Contributing to smoke-free
How can the provision and uptake of smoking cessation support be improved, including for those with mental health conditions?

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Contributing to smoke-free: How can the provision and uptake of smoking cessation support be improved, including for those with mental health conditions?

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Abstract

Background:

Smoking tobacco cigarettes is a major risk factor for cancer, chronic obstructive pulmonary disease (COPD), stroke, and heart disease. Although the United Kingdom (UK) has a comprehensive tobacco control strategy and adult smoking prevalence has reduced considerably over the past decades, from 45% in 1974 to 12.9% in 2022, smoking is still a leading preventable cause of illness and premature death in the UK and worldwide. Additionally, there are significant disparities in smoking prevalence within the population. For example, smoking prevalence is significantly higher in those with mental health conditions compared to those without, and depression and anxiety are two of the most common mental health conditions among people who smoke. Research is needed to explore how further reductions in population-level smoking prevalence can be made, including in those with mental health conditions, in order to reach national "smoke-free" or "tobacco end game" ambitions for all, which are typically defined as ≤5% adult smoking prevalence.

Aim and Objectives:

Aim: Contribute to the evidence base regarding how the provision and uptake of smoking cessation support options (including nicotine vaping products [NVPs]) could be improved.
Objective 1: Review the evidence for the effectiveness of interventions (implementation strategies), which were implemented on a national or state-wide scale, aiming to increase the provision of smoking cessation treatment in primary care.
Objective 2: Describe and characterise the extent to which NVP use has been recorded in primary care electronic health records in the UK.
Objective 3: Examine interactions between health professionals and people who smoke with and without common mental health conditions (depression and/or anxiety), about smoking cessation and nicotine vaping products.
Objective 4: Assess cessation aid utilisation by people who smoke with and without common mental health conditions (depression and/or anxiety) used in their last attempt to quit smoking.

Methods:

To achieve the four objectives, four studies were conducted.
Study 1: Systematic review and narrative synthesis of findings.
Study 2: Exploratory analysis of Clinical Practice Research Datalink (CPRD), 2006–2022: electronic primary care patient data from ~25% of the UK population.
Study 3: Using 2018 cross-sectional International Tobacco Control Four Country Smoking and Vaping Survey data from Australia, Canada, England and the United States (US), weighted logistic regression models examined the association between self-reported current diagnosis/treatment for depression and/or anxiety and health professional interactions about smoking cessation and nicotine vaping (visiting a HP; receiving advice to quit smoking from a HP; discussing NVPs with a HP; receiving a positive recommendation to use NVPs).
Study 4: Using the same survey data as in Study 3, weighted logistic regression models examined the association between self-reported current diagnosis/treatment for depression and/or anxiety and what cessation support option (any cessation support, nicotine replacement therapy [NRT], varenicline or bupropion, behavioural support, or NVPs) was used at last smoking quit attempt.

Results:

Study 1: The systematic review identified 49 studies. Implementation strategies which involved 'changing infrastructure', 'training and educating stakeholders', and 'engaging consumers' increased smoking status recording and cessation advice provision in primary care. Implementation strategies which involved 'utilizing financial strategies' increased smoking status recording and cessation advice provision, and smoking cessation. Implementation strategies which involved 'training and educating stakeholders' increased smoking status recording and cessation advice provision, and smoking cessation, but the evidence was low-quality.
Study 2: Using UK primary care data, I identified seven medical codes indicating current or former vaping. Vaping documentation was very low: 150,144 unique patients out of the estimated ~16 million patients registered in CPRD had ever received a vaping medical code. The first incidence of vaping documentation was in October 2011; vaping code incidence

increased from September 2013. The 'e-cigarette or vaping product use-associated lung injury' (EVALI) outbreak in the US (and peak media coverage in September 2019) was significantly associated with a reduction in new records of current vaping, manifested as a declining trend over a period of seven months (September 2019 to March 2020); additionally, there was an immediate increase in new records of former vaping, followed by a declining trend over the subsequent seven-month period. When patients received their first vaping code, mean age was 50.2 years, 52.4% were female, and 82.1% were White. When receiving the first vaping code, the majority of patients were either smoking or had quit smoking in the past, and <2% were recorded as having never smoked. Of those recorded as currently vaping, 98.9% had records of their previous smoking status, and 55.0% had records of their smoking status over a period greater than 12 months. Over a year after being recorded as vaping, 34.2% of people who were smoking prior to being recorded as vaping were still smoking, 23.7% quit smoking, 1.7% received a 'never smoked' status, and there was no smoking status for 40.4%.

Study 3: People with anxiety and/or depression who smoke were more likely to visit a HP than those without, but only those with depression were more likely to receive cessation advice. Among those who had visited their HP, less than half (47.9%) reported receiving advice to quit smoking. Those with both depression and anxiety were more likely to discuss NVPs, compared to those without depression/anxiety. The likelihood of receiving a positive recommendation to use NVPs did not differ by mental health condition. NVP discussions and receiving a positive recommendation to use them were rare overall.

Study 4: A large proportion (40%) of respondents did not use any cessation aid in their last quit attempt and there was a high rate of unsuccessful quit attempts: 76%. At their last smoking quit attempt, those with anxiety, and both anxiety and depression were more likely to use any cessation support than those without these mental health conditions. Specifically, those with depression and anxiety were more likely to use NRT, and those with depression and/or anxiety were more likely to use behavioural support, compared to those without depression/anxiety. However, the use of NVPs and varenicline/bupropion to quit smoking was similar among adults with and without depression/anxiety.

Conclusions:

The rate at which health professionals deliver smoking cessation advice and support is suboptimal. I found evidence towards the effectiveness of utilizing financial strategies, and some (limited) evidence towards training and educating stakeholders, on increasing smoking cessation rates. I recommend that health professionals conduct continued professional development/training to ensure that they are up to date with the smoking cessation support options that are available, and the guidance regarding their use. I recommend that cessation support options be made available to people who smoke free of charge. Also, while not all the evidence is certain for all forms of provider incentivisation, I did find some evidence that they may increase cessation rates. I recommend that future implementation strategies attempt to better align with the existing technologies and the routine systems in place. In future research, researchers could explore if there are any ways to optimise Very Brief Advice (VBA) further, and I advise that studies assess the effectiveness of implementation strategies on both (practitioner-level) provider performance as well as (patient-level) smoking outcomes.

I found that the documentation of vaping in UK primary care was low but increasing over time. Given that population-level electronic health records could be employed to investigate the long-term health effects and smoking cessation outcomes of vaping, I proposed recommendations to improve the completeness, accuracy and consistency of vaping status recording, by refining medical codes for vaping, and introducing a Quality and Outcomes Framework indicator for recording vaping status.

I found that there are missed opportunities for health professionals to provide cessation advice and recommendations about using NVPs to quit smoking, and to offer cessation support. Given that a large proportion of respondents did not use any cessation aid in their last quit attempt and there was a high rate of unsuccessful quit attempts, I advise that health professionals should systematically offer ongoing cessation support to all patients, regardless of mental health status. However, in order to address the disparity in smoking prevalence between those with and without mental health conditions, health professionals need to increase the rate of smoking cessation support provision to those who smoke and have mental health conditions (above the rate of provision to people who smoke without mental health conditions). As NVPs are potentially the most effective smoking cessation support option currently available, it is important that healthcare professionals provide accurate information about and access to NVPs to people who smoke, especially for

individuals with mental health conditions. To achieve this, people with mental health conditions could be specifically targeted as a priority population in some of the policy recommendations recently made in the Khan review and the initiatives recently announced by the UK government, such as the national ‘swap to stop’ programme, where people who smoke will be able to switch cigarettes for NVPs.

Contents

List of publications in this thesis

[1] Tildy, B. E., McNeill, A., Perman-Howe, P. R., & Brose, L. S. (2023). Implementation strategies to increase smoking cessation treatment provision in primary care: a systematic review of observational studies. *BMC Primary Care*, *24*(1), 1–61. https://doi.org/10.1186/s12875-023-01981-2

[2] Tildy, B. E., McNeill, A., Robins, J., Dregan, A., Richardson, S., & Brose, L. S. (2023). How is nicotine vaping product (e-cigarette) use monitored in primary care electronic health records in the United Kingdom? An exploratory analysis of Clinical Practice Research Datalink (CPRD). *BMC Public Health*, *23*(1), 1–13. https://doi.org/10.1186/S12889-023-17200-7

[3] Tildy, B., McNeill, A., East, K., Gravely, S., Fong, G. T., Cummings, K. M., Borland, R., Chan, G., Lim, C., Gartner, C. E., Yong, H., & Brose, L. S. (2023). Self-reported depression and anxiety and healthcare professional interactions regarding smoking cessation and nicotine vaping: Findings from 2018 International Tobacco Control Four Country Smoking and Vaping (ITC 4CV) Survey. *Tobacco Prevention & Cessation*, *9*(8), 1–12. https://doi.org/10.18332/TPC/168288

List of presentations

Implementation strategies to increase smoking cessation treatment provision in primary care: a systematic review of observational studies [Oral Presentation]. Addictions Department PhD & Early Career Research Seminar, London, Hybrid, June 2022.

Implementation strategies to increase smoking cessation treatment provision in primary care: a systematic review of observational studies [Oral Presentation]. 5th UK Implementation Science Research 2022 Conference, London, Online, July 2022.

PhD update and primary care electronic health records in the UK [Oral Presentation]. Shaping Public hEalth poliCies To Reduce ineqUalities and harM (SPECTRUM) Consortium Academy Meeting, Online, July 2022.

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Reaching smoke-free – how can we improve the provision of smoking cessation treatment? [Oral presentation]. National Centre for Youth Substance Use Research meeting, University of Queensland, Brisbane, Australia, Face to Face, October 2022.

Reaching smoke-free – how can we improve the provision of smoking cessation treatment? [Oral presentation]. National Drug and Alcohol Research Centre (NDARC) Seminar, University of New South Wales, Sydney, Australia, Online, November 2022.

Implementation strategies to increase smoking cessation treatment provision in primary care: a systematic review of observational studies [Poster Presentation]. 12th Health Services Research Association of Australia and New Zealand (HSRAANZ) 2022 Conference, Sydney, Australia, Face to Face, December 2022.

Mental health and health professional interactions regarding smoking cessation and nicotine vaping [Oral presentation]. Society for Research on Nicotine and Tobacco Europe (SRNT-E) annual conference, London, Face to Face, September 2023.

List of abbreviations

3As: Ask, Advise, Act

4CV Survey: Four Country Smoking and Vaping Survey

5As: Ask, Advise, Assess, Assist, Arrange

aOR: Adjusted Odds Ratio

APMS: Adult Psychiatric Morbidity Survey

APS: Annual Population Survey

ASH: Action on Smoking and Health

CBT: Cognitive Behavioural Therapy

CDC: Centers for Disease Control and Prevention

CFIR: Consolidated Framework for Implementation Research

CHD: Coronary Heart Disease

CI: Confidence Interval

CIS-R: Clinical Interview Schedule - Revised

CKD: Chronic Kidney Disease

CO: Carbon Monoxide

COPD: Chronic Obstructive Pulmonary Disease

COVID-19: Coronavirus Disease 2019

CPRD: Clinical Practice Research Datalink

EBP: Evidence-Based Practice

EC: Electronic Cigarettes, E-cigarettes

EHR: Electronic Health Record

ENDS: Electronic Nicotine Delivery Systems

ERIC: Expert Recommendations for Implementing Change

EVALI: E-cigarette or Vaping Product Use-Associated Lung Injury

FCTC: Framework Convention on Tobacco Control

FDA: Food and Drug Administration

GAD: Generalised Anxiety Disorder

GP: General Practice or General Practitioner

HP: Health Professional

HSE: Health Surveys for England

ID: Identification

ITC: International Tobacco Control

LCD: Last Collection Date

MH: Mental Health

MHRA: Medicines and Healthcare products Regulatory Agency

MOST: Multiphase Optimization Strategy

NCSCT: National Centre for Smoking Cessation and Training

NHS: National Health Service

NICE: National Institute for Health and Care Excellence

NRT: Nicotine Replacement Therapy

NVP: Nicotine Vaping Product, electronic cigarette (EC), e-cigarette, electronic nicotine delivery system (ENDS)

OCD: Obsessive-Compulsive Disorder

OR: Odds Ratio

ONS: Office for National Statistics

OSF: Open Science Framework

OTC: Over-the-Counter

PAD: Peripheral Arterial Disease

PCC: Primary Care Clinicians

ppm: Parts Per Million

QOF: Quality and Outcomes Framework

RCP: Royal College of Physicians

RCT: Randomised Controlled Trial

ROBINS-I: Risk Of Bias In Non-randomized Studies of Interventions

RR: Relative Risk

SMI: Severe Mental Illness

SSS: Stop Smoking Service

TABS: Tobacco Attitudes and Behaviors Survey

THC: Tetrahydrocannabinol

THIN: The Health Improvement Network

TIA: Transient Ischaemic Attack

UK: United Kingdom

US or USA: United States of America

UTS: Up-to-Standard

VBA: Very Brief Advice

WHO: World Health Organization

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PP-H: Dr Parvati Perman-Howe

RB: Professor Ron Borland

SG: Dr Shannon Gravely

SR: Dr Sol Richardson

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Chapter 1 – Introduction and Background

Smoking

Several decades of research have resulted in a robust evidence base that explains the mechanisms of smoking and underpins the cessation support options and tobacco control policies which are at our disposal. Smoking tobacco cigarettes is a major risk factor for cancer, chronic obstructive pulmonary disease (COPD), stroke, and heart disease [4]. West et al. argue that 'cigarette smoking' is not an illness, it is a "behaviour pattern" which leads to conditions that cause morbidity and mortality [5]. Instead, 'cigarette smoking' can be conceptualised as a 'cigarette addiction' ("a motivation") and 'nicotine dependence' ("a physiological abnormality … in the central nervous system, [which includes] upregulation of nicotinic acetylcholine receptors, sensitisation of parts of the nucleus accumbens to nicotine and reduced tonic firing of the central nervous system pathway concerned") [5]. Smoke from combustible tobacco contains thousands of constituents, but nicotine is recognised to be the primary addictive constituent of tobacco [6]. The addictive properties of nicotine are enhanced by the presence of other constituents (such as monoamine oxidase inhibitors) and delivery through inhalation [6]. Smoking delivers nicotine to the lung in aerosol form, which results in the delivery of nicotine (via the pulmonary circulatory system) to the brain within 10 to 15 seconds [6].

The field of tobacco control aims to address tobacco use and reduce the morbidity and mortality it causes. A comprehensive tobacco control strategy incorporates three approaches: prevention, cessation, and harm reduction [7]. The strategy contains both population- and individual-level approaches which can help prevent people from initiating smoking, motivate people who smoke to try to quit, as well as provide support for people who smoke to successfully quit smoking. The MPOWER package contains the six evidence-based tobacco control measures of the World Health Organisation (WHO) Framework Convention on Tobacco Control (FCTC) [8]: Monitoring tobacco use and tobacco control measures; Protecting people from tobacco smoke; Offering help (e.g., treatments) to quit tobacco use; Warning people about the dangers of tobacco; Enforcing bans on tobacco advertising, promotion and sponsorship; and Raising taxes on tobacco products.

Additionally, tobacco harm reduction can be defined as "decreasing the burden of death and disease, without completely eliminating nicotine and tobacco use" [7,9]. The harm reduction approach recognises that tobacco abstinence or never using tobacco is the ideal outcome but promotes providing those who are unable or unwilling to quit smoking with less harmful nicotine-containing products for continued use [10]. This approach is based on the concept that nicotine itself is not a highly hazardous drug and that most of the morbidity and mortality from smoking arises from direct exposure of the lungs to the other constituents of tobacco smoke [11]; one of the key international experts in nicotine addiction, Professor M. A. H. Russell, coined the phrase: "people smoke for nicotine but they die from the tar" [12].

Although the United Kingdom (UK) has a comprehensive tobacco control strategy and adult smoking prevalence has reduced considerably over the past decades, from 45% in 1974 [13] to 12.9% in 2022 [14], smoking is still a leading preventable cause of illness and premature death in the UK [4] and worldwide [15]. Additionally, there are significant disparities in smoking prevalence between individuals in 'disadvantaged groups', such as those with mental health conditions, and individuals in the general population [16]. This thesis aimed to explore how further reductions in population-level smoking prevalence can be made, to reach national "smoke-free" [17,18] or "tobacco end game" [19] ambitions, which are typically defined as ≤5% adult smoking prevalence.

Smoke-free ambition

In 2019, the English government set a "smoke-free 2030" ambition which aimed for adult smoking prevalence to be ≤5% in England by the year 2030 [17]. However, Cancer Research UK models, which extrapolated 2011–2017 English smoking prevalence Annual Population Survey (APS) data, predicted that adult smoking prevalence in England will be 7.7% in 2030 [20]; and models which used 2011–2021 data predicted that adult smoking prevalence in England will be 8.3% in 2030 [21].

In England, the 'Tobacco Control Plan for England' outlines the government's strategy to reduce smoking; the most recent report set out the strategy for 2017 to 2022 [22]. A new

Tobacco Control Plan for England was expected to be published in 2022. Instead, the UK government commissioned an independent review; this was conducted by Javed Khan OBE and published on 9 June 2022: 'The Khan Review: Making Smoking Obsolete' [18]. The review cited the Cancer Research UK predictions, that "… England will miss the smoke-free 2030 target by at least 7 years …" [18], acknowledging that the 5% prevalence target in 2030 will not be met. The Khan review instead set out recommendations for how to further decrease smoking prevalence and reach below 5% prevalence "in every community in every area" by 2035, and to "make smoking obsolete" (0%) by 2040 [18]. The review [18] included four central recommendations: reducing the number of people taking up smoking (via policies such as raising the age of sale of tobacco from 18, by one year, every year); increased investment into Stop Smoking Services; that vaping is offered as a substitute for smoking and health professionals are provided with accurate information about vaping; increased investment into a national media campaign to direct people who smoke to access cessation support or switch to vaping; improved integration of smoking cessation in the National Health Service (NHS) (for example, by making stopping smoking a key part of mental health treatment in acute and community mental health services, and in primary care).

Aiming to respond to the Khan review, Public Health Minister Neil O'Brien delivered a speech on 11 April 2023 [23] and did not acknowledge the high likelihood that the ≤5% smoking prevalence in 2030 target will not be met.

Most recently (at the time of writing), the Prime Minister gave a speech on 4 October 2023 [24], announcing that they will: legislate to raise the age of sale of tobacco one year every year from 2027 onwards; increase funding for local authority Stop Smoking Services; implement a national 'swap to stop' scheme where people who smoke will be able to switch cigarettes for nicotine vaping products; increase funding for awareness raising campaigns; increase funding for enforcement on illicit tobacco and nicotine vaping products; and launch a consultation on specific measures to tackle the increase in youth vaping.

Inequalities in smoking prevalence

A significant challenge in reducing overall smoking prevalence is inequalities in smoking prevalence in the UK [16] – smoking prevalence is considerably higher among people in 'disadvantaged groups'.

For example, although smoking prevalence has declined in all socioeconomic groups in recent years, smoking prevalence is considerably higher in deprived sociodemographic groups [20,21,25]. According to the Smoking Toolkit Study, a monthly household survey of people (aged ≥16 years) who smoke in England, in July 2023, smoking prevalence in lower socioeconomic groups was 18.6%, and 12.1% in higher socioeconomic groups [26]. A recent Royal College of Physicians report, 'Smoking and health 2021: A coming of age for tobacco control?' [6], found, using 2013–2018 Health Survey for England (HSE) data, that if smoking prevalence trends were extrapolated in the most optimistic scenario (decreased smoking initiation probabilities, increased smoking quitting probabilities), the predicted smoking prevalence amongst 11–89-year-olds in England in 2030 would be 3.0% for females and 5.6% for males in the least deprived sociodemographic category, and 15.0% for females and 17.7% for males in the most deprived sociodemographic category. Similarly, Cancer Research UK modelling suggested that the most deprived would only reach ≤5% smoking prevalence in the year 2047 [20].

Another 'disadvantaged group', in which smoking prevalence is disproportionately high, is people who have a mental health condition. Smoking prevalence is significantly higher among adults with a mental health condition compared to adults without a mental health condition [25,27–32], but smoking rates vary based on the mental health severity and disorder type (smoking prevalence increases as the number and severity of lifetime mental disorders increases) [33]. In England, smoking prevalence in adults with a long-term mental health condition was 25.2% in 2021/22 [34] (compared to 12.9% smoking prevalence among all adults in 2021 [14]), and a third of people who smoked in 2016–17 had mental health conditions [31]. Using the most recent Adult Psychiatric Morbidity Survey (APMS) data available, which was last collected in 2014, Richardson et al. found that in England in 2014, among those with a current common mental health condition, smoking prevalence was 34.1%, compared to 19.6% in people without [30,35]. Richardson et al. also extrapolated

trends into the future, assuming no change based on mean annual percentage point decrease in smoking prevalence using weighted APMS data (based on a 0.60% percentage-point decrease in smoking prevalence per year for the non-mental health condition group and a 20.74% percentage-point decrease in smoking prevalence per year for the mental health condition group) (Richardson & Robson, adapted from [30]). They predicted that smoking prevalence in those without a mental health condition would reach 5% in the year 2039 (95% CI: 2037.6–2040.4 years), and smoking prevalence in those with a mental health condition would reach 5% in the year 2054 (95% CI: 2051.1–2057.5 years), 24 years later than the target date (Richardson & Robson, adapted from [30]).

Smoking and mental health

Smoking is a significant contributor to the large discrepancy in life expectancy between people with and without mental health conditions [27,36–38]. As well as being more likely to smoke, people with mental health conditions are more likely to smoke heavily and be highly dependent on cigarettes [30,39]. People with mental disorders experience substantial physical health disparities compared to those without such disorders (for a 2021 summary, see: [33]). Most of this excess morbidity and mortality can be attributed to physical health illnesses caused by smoking [33].

In the past, it was not well established whether there was a causal effect between smoking and mental health, and the direction of this association [33]. The 'self-medication' hypothesis assumed that people with mental health conditions may initiate smoking and smoke more heavily in an attempt to self-medicate or cope with their psychiatric symptoms [33] or the side effects of their psychiatric medications [40]. However, there is a growing body of evidence (for a 2022 summary, see: [40]) which suggests that smoking may be a causal risk factor for mental illness [41] and that smoking cessation may be beneficial for long-term mental health outcomes [42]. Furthermore, because the inhaled polycyclic aromatic hydrocarbons in smoke induce cytochrome P450 (CYP) CYP1A2 isoenzymes, which increase the metabolism of several antipsychotics (e.g., clozapine, olanzapine, chlorpromazine, haloperidol, fluphenazine) and antidepressants (e.g., fluvoxamine,

duloxetine, tricyclic antidepressants), smoking cessation may allow for a reduction in the dose of some psychotropic medications, which may, in turn, reduce their side effects [27,33].

It is now generally established that successful smoking cessation is associated with improved physical and mental health [42]. However, historically, people with people with mental health conditions who smoke have had low long-term cessation rates [33].

It is notable to mention here that the definition of 'mental health conditions' can vary. According to the World Health Organization (WHO) [43], 'mental health conditions' can be a broader term to include "mental disorders, psychosocial disabilities and (other) mental states associated with significant distress, impairments in functioning, or risk of self-harm". Globally, in 2019, 1 in 8 people were living with a mental disorder [43], with anxiety and depressive disorders being the most common [43,44]: 280 million people were living with depression, and 301 million people were living with an anxiety disorder [43]. In 2014, 1 in 6 (17.0%) people (aged ≥16 years) surveyed in England by the APMS met the criteria for a common mental health problem (most commonly: 'mixed anxiety and depression', generalised anxiety disorder [GAD], and depression) [45]. Brose et al. [31] found that in England, 35.9% of people who smoked in the past year (were currently smoking or recently quit) reported ever having been diagnosed with at least one mental health problem since the age of 16 – two of the most common conditions were depression and anxiety: 27.2% had ever been diagnosed with depression, and 20.6% with anxiety. Regarding my *Thesis aim and objectives*, I decided to focus on these common mental health conditions (depression and anxiety) because people who have these conditions typically live in the general population and may not have frequent contact with health professionals (compared to those who live in mental health settings) [46], which may reduce their likelihood of being screened for smoking and receiving smoking cessation support.

Researchers have found that the way that mental health conditions are defined/measured in research studies can have an effect on the outcome measures (such as smoking cessation) [47,48]. For example, mental health can be measured by asking participants if they have 'ever' received a diagnosis or treatment for a specific condition from a health professional, or if they have a 'current' diagnosis or treatment for a specific condition. Another approach

is asking participants if they are experiencing any symptoms of mental health conditions, currently or in the last week or 30 days, using scales such as the Kessler psychological distress scale (K6) [49]. To be mindful of the differing measures of mental health, in the *Increasing smoking cessation likelihood* section, I have aimed to accurately describe how 'mental health condition' was defined in the individual studies I included.

Smoking cessation

Population smoking prevalence can be reduced by reducing the uptake (initiation) of smoking or by increasing smoking cessation [50]. Smoking cessation is important at both the individual- and population-level. For individuals who manage to quit smoking, the health benefits that are gained are significant, both in improving life expectancy and morbidity, because their risk of experiencing some smoking-related diseases are either halted or returned to the risk levels of people who have never smoked [51,52]. For the population, numerous economic analyses have estimated the burden of smoking on society to be significant. For example, the cost of smoking to society in England was recently estimated to be £17 billion per year [53] – made up of the impact of smoking on productivity (people of working age who smoke are more likely to be out of employment and to die while they are of working age), and the impact of smoking on health and social care budgets (people who smoke require more expenditure on health and social care from a younger age, compared to people who do not smoke).

Motivation to quit and making quit attempts

General population

Since the mid-2000s, studies have consistently shown that most adults who smoke say they want to quit smoking. For example, in the US, the prevalence of quit attempts among adults aged ≥16 years who smoked increased between 2000 and 2015 [54]; in 2015, 68.0% of adults who smoked wanted to stop smoking, and 55.4% had made a quit attempt in the past year [54]. In 2018 in the US, 55.1% of adults aged ≥18 years who smoked had made a

smoking quit attempt in the past year [55]. A more recent example from the UK is from the Office for National Statistics (ONS) survey of adults conducted in 2022 [14], which found that of those who currently smoke, 45.4% indicated that they intended to quit smoking, and 22.0% of people who currently smoke intended to quit within three months of the time of the survey. The latter figure is consistent with the proportion found by the Smoking Toolkit Study, a monthly household survey of people (aged ≥16 years) who smoke: the proportion of people who smoke who want to stop and "intend to stop soon" ranged between 39.0% to 23.4% between 2009 and 2023 [26]. In terms of actually making quit attempts, the Smoking Toolkit Study found that the proportion of those who currently smoked who made quit attempt(s) in the past 12 months ranged between 26.9% and 45.1% between 2007 and 2023 [26]. It is worth noting here that tobacco control faces different challenges internationally; the rate of quit attempts significantly differs between countries – for example, in 2016, in England, 46.3% of people who smoke indicated making a quit attempt in the last 12 months, while in the Netherlands it was 31.5%, in Spain it was 17.7%, and in Hungary it was 10.4% [56].

People with mental health conditions

Studies have found that people who smoke and have mental health conditions are as motivated or more motivated to quit smoking as people who smoke in the general population [30,33,57–64], and they make a similar or a greater number of quit attempts compared to people who smoke who do not have mental health conditions [31,33,64–70]. Using England APMS data from the year 2000 (the most recent data where the outcome was available), Richardson et al. [30] found that those (aged 16–64 years) with generalised anxiety disorder (GAD) were more likely to report a desire to quit, compared to those without. Those with other common mental health conditions (depressive episode, phobia, and mixed anxiety and depressive disorder) were as likely to report a desire to quit, compared to those without [30]. In terms of actually making quit attempts, using survey data from England collected between January 2016 and December 2017, Brose et al. [31] found that overall, just under a third (32.5%) of people (aged ≥16 years) who smoked in the past year had made at least one quit attempt in the past 12 months; people who smoked

and had mental health conditions were more likely to have made a quit attempt compared to people who smoked without these indicators of a mental health problem – this applied to all those who had ever been diagnosed with a mental health condition, those who indicated moderate or serious past-month distress (measured using the K6 screener for mental distress [49]) in the past 30 days), and those who received past-year treatment. Similarly, using 2016 [71] and 2018 [72] survey data from Australia, Canada, England, and the US, Li et al. found that those with self-reported current treatment/diagnosis of depression or anxiety were more likely to report making quit attempts than those without depression or anxiety. Lastly, Yimsaard et al. [73] analysed 2018 and 2020 waves of survey data from Australia, Canada, England, and the US and found that those who self-reported depressive symptoms in 2018 were more likely to have made a quit attempt between 2018 and 2020, compared to those who did not report having depressive-symptoms or a diagnosis of depression; and those who self-reported having a diagnosis/treatment for depression in 2018 were equally likely to have made a quit attempt between 2018 and 2020, compared to those who did not report having depressive-symptoms or a diagnosis of depression. Those who self-reported having a diagnosis/treatment for anxiety in 2018 were as likely to have made a quit attempt between 2018 and 2020, as those who did not report having anxiety [73].

Summary

Most adults who smoke say they want to quit smoking, and more than a quarter of people (in the UK and USA) have made a smoking quit attempt in the past year. People who smoke and have mental health conditions are just as motivated or more motivated to quit smoking as people who smoke in the general population, and they make a similar or a greater number of quit attempts compared to people who smoke who do not have mental health conditions.

Quit success rate

General population

There have been various estimations made as to how many quit attempts it takes, on average, for a person who smokes to successfully quit smoking long-term. Various organisations (e.g., American Cancer Society, Australian Cancer Council, Centers for Disease Control and Prevention) have estimated that it takes more than 8 quit attempts before the person succeeds in long-term smoking cessation [74], and a US cross-sectional study reported 6.1 attempts [75]. One study, using longitudinal (2002–2008) survey data from Australia, Canada, England, and the US, estimated that the average 40-year-old who smokes who started in their teens will have made over 20 failed quit attempts [76]. Chaiton et al. have argued that these estimations are too low and calculated that for many people who smoke, it may take 30 or more quit attempts before being successful [74]. Hughes et al. [77] estimate the unaided quit rate (percentage succeeding in smoking cessation for at least 12 months) to be 3 to 5%. As outlined in the sub-section above, most adults who smoke want to quit smoking and a high proportion of them make smoking quit attempts. However, it has been well documented that most quit attempts end in relapse to smoking within 12 months [54,55,77,78]. As a recent example, in the US in 2018, among adults aged ≥18 years who currently smoke or those who quit smoking in the past year, only 7.5% were smoking abstinent for ≥6 months during the past year [55]. In England, the Smoking Toolkit Study found that the success rate for stopping in those who tried to stop smoking in the past year was 14.2% (95% CI: 11.9–16.3) in 2019 and 24.9% in 2023 (95% CI: 21.9–27.9) [79]; between 2007 and 2018, on average, 16.2% (95% CI: 15.5–17.0) of respondents reported a successful quit attempt [80].

People with mental health conditions

As previously outlined, people who smoke and have mental health conditions are equally or more motivated to quit smoking [30,33,57–63] and make similar amounts or more quit attempts [31,33,65–70], compared to people who smoke without mental health conditions.

Also previously mentioned, for people who do not have mental health conditions, the smoking quit success rate is low. Studies which have compared the quit success rate between people who smoke with and without mental health conditions have found that the quit success rate for people with mental health conditions is lower [65,67,72,73,81–83] or equal [30,66,70,72,73,83–89], compared to those with no mental health conditions. For example, using survey data from England collected between January 2016 and December 2017, Brose et al. [84] found that people (aged ≥16 years) who had made a quit attempt who smoked with mental health problems (ever diagnosis [18.3% no vs 18.1% yes], past-year treatment [18.3% no vs 18.0% yes], past-month distress [19.9% no vs 16.2% moderate vs 15.3% serious]) were as likely to be quit smoking for >1 month at the time of the survey as those without mental health problems. Additionally, using ITC survey data from Australia, Canada, England, and the US, Li et al. [72] found that those who self-reported having depression (23.1%) or anxiety (20.8%) in 2016 and had made a quit attempt were equally likely to have successfully quit between 2016 and 2018. Using the same data but from 2018 and 2020, Yimsaard et al. [73] found that those who had self-reported having depressive symptoms in 2018 and had made a quit attempt were significantly less likely to have successfully quit between 2018 and 2020 (19.4%), compared to those who did not report having depressive-symptoms or a diagnosis of depression (30.5%); however, those who self-reported having a current diagnosis/treatment for depression in 2018 and had made a quit attempt were equally likely to have successfully quit between 2018 and 2020 (29.5%), compared to those who did not report having depressive-symptoms or treatment/diagnosis of depression (30.5%). Those who self-reported having a current diagnosis/treatment for anxiety in 2018 and had made a quit attempt were equally likely to have successfully quit between 2018 and 2020 (26.7%), compared to those who did not report having anxiety (27.7%). Notably, Brose et al., Li et al., and Yimsaard et al. measured 'successful smoking cessation' as respondents who reported that they quit smoking at least one month ago, hence this may not be a marker of long-term smoking cessation. Richardson et al. [30] used England APMS survey data (1993, 2000, 2007 and 2014 waves) of people aged 16–64 years, where respondents were categorised as having a mental health condition if they met the criteria for any common mental health condition (depression, phobia, generalised anxiety disorder (GAD), panic disorder, obsessive-compulsive disorder (OCD) and mixed anxiety and depressive disorder) on the revised Clinical Interview Schedule (CIS-R) within the last week.

Richardson et al. [30] found that having any common mental health condition was associated with lower odds of >6-month successful smoking cessation; however, the association was not significant after adjustment for heavy smoking – i.e., people with common mental health conditions were equally likely to successfully quit smoking, compared to those with no common mental health condition.

Summary

In summary, the quit success rate for people who smoke both with and without mental health conditions is low. It usually takes people who smoke multiple quit attempts before they successfully quit smoking. Some studies found that the quit success rate is lower in those with mental health conditions, compared to those without [65,67,72,73,81–83], while other studies found that the quit rate in people with mental health conditions is generally equal to the quit success rate in people without mental health conditions [30,66,70,72,73,83–89] (especially when heaviness of smoking is taken into account [30]).

Increasing smoking cessation likelihood

In this section, I outline ways in which the likelihood of successful smoking cessation can be increased.

Smoking cessation support options – What are they?

As mentioned above, the unaided 12-month smoking cessation rate is estimated to be 3 to 5% [77]. A way to increase the likelihood of successful long-term smoking cessation is by using evidence-based cessation options during smoking quit attempts. This sub-section outlines the smoking cessation support options that are currently available to support quit attempts.

Following England's first 'Tobacco Control Plan' in 1998 [90], the English government recognised that people who smoke should be supported to quit smoking. NHS Stop Smoking Services (SSSs), to which people who smoke could be self-referred or referred by their general practitioner, were introduced in 1999 [91]; this and several smoking cessation pharmacotherapies became accessible in the years that followed. For example, nicotine gum was available for general sale in 1999 [92]; bupropion became available on NHS prescription in 2000 [92]; nicotine gum, nicotine lozenge, and all nicotine patches were available on NHS prescription as well as general sale in 2001 [92]; and varenicline became available on NHS prescription in 2006 [93]. Several studies since then have shown that the treatment of people who smoke is highly cost-effective as it reduces the chronic conditions caused by smoking and acute events in secondary care [6,94].

The most commonly recommended cessation support options in many countries [95–98] currently are: nicotine replacement therapy (NRT), varenicline, bupropion and behavioural support, while some countries also recommend cytisine [96]. (Cytisine has similar properties to varenicline; it is currently licensed in England but not yet supplied [99,100].)

In the UK, the most recent (2021) National Institute for Health and Care Excellence (NICE) tobacco guideline [95] recommends that the following are accessible to adults who smoke:

- Behavioural interventions:
    - Behavioural support (individual and group) – sessions which provide people who smoke with information, advice, encouragement and some form of behavioural intervention.
    - Very brief advice – aims to identify and support patients who smoke to make a quit attempt. Healthcare professionals 'Ask' (ask a patient if they smoke), 'Advise' (advise that the best way to stop smoking is with a combination of medication and specialist support), and 'Act' (offer a referral to specialist support and prescribe medication if appropriate) [101].

- Medicinally licensed products:
    - Nicotine replacement therapy (NRT) – a medication which provides an alternative source of nicotine.

    - Bupropion (Zyban) – an antidepressant medication which also supports smoking cessation.
    - Varenicline (Champix) – a medication which acts as a selective nicotine-receptor partial agonist, which reduces the cravings for nicotine and alleviates the withdrawal symptoms a person experiences when they stop smoking.

- Nicotine-containing e-cigarettes – also known as nicotine vaping products (NVPs), electronic cigarettes (e-cigarettes) or electronic nicotine delivery systems (ENDS), are an alternative to combustible tobacco cigarettes and have been demonstrated to be an effective smoking cessation support option [102] (see sub-sections below). Vaping products are electronic devices which contain a battery-powered heating element that heats up and aerosolises an 'e-liquid' solution consisting of water, propylene glycol and/or glycerol, and usually also nicotine and flavourings [103]. Extensive evidence suggests that using NVPs is substantially less harmful than smoking combustible tobacco in the short- to medium-term (evidence regarding long-term benefits/harms is currently lacking) [104] – I expand on NVPs in the section *Nicotine vaping products (NVPs)*, below.

- Allen Carr's Easyway in-person group seminar – a multicomponent programme that includes group cognitive behavioural and relaxation therapies without pharmacotherapy.

The 2021 NICE guideline [95] advises that varenicline, a combination of short-acting and long-acting NRT, and NVPs are most likely to result in successful smoking cessation when these are combined with behavioural support.

Here, it is worth noting that effective pharmaceutical options for smoking cessation in the UK are currently limited, as varenicline and bupropion have been unavailable internationally since 2021 [105] and 2022 [106], respectively, and cytisine is not supplied [99,100].

Smoking cessation support options – Efficacy in RCTs

The evidence that underpins the smoking cessation support options recommended in clinical guidelines (above) is based on high-quality randomised controlled trials (RCTs) whose results have been meta-synthesised in gold-standard systematic reviews.

General population

For the general population of people who smoke, there are Cochrane systematic reviews for nicotine receptor partial agonists (varenicline and cytisine) (studies that directly compared cytisine and varenicline found that there may be no difference between them for quitting smoking) [107], NRT [108,109], bupropion [110], comparing different pharmacological interventions [111], behavioural support [112,113], combining behavioural support with pharmacotherapy [114,115], NVPs [102,116]. The Cochrane review for NVPs found that NVPs improve smoking cessation likelihood compared to NRT and non-nicotine containing vaping products [102]. NICE conducted its own systematic review regarding Allen Carr's Easyway in-person group seminar, including two RCTs [117]. Table 1.1 shows some RCT efficacy estimates of these interventions, adapted from the respective Cochrane reviews:

Table 1.1. Systematic reviews of RCT efficacy of smoking cessation support options – general population

Intervention **(proportion [%] of participants who obtained the outcome, 95% CI)**	**Comparison** **(median proportion [%] of participants who obtained the outcome)**	**Percentage point increase**	**Relative effect (RR)**	**Certainty**
Varenicline [107] 23.0 95% CI: 21.3–24.9	Placebo or no medication 9.9	13.1	RR 2.32 95% CI: 2.15–2.51	High

Intervention **(proportion [%] of participants who obtained the outcome, 95% CI)**	**Comparison** **(median proportion [%] of participants who obtained the outcome)**	**Percentage point increase**	**Relative effect (RR)**	**Certainty**
Cytisine [107] 20.5 95% CI: 18.1–23.3	Placebo or no medication 15.8	4.7	RR 1.30 95% CI: 1.15–1.47	Moderate
Bupropion [110] 19.0 95% CI: 18.0–20.0	Placebo/no pharmacological treatment 12.0	7.0	RR 1.60 95% CI: 1.49–1.72	High
NRT in any form [108] 16.2 95% CI: 15.6–16.8	Control 10.5	5.7	RR 1.55 95% CI: 1.49–1.61	High
Individual behavioural support without pharmacotherapy [113] 11.0 95% CI: 10.0–12.0	Control 7.0	4.0	RR 1.57 95% CI: 1.40–1.77	High
Individual behavioural support with pharmacotherapy offered [113] 13.0 95% CI: 11.0–16.0	Control (with pharmacotherapy offered) 11.0	2.0	RR 1.24 95% CI: 1.01–1.51	Moderate
Nicotine e-cigarette (NVP) [102] 10.0 95% CI: 8.0–12.0	NRT 6.0	4.0	RR 1.63 95% CI: 1.30–2.04	High

Intervention **(proportion [%] of participants who obtained the outcome, 95% CI)**	**Comparison** **(median proportion [%] of participants who obtained the outcome)**	**Percentage point increase**	**Relative effect (RR)**	**Certainty**
Nicotine e-cigarette (NVP) [102] 14.0 95% CI: 9.0–23.0	Non-nicotine e-cigarette 7.0	7.0	RR 1.94 95% CI: 1.21–3.13	Moderate

Outcome: Smoking cessation at 6+ months.
RR: relative risk

People with mental health conditions

Reviews which have synthesised findings from RCTs which included people who smoke who have mental illness found that people with serious mental illness can successfully quit smoking using some of the cessation options that have been shown to be efficacious for the general population [33,118–125]. However, there have been fewer RCTs conducted in this patient population compared to the general population. Lightfoot et al. [122] found that NRT, bupropion or varenicline in combination with psychological treatment showed efficacy. Peckham et al. [119] found sufficient evidence to meta-analyse findings for bupropion, varenicline and specialised smoking cessation programmes: bupropion was found to be efficacious at medium- and long-term smoking cessation; there were no long-term cessation studies of varenicline but varenicline was found efficacious at medium-term smoking cessation; and specialised smoking cessation programmes were not found to be efficacious at either the medium- or long-term. Spanakis et al. [123] found sufficient evidence that bespoke person-based behavioural interventions were efficacious for medium- and long-term smoking cessation. Table 1.2 includes some efficacy estimates from RCTs for people who smoke who have severe mental ill health from Peckham et al.'s [119] and Spanakis et al.'s systematic reviews [123].

Table 1.2. Systematic reviews of RCT efficacy of smoking cessation support options – mental health population

Intervention	Comparison	Outcome	Relative effect (relative risk, RR)	Number of RCTs
Bupropion [119]	Placebo	Long term	RR 3.04 95% CI: 1.10–8.42	4
Varenicline [119]	Placebo	Medium term	RR 4.13 95% CI: 1.36–12.53	4
Specialised smoking cessation programme [119]	Placebo	Long term	RR 1.33 95% CI: 0.85–2.08	4
Bespoke person-based behavioural interventions [123]	Usual care	Long term	RR 1.58 95% CI: 1.09–2.30	3

Outcomes: Medium term: smoking abstinence at longest follow-up (up to 6 months); Long term: smoking abstinence at longest follow-up (6+ months).
RR: relative risk

There were concerns that varenicline may cause adverse neuropsychiatric events; however, a large RCT (EAGLES) showed that there was no significant risk in patients with and without common mental health conditions or serious mental illness when prescribed varenicline [126], and further RCTs and large observational studies also found that varenicline does not increase the risk of neuropsychiatric or cardiovascular adverse events [127–129]. A 2018 position statement from the Royal College of Psychiatrists [130] recommended that health professionals consider prescribing varenicline when clinically indicated as one of the options to support patients with serious mental illness to stop smoking. The position statement also advised health professionals to recommend NVPs to people who smoke and have mental health conditions, as using NVPs is safer than continued smoking [130]. The 2020 'Vaping in England: An Evidence Update March 2020: Including Mental Health and Pregnancy' by McNeill et al. [131] found that there were no published RCTs evaluating NVPs for smoking

cessation or reduction for people who smoke with mental health conditions. Since then, the 2022 update of the 'Electronic cigarettes for smoking cessation' Cochrane systematic review by Hartmann-Boyce et al. [102] identified one RCT, by Pratt et al. [132], where the trial participants (who had serious mental illness) (n=240), who were currently unwilling to quit smoking, were randomly assigned to either receive disposable NVPs for 8 weeks or no product. The NVP group reduced their cigarette use and expired-air carbon monoxide (CO) concentration compared to the control group across the 8-week NVP provision period; 19%–22% of the NVP group fully substituted NVPs for cigarettes during the NVP provision period [132].

Summary

For the general population of people who smoke, there is extensive evidence – based on high-quality RCTs – that there are several smoking cessation support options which people who smoke can use to support their smoking quit attempts, which can increase the likelihood of successful smoking cessation. The RCT evidence regarding the efficacy of cessation options for people who smoke with mental health conditions is less, however, systematic reviews indicate that people with mental health conditions can successfully quit smoking using some of the cessation options that have been shown to be efficacious for the general population.

Smoking cessation support options – Effectiveness in the 'real world'

As outlined above, there is extensive evidence from RCTs that using smoking cessation support options can increase the likelihood of successful smoking cessation. However, the smoking cessation rates that are observed in RCTs do not always translate to the same rates in 'real world' settings. There are many reasons why efficacy estimates from RCTs might not translate into the same level of effectiveness in the 'real world' [133,134]. For example [135], the general population of people who smoke may differ from those who are eligible to participate in RCTs; the quantity/quality of support individuals receive when using

cessation aids may be higher in the RCT setting compared to the 'real world' setting; or people may use cessation products suboptimally (e.g. by being less compliant with the optimal treatment regime [136,137]) in the 'real world' setting. Observational studies can examine the effectiveness of cessation support options in the 'real world' (outside an experimental setting [135]).

General population

In observational studies to examine the 'real world' cessation rate of cessation support options, it is important to adjust for confounding factors, such as: age, sex, social grade (or education, ethnicity), alcohol consumption, previous quit attempts, and level of cigarette dependence (people who smoke who are more dependent are more likely to choose more intensive cessation aids and are less likely to quit successfully [135]). In the published literature, a criticism [138–142] of – usually cross-sectional – studies is that these fail to control adequately for important confounding factors (such as cigarette dependence) or fail to adequately consider that respondents may forget about previous failed quit attempts (especially those which did not include a cessation aid), which leads to the underestimation of 'real world' effectiveness. The effectiveness estimates of some of the more robust studies are summarised in Table 1.3. Some of these studies investigating the 'real world' effectiveness of cessation aids found that the likelihood of smoking cessation is the same between those who do and those who do not use cessation aids in quit attempts. However, generally, studies found that varenicline, prescription medicine combined with behavioural support, and NVPs increase the likelihood of successful cessation, compared to using no aid in a quit attempt. The evidence for NRT (especially over-the-counter NRT) and bupropion appears less convincing. Differences between these observational studies could come from differences between:

- study methodology – longitudinal vs cross-sectional; the confounding variables controlled for; the outcome measure of smoking abstinence (e.g., 30-day vs >6 months),

- the year the survey took place – it has been suggested that smoking cessation effectiveness estimates for a given cessation aid may differ over time, from when a specific support option is first accessible to a population due to novelty [142],
- regulatory environment of the setting – a restrictive regulatory environment regarding NVPs has been shown to reduce the 'real world' effectiveness estimates of NVPs [143].

Table 1.3. 'Real world' effectiveness of smoking cessation support options – general population

Study	Year	Setting, Design	Participants	Findings
West et al. [140]	2003–2004	Canada, France, UK, USA, Spain Multinational cohort study	35–65-year-olds who made a quit attempt in the past 3 months	Those who used NRT more likely to achieve 6-month continuous smoking abstinence, compared to those not using NRT
Boutou et al. [144]	2004–2005	Greece Smoking Cessation Clinic cohort	≥18-year-olds who attended the smoking cessation clinic and had 6-month follow-up	Those who used bupropion more likely to achieve 6-month continuous smoking abstinence, compared to those using no aid; those who used NRT equally likely to succeed, compared to those using no aid
Kasza et al. [145]	2006–2009	Australia, Canada, England, US Longitudinal survey	≥18-year-olds who reported making a quit attempt between two consecutive survey waves	Those who used varenicline or nicotine patch more likely to maintain 6-month continuous smoking abstinence; those who used oral nicotine/nicotine gum or bupropion equally likely to succeed, compared to those who attempted to quit without medication
Brose et al. [146,147]	2009–2010 [147]	UK Stop Smoking Services	Any client and had 4-week follow-up	Those who used single NRT equally likely to succeed in smoking cessation, compared to those using no medication; those who used combination NRT, bupropion or varenicline more likely to succeed, compared to those using no medication;

Study	Year	Setting, Design	Participants	Findings
	2009–2011 [146]			those who used combination NRT and varenicline more likely to succeed, compared to those using single NRT; those who used bupropion equally likely to succeed, compared to those using single NRT Outcome measure: participant must report 4 weeks after the designated quit date that they have not smoked for at least 2 weeks and their expired-air CO concentration is <10 ppm
Chaiton et al. [148]	2005–2011	Canada Longitudinal survey	≥18-year-olds who reported making a first quit attempt between two consecutive survey waves	Those who used varenicline more likely to succeed in >6-month smoking cessation, compared to those using no pharmaceutical aid; those who used nicotine patch and nicotine gum less likely to succeed, compared to those using no pharmaceutical aid; those who used bupropion equally likely to succeed, compared to those using no pharmaceutical aid
Kotz et al. [142]	2006–2012	England Cross-sectional survey	≥16-year-olds who reported making a quit attempt	Those who used over-the-counter NRT equally likely to succeed in self-reported non-smoking up to the time of the survey, compared to those using no cessation aid; those who used prescription medication (prescription NRT, varenicline, bupropion) plus specialist behavioural support, or

Study	Year	Setting, Design	Participants	Findings
				prescription medication combined with brief advice more likely to succeed, compared to those using no cessation aid
Kotz et al. [149]	2006–2012	England Longitudinal survey	≥16-year-olds who reported making a quit attempt between two consecutive survey waves	Those who used over-the-counter NRT less likely to succeed in 6-month smoking cessation, compared to those using no cessation aid; those who used prescription medication (prescription NRT, varenicline, bupropion) combined with specialist behavioural support, or prescription medication combined with brief advice more likely to succeed in 6-month smoking cessation, compared to those using no cessation aid
Bauld et al. [150]	2012/2013	UK Stop Smoking Services	≥16-year-old clients and had achieved self-reported quitting at 4 weeks	Those who used varenicline more likely to be smoking abstinent, compared to those who did not use varenicline Outcome measure: exhaled breath carbon monoxide-validated smoking abstinence at 52 weeks after quit date
Brown et al. [151]	2009–2014	England Cross-sectional survey	≥16-year-olds who reported making a quit attempt	Those who used NVPs more likely to succeed in in self-reported non-smoking up to the time of the survey, compared to those who used over-the-counter NRT or no aid

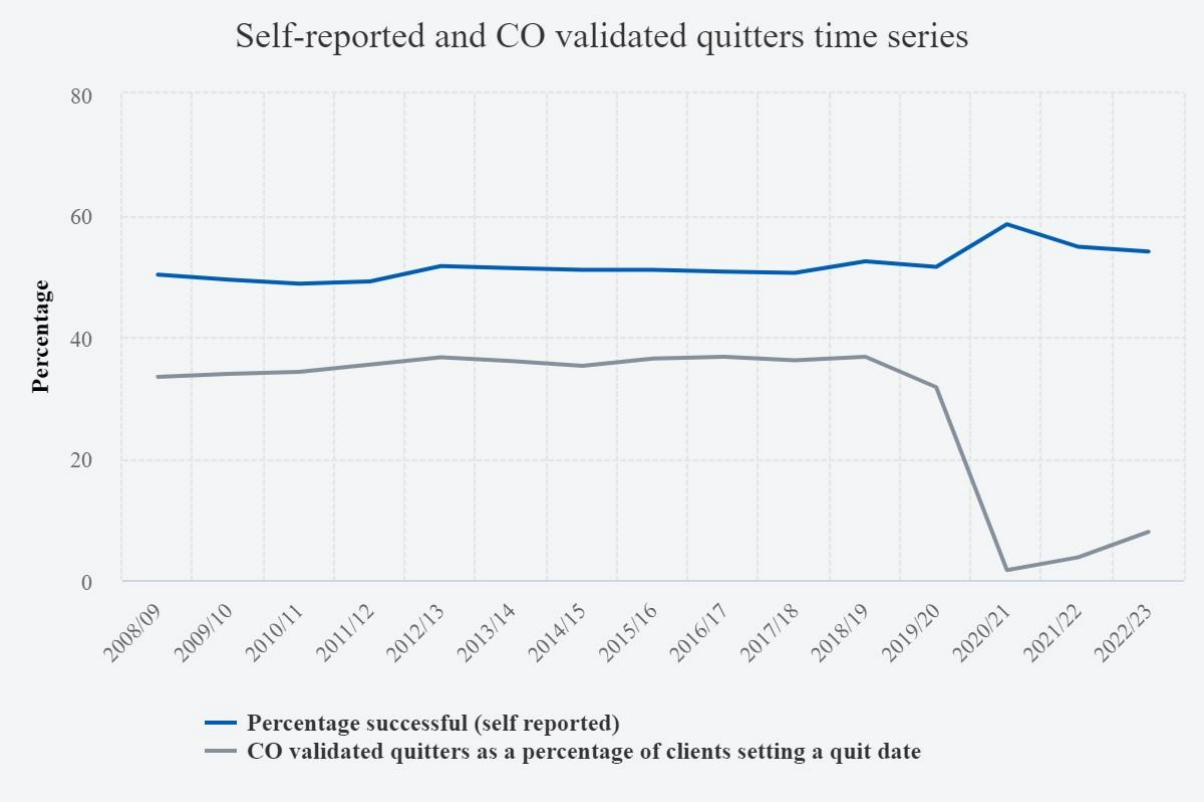
Study	Year	Setting, Design	Participants	Findings
Taylor et al. [152]	2006–2015	UK Longitudinal primary care electronic health records	≥18-year-olds who were prescribed NRT or varenicline	Those who were prescribed varenicline more likely to be quit smoking (lasting up to 4 years), compared to those who were prescribed NRT
Benmarhnia et al. [153]	2013–2015	US Longitudinal survey	≥18-year-olds who reported making a quit attempt between two consecutive survey waves	Those who used NVPs more likely to report 30-day cigarette smoking abstinence, compared to those using no cessation aid; Those who used NRT, varenicline or bupropion had no statistically significant risk difference for smoking abstinence; There was no statistically significant difference when comparing NVPs with approved cessation aids (NRT, varenicline, bupropion)
Brose et al. [84]	2016–2017	England Cross-sectional survey	≥16-year-olds who reported making a quit attempt	Those who used NVPs more likely to be quit smoking >1 month after the quit attempt, compared to those who used non-evidence-based cessation aids (e.g., booklets, websites, apps); those who used over-the-counter NRT or prescription medication and/or behavioural support equally likely to be quit smoking >1 month after the quit attempt, compared to those who used non-evidence-based cessation aids

Study	Year	Setting, Design	Participants	Findings
Jackson et al. [154]	2006–2018	England Cross-sectional survey	≥16-year-olds who reported making a quit attempt	Those who used prescription NRT, varenicline, or NVPs more likely to succeed in self-reported abstinence from quit date up to the survey, compared to those using no aid; those using over-the-counter NRT, bupropion, face-to-face behavioural support equally likely to succeed, compared to those using no aid
Jackson et al. [135]	2015–2020	England Longitudinal survey	≥18-year-olds who reported making a quit attempt between two consecutive survey waves	Those who used varenicline more likely to be self-reported smoking abstinent at 12 months, compared to those not using varenicline; data were inconclusive for using NVPs, prescription NRT, over-the-counter NRT, and behavioural support; sample size was too small for bupropion-only analyses
Jackson et al. [155] (under review)	2016–2017 & 2020–2023	England Cross-sectional survey	≥16-year-olds* who reported making a quit attempt *data not collected from 16- and 17-year-olds between April 2020 and December 2021	Those who used NVPs, varenicline or heated tobacco products more likely to succeed in self-reported abstinence from quit date up to the survey, compared to those not using these aids; those who used Allen Carr's Easyway method less likely to succeed, compared to those not using this; those who used other aids (over-the-counter NRT, prescription NRT, bupropion, face-to-face behavioural support, telephone support, websites, hypnotherapy, written self-help materials, nicotine

Study	Year	Setting, Design	Participants	Findings
				pouches) equally likely to succeed, compared to those not using these aids

In England, NHS Stop Smoking Service monitoring data [156,157] has found that, among those who use the service (which offers intensive group therapy or one-to-one support), approximately 50% self-report being smoking abstinent for at least 15–28 days following their quit attempt day. The monitoring data consider a self-reported quitter to be a verified quitter if the self-reported quitter is assessed 28 days after their quit date and the exhaled breath carbon monoxide (CO) reading is less than 10 parts per million (ppm) [156]. The percentage of CO-verified quitters is significantly lower than the percentage of self-report quitters, indicating that the self-reported data is prone to bias [156,157]. See Figure 1.1 showing the proportion of Stop Smoking Service attendees who are self-reported quitters and CO-verified quitters between 2008 and 2023. (The substantial decrease in CO-verified quitters for the 2020 to 2023 period is due to disruption to data monitoring due to the COVID-19 pandemic.)

Figure 1.1. NHS Stop Smoking Service graph



Reproduced from [156]

People with mental health conditions

There are only a few studies which have examined whether the effectiveness of smoking cessation aids differ between people with and without mental health conditions in the 'real world', and they have not appeared to find a significant difference between the two populations. The mental health variables used in these studies are defined in Table 1.4.

Cooper et al. [67] used four annual wave survey data from 2006/2007–2010/2011 from Australia, Canada, the UK, and the USA, finding that the interactions between depression and use of behavioural support and pharmacological cessation support were not significant, on 1-month abstinence.

Taylor et al. [158] used 2010–2015 primary care electronic health records from England to find that patients who smoked who were prescribed varenicline had higher odds of quitting at 2 years for all mental disorder subgroups, compared to those who were prescribed NRT. They found that there was some evidence that the odds of 2-year smoking cessation in those prescribed varenicline compared with NRT was smaller in those prescribed antidepressants, when compared to patients without mental disorders. However, they did not find evidence for this difference between the other mental disorder groups and patients without mental disorders.

Brose et al. [84], using Smoking Toolkit Study survey data collected between January 2016 and December 2017 from ≥16-year-olds in England, found no significant interactions between mental health condition and cessation support option used, on >1-month quit success rate.

Jackson et al. [155] (under review) used survey data collected between January 2016 and December 2017, and October 2020 and June 2023 from ≥16-year-olds in the Smoking Toolkit Study in England (*data were not collected from 16 and 17-year-olds between April 2020 and December 2021) to find that the interactions between history of mental health conditions and use of cessation aid, on self-reported continuous abstinence, were not significant. However, Bayes factors indicated that they were unable to rule out potential differences in effectiveness by history of mental health condition, except for NVPs, where

there was an indication that the effectiveness of NVPs for smoking cessation did not differ significantly between those with and without a history of mental health conditions.

Summary

Studies investigating the 'real world' effectiveness of cessation aids generally found that varenicline, prescription medicine combined with behavioural support, and NVPs increase the likelihood of successful cessation, compared to using no aid in a quit attempt. However, the evidence for over-the-counter NRT and bupropion is less convincing.

It is noteworthy to highlight that the efficacy estimations of these cessation aids even under 'perfect', controlled RCT conditions are only moderate. In section *Smoking cessation support options – Efficacy in RCTs,* I outlined that Cochrane reviews of RCTs found that only 11.0–23.0% of participants who used cessation support options were successfully >6 months smoking abstinent (Table 1.1). Hence, it should be acknowledged that although using these cessation aids in quit attempts does increase smoking cessation likelihood, even if cessation aid utilisation is 100%, the majority of people will not successfully quit smoking.

There have been only a few studies conducted which have examined whether the effectiveness of smoking cessation aids differ between people with and without mental health conditions in the 'real world', and they have not appeared to find a significant difference between the two populations.

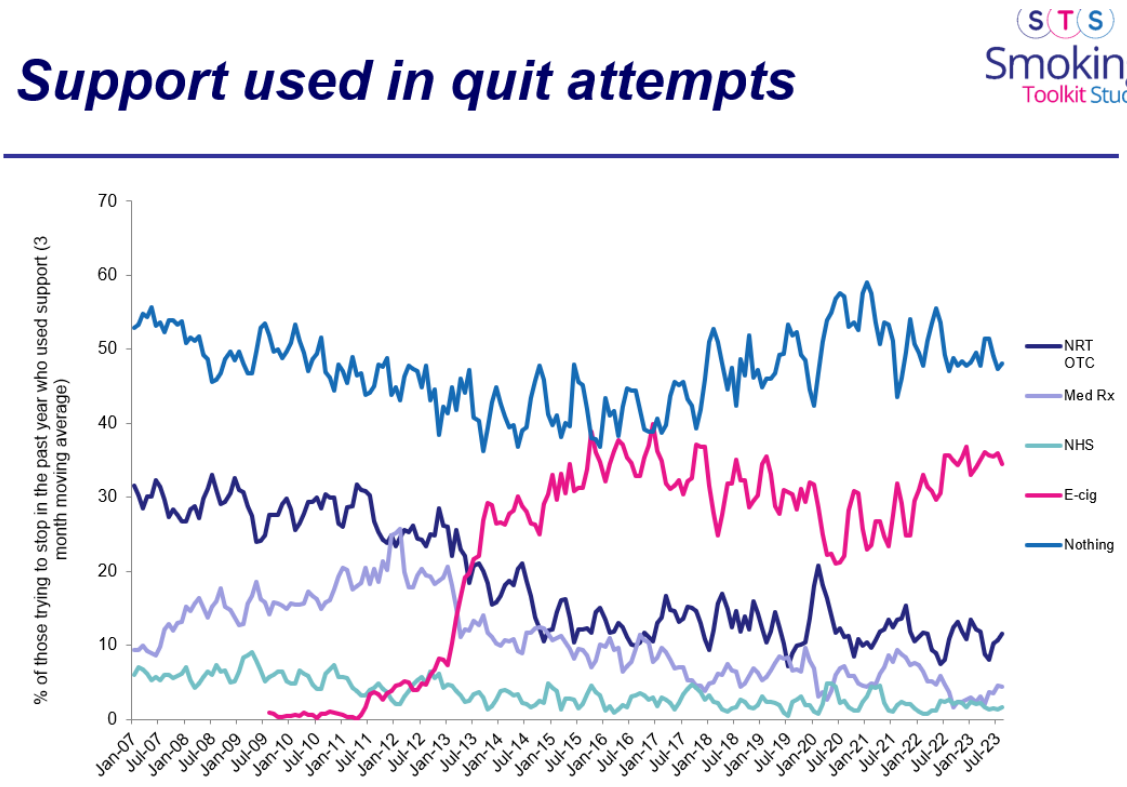
Smoking cessation support options – Rate of use in the 'real world'

General population

In addition to the low success rates even with cessation aids, many people who make a smoking quit attempt do not use cessation aids to support their quit attempt. Although the proportion of quit attempts in the 'real world' which are made without cessation aids fluctuates, the most popular form of support is no support – in England, approximately half

(50%) of quit attempts use no support [26]. For example, in August 2023, 48.1% of quit attempts in England did not use a cessation aid; 34.5% of quit attempts included NVPs, 11.5% included over-the-counter NRT, and 4.4% included prescription medication [26]. NVPs have become the most popular smoking cessation aid in the UK [104]. Figure 1.2 illustrates how the proportion of people who used NVPs in their quit attempt has increased since 2011 [26]. For example, a recent study by Jackson et al. [135] which used survey data of ≥18-year-olds who smoke in England from 2015–2020, found that of those who had 12-month follow-up responses available, just over half (57.8%) had used one or more cessation aids in their most recent smoking quit attempt, including 14.6% who used any prescription medication: 9.8% had used prescription NRT, 5.2% used varenicline, and 0.4% used bupropion. For non-prescription aids, 16.1% used over-the-counter NRT, 32.9% used NVPs, and 8.2% used behavioural support. While 45.8% used one of these cessation aids on their own, 12.0% used 2–4 aids, and 42.2% used none of these cessation aids [135].

Figure 1.2. Support used in quit attempts in England



NRT OTC: Nicotine replacement therapy bought over the counter; Med Rx: Prescription medication; NHS: NHS Stop Smoking Service; E-cig: E-cigarette. Method is coded hierarchically with smokers using more than one method classified into most intensive by the following scheme: 1. Nothing, 2. NRT OTC, 3. E-cigarette, 4. Med Rx, 5. NHS. In updates until June 2015, NRT OTC was coded above e-cigarette - earlier figures have now been revised. See e-cigarette tracking slides for any use of different treatments.

Reproduced from [26]

The low rate of cessation aid use in quit attempts is generalisable to other countries, too. In comparison to many other countries, the proportion of people using cessation aids in quit attempts appears to be highest in England [159,160]. For example, using 2017/2018 survey data from the ITC Project in England, Germany, Greece, Hungary, Poland, Romania, and Spain, Papadakis et al. [160] found that during the most recent quit attempt, England had the highest proportion who used any cessation support (64.1%); followed by 44.0% using any cessation support in Greece; the other countries had smaller proportions, with Romania having the smallest at 16.0%. NVPs were the most widely used cessation aid in England (51.7%), Greece (26.3%) and Germany (15.0%), with lower rates reported in the other countries. In England, after NVPs, the most frequently used cessation aid was NRT (23.8%), while the other cessation medications were less popular (varenicline: 6.4%, bupropion: 2.6%). In England, 7.5% of the most recent quit attempts included face-to-face advice from a health professional, 6.8% included the use of a smoking cessation service, and 23.1% of quit attempts used either quitline, apps, the internet or printed materials [160].

Gravely et al. [161] used more recent 2020 survey data from England, the USA, Canada and Australia to calculate what proportion of people who smoke used cessation aids (including NVPs) in their last quit attempt: among all respondents, 38.6% used no cessation aid/assistance, 28.8% used NRT, 28.0% used NVPs, 12.0% used other pharmacotherapy (varenicline/bupropion/cytisine) and 7.8% used a cessation service (stop smoking service/counselling/advice from a doctor/quitline). The study found some significant differences between the four countries. For example, a higher proportion used NVPs in quit attempts in England (36.7%), relative to Canada (26.7%), the US (22.1%), and Australia (21.5%). For NRT, respondents in Australia (34.5%) and Canada (33.0%) had a significantly higher use rate compared to England (22.8%), and England was significantly lower compared to the US (29.5%). For other pharmacotherapy, 14.4% of Australian respondents reported using these medications; while respondents in the US (15.5%) had a significantly higher use rate compared to Canada (11.2%) and England (10.1%). Lastly, for cessation services, the proportion of use was significantly higher in Australia (9.4%) and England (10.8%), compared to the US (5.0%); and England had a significantly higher rate compared to Canada (6.4%).

People with mental health conditions

There is less research which has investigated what cessation aids people who smoke with mental health conditions use, and what proportion of smoking quit attempts are made with the support of cessation aids. The studies I identified are summarised in Table 1.4. These studies found that people who smoke and have mental health conditions are either equally likely [66–68,162,163] or more likely [68,71,155,158,164] to use some cessation support in quit attempts, compared to people who smoke and do not have mental health conditions. One study [165], using 2009–2010 electronic health record data from the UK, found that a higher proportion of people with a mental health condition had a cessation medication (NRT, bupropion or varenicline) prescribed to them, compared to people without a mental health condition, but the proportion of *consultations* in which a cessation medication was prescribed was lower in patients with mental health conditions. Brose et al. [84] found mixed findings using 2016–17 survey data from England – people with mental health conditions were less likely to use over-the-counter NRT but more likely to use prescription medication and/or behavioural support, and there was no difference in the use of NVPs during the last quit attempt between people who smoke with and without mental health conditions.

Table 1.4. Use of smoking cessation support options in smoking quit attempts in the 'real world' by mental health

Study	Data source	Mental health condition measure	Findings
Morris et al. [66]	2008 survey data from the >18-year-olds Colorado Tobacco Attitudes and Behaviors Survey (TABS)	1. Limitations: 'Yes' to: "Are you limited in any way in any activities because of mental or emotional problems?" 2. Self-reported mental health diagnosis: 'Yes' to: "Has a doctor or healthcare provider ever told you that you have a mental health problem or mental illness? Please tell me what the problem or illness is called."	<u>Used NRT:</u> Limitations: 40.2% No limitations: 23.4% ($p<0.05$) Those with and without a mental health diagnosis equally likely
Cooper et al. [67]	2006/2007–2010/2011 ITC survey, adults in Australia, Canada, UK, USA	Depression symptoms: Bothered by either symptom but no diagnosis in the previous year: 'Yes' to "During the last month, have you often been bothered by little interest or pleasure in doing things?" and/or 'Yes' to "During the last month, have you often been bothered by feeling down, depressed, or hopeless?"; and 'No' to "In the last year, have you been told by a doctor or other health care provider that you have depression?" Depression diagnosis: Bothered by either symptom and reported a diagnosis in the previous year: 'Yes' to "During the last month, have you often been bothered by little interest or pleasure in doing things?" and/or 'Yes' to "During the last month, have you often been bothered by feeling down, depressed, or hopeless?"; and 'Yes' to "In	<u>Used stop smoking medication:</u> Either symptom: 48.9–54.2% Depression diagnosis: 51.2–66.4% Vs no depression: 50.2–52.5% (n.s.) <u>Used behavioural support:</u> Either symptom: 19.1–29.6% Depression diagnosis: 20.1–38.4% Vs no depression: 18.0–27.5% (n.s.)

Study	Data source	Mental health condition measure	Findings
		the last year, have you been told by a doctor or other health care provider that you have depression?"	
Petroulia et al. [68]	2016 ITC survey, adults in Germany, Greece, Hungary, Poland, Romania, Spain	1. Self-reported current treatment/diagnosis of anxiety 2. Self-reported current treatment/diagnosis of depression 3. Positive screen for depression: Answered 'Yes' to "During the last 30 days, have you often been bothered by little interest or pleasure in doing things?" or/and "During the last 30 days, have you often been bothered by feeling down, depressed, or hopeless?" 4. Probable anxiety or depression: 'Yes' to 1. or 'Yes' to 2. or Positive screen for 3.	<u>Used any cessation support:</u> 1. 48.3% (p<0.01) 2. 41.1% (n.s.) 3. 27.7% (n.s.) 4. 29.5% (n.s.) Vs no probable anxiety or depression (28.1%) <u>Used NRT:</u> 1. 32.8% (p<0.001) 2. 25.0% (p<0.01) 3. 8.6% (n.s.) 4. 11.3% (n.s.) Vs no probable anxiety or depression (10.1%) <u>Used pharmacotherapy (varenicline, bupropion, cytisine):</u> 1. 11.6% (n.s.) 2. 24.0% (p<0.01) 3. 15.2% (n.s.) 4. 15.4% (n.s.) Vs no probable anxiety or depression (7.9%)

Study	Data source	Mental health condition measure	Findings
			Used local quit services: 1. 9.9% (p<0.001) 2. 6.9% (p<0.01) 3. 0.4% (n.s.) 4. 1.8% (p<0.05) Vs no probable anxiety or depression (0.9%) Used face-to-face advice from health professional: 1. 17.5% (p<0.001) 2. 15.0% (p<0.01) 3. 7.0% (n.s.) 4. 8.5% (p<0.05) Vs no probable anxiety or depression (4.3%) Used telephone/quitline services: 1. 6.0% (p<0.001) 2. 9.0% (p<0.001) 3. 1.9% (p<0.001) 4. 2.4% (p<0.001) Vs no probable anxiety or depression (0.1%) Used NVPs: 1. 22.5% (n.s.) 2. 13.4% (n.s.) 3. 12.9% (n.s.)

Study	Data source	Mental health condition measure	Findings
			4. 13.7% (n.s.) Vs no probable anxiety or depression (14.3%)
McGowan et al. [162]	2012 Smoking Toolkit Study survey, ≥40-year-olds in England	Anxiety/depression present (vs not present): respondent chooses one from: (1) "I am not anxious or depressed", (2) "I am moderately anxious or depressed" or (3) "I am extremely anxious or depressed".	<u>Used prescription medication:</u> Anxiety/depression: 34.1% Vs no anxiety/anxiety: 31.5% (n.s.) <u>Used prescription NRT:</u> Anxiety/depression: 22.7% Vs no anxiety/anxiety: 15.2% (n.s.) <u>Used varenicline:</u> Anxiety/depression: 11.4% Vs no anxiety/anxiety: 14.6% (n.s.) <u>Used bupropion:</u> Anxiety/depression: 5.7% Vs no anxiety/anxiety: 4.0% (n.s.) <u>Used over-the-counter NRT:</u> Anxiety/depression: 39.8%

Study	Data source	Mental health condition measure	Findings
			Vs no anxiety/anxiety: 35.1% (n.s.) <u>Used NVPs:</u> Anxiety/depression: 1.1% Vs no anxiety/anxiety: 0.0% (n.s.) <u>Used NHS support (group or one-to-one):</u> Anxiety/depression: 12.5% Vs no anxiety/anxiety: 7.3% (n.s.)
Szatkowksi et al. [165]	2009–2010 primary care electronic health records (THIN), ≥16-year-old patients in the UK	MH diagnosis: Patients with a diagnosis of one or more specific conditions in the study period (schizophrenia, bipolar affective disorder, depression, neurotic, stress-related and somatoform disorders, eating disorders, specifical personality disorders, hyperkinetic disorders) MH medication: Patients prescribed one or more psychoactive medications in the study period (antipsychotic, lithium, antidepressant or anxiolytic)	<u>Prescribed a cessation medication (prescription NRT, bupropion or varenicline):</u> MH diagnosis: 11.2% MH medication: 11.0% No MH: 6.7% <u>Mean number of consultations per year:</u> MH diagnosis: 10.00 MH medication: 9.80 No MH: 3.89 <u>Proportion of consultations where cessation medication was prescribed:</u> MH diagnosis: 2.90%

Study	Data source	Mental health condition measure	Findings
		No MH diagnosis or MH medication: Patients without a diagnosis of a mental health condition or a prescription for a psychoactive medication	MH medication: 3.15% No MH: 4.37%
Falcaro et al. [164]	2007–2014 primary care electronic health records (THIN), ≥18-year-olds patients in England	History of SMI: a record of SMI (bipolar disorder, schizophrenia and other non-organic psychotic illnesses) diagnosis at any time in their healthcare record Depression: No history of SMI but recent recorded diagnoses or symptoms of depression No SMI nor depression: No history of SMI nor recent recorded diagnoses or symptoms of depression	<u>Proportion with referral to Stop Smoking Services:</u> History of SMI: 2.1% in 2007; 3.6% in 2014 Depression: 1.7% in 2007; 4.3% in 2014 No SMI nor depression: 1.6% in 2007; 3.4% in 2014 (No significant difference between groups) <u>Proportion prescribed NRT:</u> History of SMI: 12.3% in 2007; 6.3% in 2014 Depression: 11.9% in 2007; 4.5% in 2014 No SMI nor depression: 8.3% in 2007; 3.1% in 2014 (NRT prescribing higher in history of SMI and depression vs no SMI nor depression) <u>Proportion prescribed bupropion:</u> History of SMI: 0.4% in 2007; 0.1% in 2014 Depression: 1.0% in 2007; 0.1% in 2014 No SMI nor depression: 1.1% in 2007; 0.1% in 2014

Study	Data source	Mental health condition measure	Findings
			(Bupropion prescribing very low, especially in history of SMI) <u>Proportion prescribed varenicline:</u> History of SMI: 1.0% in 2007; 1.6% in 2014 Depression: 2.5% in 2007; 2.2% in 2014 No SMI nor depression: 2.3% in 2007; 2.7% in 2014 (Varenicline prescribing very low, especially in history of SMI)
Taylor et al. [158]	2006–2015 primary care electronic health records (CPRD), ≥18-year-old patients in England	MH: have past-year record of diagnosis of depression or neurotic disorder; have ever record of diagnosis of bipolar disorder, schizophrenia or other nonaffective psychotic disorders; or have past-year record of a psychoactive medication prescription (antidepressants, antipsychotics, hypnotics or anxiolytics, or mood stabilizers)	<u>Proportion prescribed NRT:</u> MH: 14.4% in 2007; 3.9% in 2015 No MH: <4% in 2007; <2% in 2015 <u>Proportion prescribed varenicline:</u> MH: 2.5% in 2007; 2.0% in 2015 No MH: <2% in 2007; <2% in 2015 Higher proportion of people who smoke with MH were prescribed NRT and varenicline, compared to people who smoke without MH (number of consultations not adjusted for)
Lin Li et al. [71]	2016 ITC survey, ≥18-year-olds in	Self-reported current treatment/diagnosis of anxiety	<u>Used cessation medication (NRT/varenicline/bupropion):</u>

Study	Data source	Mental health condition measure	Findings
	Australia, Canada, England, USA	Self-reported current treatment/diagnosis of depression	Anxiety: 46.5% No anxiety: 39.4% (p<0.01) OR: 1.5, 95% CI: 1.2–1.9 Depression: 46.6% No depression: 39.2% (p<0.01) OR: 1.4, 95% CI: 1.1–1.7
Lin Li et al. [163]	2016 ITC survey, ≥18-year-olds in Australia, Canada, England, USA	Self-reported current treatment/diagnosis of anxiety Self-reported current treatment/diagnosis of depression	<u>Used NVPs (in last smoking quit attempt):</u> Anxiety: 29.42% No anxiety: 26.83% (n.s.) OR: 1.12, 95% CI: 0.81–1.34 Depression: 30.43% No depression: 26.41% (n.s.) OR: 1.12, 95% CI: 0.91–1.43
Brose et al. [84]	2016–2017 Smoking Toolkit Study survey, ≥16-year-olds in England	Ever diagnosis: "Since the age of 16, which of the following, if any, has a doctor or health professional ever told you that you had? Depression; anxiety; obsessive-compulsive disorder; panic disorder or a phobia; post-traumatic stress disorder; psychosis; personality disorder; ADHD; an eating disorder alcohol misuse or dependence; drug use or dependence; problem gambling"	<u>Used non-evidence-based treatment:</u> Ever diagnosis: 41.6% No, ever diagnosis (ref): 42.3% (n.s) OR: 0.91, 95% CI: 0.74–1.10

Study	Data source	Mental health condition measure	Findings
		Past-year treatment: "In the last 12 months, which of the following conditions, if any, have you had any treatment or taken any prescribed medication for? response options were any conditions that had been selected in the previous question" Past-month distress: "During the past 30 days, about how often, if at all, did you feel… nervous; hopeless; restless or fidgety; so depressed that nothing could cheer you up; that everything was an effort; worthless" For each, the respondent indicated: all of the time (scored 4), most of the time (3), some of the time (2), a little of the time (1), or and none of the time (0). Total score: 5–12: moderate distress; >13: serious distress	Past-year treatment: 40.0% No, past-year treatment (ref): 42.6% (n.s) OR: 0.90, 95% CI: 0.72–1.12 Past-month distress, serious: 45.5%, (n.s) OR: 1.15, 95% CI: 0.85–1.56 Past-month distress, moderate: 42.5%, (n.s) OR: 1.07, 95% CI: 0.86–1.32 No, past-month distress (ref): 41.1% <u>Used over-the-counter NRT:</u> Ever diagnosis: 9.8% No, ever diagnosis (ref): 13.5% (p=0.006) OR: 0.66, 95% CI: 0.48–0.89 Past-year treatment: 10.9% No, past-year treatment (ref): 12.4% (n.s.) OR: 0.83, 95% CI: 0.59–1.16 Past-month distress, serious: 6.1%, (p=0.001) OR: 0.35, 95% CI: 0.19–0.64 Past-month distress, moderate: 10.2%, (p=0.030) OR: 0.69, 95% CI: 0.50–0.97 No, past-month distress (ref): 14.1%

Study	Data source	Mental health condition measure	Findings
			<u>Used NVPs:</u> Ever diagnosis: 37.0% No, ever diagnosis (ref): 33.9% (n.s) OR: 1.17, 95% CI: 0.96–1.43 Past-year treatment: 36.1% No, past-year treatment (ref): 34.9% (n.s) OR: 1.03, 95% CI: 0.83–1.29 Past-month distress, serious: 34.0%, (n.s) OR: 0.91, 95% CI: 0.66–1.24 Past-month distress, moderate: 37.6%, (n.s) OR: 1.06, 95% CI: 0.85–1.32 No, past-month distress (ref): 34.2% <u>Used prescription and/or behavioural support</u> (prescription NRT, varenicline, bupropion, Stop Smoking Group, Stop Smoking one-to-one counselling/advice/support session/s, or Telephone quitline): Ever diagnosis: 11.6% No, ever diagnosis (ref) 10.2% (n.s) OR: 1.34, 95% CI: 0.99–1.82

Study	Data source	Mental health condition measure	Findings
			Past-year treatment: 12.8% No, past-year treatment (ref): 10.1% (p=0.039) OR: 1.42, 95% CI: 1.02–1.97 Past-month distress, serious: 14.3%, (p=0.001) OR: 2.05, 95% CI: 1.32–3.18 Past-month distress, moderate: 9.8%, (n.s) OR: 1.11, 95% CI: 0.78–1.57 No, past-month distress (ref): 10.5%
Jackson et al. [155] (under review)	2016–2017 & 2020–2023 Smoking Toolkit Study survey, ≥16-year-olds (data not collected from 16- and 17-year-olds between April 2020 and December 2021), in England	MH: 'Yes' to : "Since the age of 16, which of the following, if any, has a doctor or health professional ever told you that you had?" followed by: depression; anxiety; obsessive compulsive disorder; panic disorder or a phobia; post-traumatic stress disorder; psychosis; personality disorder; attention deficit hyperactivity disorder; an eating disorder; alcohol misuse or dependence; drug use or dependence; and problem gambling. Between 2020 and 2023, also: autism or autism spectrum disorder; and bipolar disorder.	<u>Used any cessation aid:</u> MH: 52.9% No MH: 58.9% Significant difference <u>Used prescription NRT:</u> MH: 4.8% No MH: 2.7% Significant difference <u>Used NVPs:</u> MH: 38.8% No MH: 30.7% Significant difference <u>Used websites:</u> MH: 4.0%

Study	Data source	Mental health condition measure	Findings
			No MH: 2.2% Significant difference <u>Use of other aids did not significantly differ between MH and no MH:</u> Used over-the-counter NRT: 16.7% vs 17.8% Used varenicline: 3.4% vs 3.5% Used bupropion: 0.6% vs 0.4% Used face-of-face behavioural support: 2.8% vs 1.8% Used Allen Carr's Easyway: 1.4% vs 1.2% Used written self-help materials: 0.7% vs 1.1% Used telephone support: 0.9% vs 0.7%

n.s.: not (statistically) significant

Summary

Studies of smoking cessation support option use in people who smoke in the general population have shown that usually, there are at least 35% of quit attempts which are still being made without cessation support. In recent years, NVPs have become the most popular cessation aid – with some studies showing that they are used in up to 50% of quit attempts.

Regarding people who smoke and have mental health conditions, there have been fewer studies conducted looking at the rate of cessation support use in this population. The studies identified found that people who smoke and have mental health conditions are either equally likely or more likely to use some cessation support in quit attempts, compared to people who smoke and do not have mental health conditions. However, one study [165] suggests that because the proportion of *consultations* in which a cessation medication was prescribed was lower in patients with mental health conditions, given equal opportunity to do so, health professionals appear less likely to intervene with people who smoke with indicators of poor mental health compared to those without. Overall, NVPs appear to be a popular cessation option for people who smoke and have mental health conditions, as well as those without. However, overall, there is a large proportion of quit attempts which are made without the use of cessation support.

Nicotine vaping products (NVPs)

Uncertainties surrounding NVPs

In the above sub-sections, I have mentioned that NVPs are a type of electronic device which can aerosolise a vapour which can be inhaled, which may or may not contain nicotine and/or flavourings [103]. I have also outlined that NVPs have been shown to be efficacious in RCTs and effective in 'real world' studies on smoking cessation as an outcome.

Although researchers have been able to gather evidence which has demonstrated that using NVPs is likely to be substantially less harmful than smoking in the short- to medium-term

[104], evidence regarding the longer-term use of NVPs is currently lacking because robust long-term longitudinal studies do not yet exist [104]. Studies which have investigated biomarkers of toxicant exposure (measuring potentially harmful substance levels in the body) have found that the level of some biomarkers associated with the risk of cancer, respiratory and cardiovascular conditions was higher in people who have used NVPs, compared to people who have not used NVPs (but some of this could be due to these people smoking cigarettes before they switched to vaping) [104]. Therefore, although using NVPs is likely to be substantially less harmful than smoking in the short- to medium-term [104], using NVPs cannot be considered 'risk-free' and McNeill et al. [104] emphasise that inhaling any substance into the lungs on a sustained and regular basis is likely to be harmful in the long-term; hence those who do not smoke or vape should not initiate NVP use.

Hence, not all researchers and public health advocates agree that NVPs should be recommended as a smoking cessation tool. The opponents of NVPs focus on their health risks for young people; the possibility that NVPs may 'renormalise' smoking; the lack of evidence regarding any long-term harms of NVPs; views that people who do not smoke should be nicotine abstinent; and a worry that NVPs may be a consumer product liable to industry manipulation (as was the case with Big Tobacco historically). In contrast, supporters of NVPs emphasize the potential for NVPs to assist people who smoke in quitting smoking; believe that using NVPs poses less harm to health when compared to smoking and is, therefore, an effective tobacco harm reduction approach; believe that there is insufficient evidence for the gateway hypothesis (that using NVPs leads to smoking) or that using NVPs leads to the 'renormalisation' of smoking; do not necessarily believe in nicotine abstinence as a societal aim; and although they are wary of policy-manipulating tobacco industry tactics, regard NVPs as a separate, non-tobacco product. Further discussion of this is out of the scope of this thesis, for further critical reading, see: [104,166–170].

There are concerns about increased rates of youth uptake of vaping. For example, in Great Britain, the proportion of young people (11–17-year-olds) who indicated that they regularly use (more than once a week) NVPs increased from 0.3% in 2013 to 3.7% in 2023 [171]. Some researchers have argued that the cause of the increase in youth vaping is the current increase in availability of disposable (single-use) NVPs – the increase in availability occurred concurrently with higher levels of youth use [171].

Research has shown that members of the general population have inaccurate harm perceptions about NVPs. For example, in Great Britain, the proportion of young people (11–17-year-olds) who thought that vaping was less harmful than smoking was 73% in 2013 and decreased to 33% in 2023 [171]. In Great Britain, the proportion of adults (≥18-year-olds) who thought that vaping was less harmful than smoking was 42% in 2013 and decreased to 34% in 2023 [172]. Studies have shown that people (in England/UK) who smoke and have mental health conditions also hold inaccurate harm perceptions about vaping [173,174]. One recent phenomenon that affected harm perceptions of youth was the 'e-cigarette or vaping product use-associated lung injury' (EVALI) outbreak – research suggests that EVALI may have exacerbated young people's perceptions of vaping harms internationally [175]. EVALI was a multistate outbreak of severe lung injuries which were confined largely to the US [176]. EVALI was first identified in July 2019, with a sharp increase in cases in August 2019, followed by a peak in case counts in September 2019, which then steadily declined through early 2020 [176]. News coverage about EVALI peaked in the US in September 2019 [177]. EVALI was initially incorrectly purported to be associated with NVP use, however, the US Centers for Disease Control and Prevention (CDC) concluded that tetrahydrocannabinol (THC)-containing vaping products and Vitamin E acetate were linked to most EVALI cases [104,176,178].

Regulation of NVPs varies internationally

The way that NVPs are regulated varies widely internationally, for example:

- Since 2021, Australia has prohibited the sale of nicotine-containing vaping products, unless on prescription from a licensed health professional [179,180].
- In Canada, NVPs are widely available in various retail locations, but are not included in smoking cessation clinical practice guidelines [96].
- In the US in 2020, the Food and Drug Administration (FDA) announced a nationwide ban on any non-tobacco and non-menthol flavoured vaping products that used pod or cartridge systems [181]. Also, the FDA has issued marketing denials through its Premarket Tobacco Product Application process for millions of NVPs, and has only approved a small number of tobacco-flavoured e-cigarettes [182]; at the time of

writing (October 2023), no non-tobacco flavoured products have been approved, however the ones not approved have not been taken off the market.

Policies in the UK regarding NVPs

The first NVP was marketed in China in 2004, and NVPs started to appear in England in 2006/7, increasing rapidly by 2010 [103] – for example, 1.7% of adults in Great Britain regularly used NVPs in 2012 [172].

The UK NICE guideline published in 2018 recommended that switching from smoking to using NVPs is an effective form of harm reduction [183]. Since 2021, the NICE clinical guidelines recommend that NVPs should be accessible to adults who smoke, alongside other smoking cessation interventions [95]. In the UK, there are no medicinally licensed NVPs; NVPs are regulated as consumer products and are widely available on the open market to those aged ≥18 years [104].

Although health professionals cannot prescribe specific vaping products, a survey in England found that in 2022, 52% of local authorities offered NVPs to clients of stop smoking services, by either providing them directly or via vouchers or other arrangements with local vape shops [184]. NVPs are the most popular smoking cessation aid in the UK [104], and 9.1% of adults in Great Britain regularly used NVPs in 2023 [172]. Additionally, the English government announced in 2023 that people who smoke "will be provided with a vape starter kit alongside behavioural support" ('swap to stop' scheme) [185].

Table 1.5 shows a timeline of UK policies and policy statements from public health stakeholders between 2016 and 2023.

Table 1.5. Timeline of NVP policies in the United Kingdom

Year	Policy	Citation
2016	The 2016 Royal College of Physicians 'Nicotine without smoke: Tobacco harm reduction' report recommends "…in the interests of public health it is important to promote the use of e-cigarettes, NRT and other non-tobacco nicotine products as widely as possible as a substitute for smoking in the UK." (Key recommendations section)	[11]
2017	Royal College of General Practitioners position statement on NVPs "Recommendations: • Primary Care Clinicians (PCCs) should provide advice to smoking patients on the relative risks of smoking. • Patients should be advised that behavioural support and prescription medication from local Stop Smoking Services (SSS) is the most effective quit method. PCCs should provide referral to SSS where these services exist, and the patient wishes to access this support. • Using their clinical judgement on an individual patient basis, PCCs may wish to promote e-cigarette (EC) use as a means to stopping. Patients choosing to use an e-cigarette in a quit attempt should be advised that seeking behavioural support alongside e-cigarette use increases the chances of quit success further. Most SSS are EC friendly, and patients can be advised to bring one to their appointment if they would like to quit using their device. • PCCs recognise ECs offer a wide reaching, low-cost opportunity to reduce smoking (especially in deprived groups in society and those with poor mental health, both having elevated rates of smoking). In the UK, though start-up costs can be higher, it is likely to be less expensive to use an EC over time than it is to smoke."	[186]
2018	The 2018 Royal College of Physicians 'Hiding in plain sight: Treating tobacco dependency in the NHS' report recommended:	[187]

Year	Policy	Citation
	• "E-cigarettes are the most popular smoking cessation aid in the UK and are also effective in helping people to stop smoking." (pg 118) • "Allowing e-cigarettes to be used on NHS sites can support smokers in remaining smoke free and help to sustain smoke-free policy." (pg 214) • "10.4 How should tobacco dependency be treated in the NHS? Smoking cessation interventions have been extensively researched and there is an extensive evidence base demonstrating that advice to quit, behavioural support, licensed pharmacotherapies and the use of e-cigarettes to replace nicotine are all effective, and especially so if delivered in combination rather than alone. They are also highly cost-effective, and typically far more so than many of the treatments offered routinely by the NHS, and many of those used as a routine to treat the chronic diseases that smoking causes or exacerbates. … The challenge in addressing smoking in NHS patients is therefore not one of a lack of treatment options: it is to ensure that smokers are identified and receive treatment; and that this treatment is supported by a standard tariff for treating tobacco dependence, and a comprehensively smokefree environment. … Providing stop smoking support as a default (opt-out) service, on site, doubles quit rates. The NHS should therefore make opt-out, on-site treatment of tobacco dependency a systematic and routine component of all NHS care." (pg 227-228)	
2018	A Royal College of Physicians 2018 consultation on 'Information standards for recording tobacco use in electronic health records' recommended "recording use of electronic cigarettes" in electronic health records. (pg 6)	[188]
2018 to 2023	QOF guidelines (2018/19 [189] to 2022/23 [190]) recommend that "users of electronic cigarettes who have never smoked or given up smoking should be classified as non-smokers or ex-smokers respectively", which may lead to under-recording of NVP use in electronic health records.	QOF guidelines 2018/19 [189] to 2022/23 [190]

Year	Policy	Citation
2018	NICE tobacco guideline recommended that switching to vaping from smoking is an effective form of harm reduction but emphasise that NVPs are not risk free. NVPs were not included in the list of "evidence-based stop smoking interventions". "1.5 Advice on e-cigarettes These recommendations are for health and social care workers in primary and community settings. 1.5.1 For people who smoke and who are using, or are interested in using, a nicotine-containing e-cigarette on general sale to quit smoking, explain that: • although these products are not licensed medicines, they are regulated by the Tobacco and Related Products Regulations 2016 • many people have found them helpful to quit smoking cigarettes • people using e-cigarettes should stop smoking tobacco completely, because any smoking is harmful • the evidence suggests that e-cigarettes are substantially less harmful to health than smoking but are not risk free • the evidence in this area is still developing, including evidence on the long-term health impact. [2018]"	[183]
2020	UK Medicines and Healthcare products Regulatory Agency's (MHRA) advice in 2020: "Routinely document e-cigarette history: As part of routine clinical practice, clinicians are advised to document use of e-cigarettes or vaping devices in medical records for all patients as they would with smoking. Clinicians should routinely document:	[191]

Year	Policy	Citation
	• Name or brand of product used • Type of product (if known) • Duration and frequency used • Substances vaped (for example, nicotine or recreational substances) • Strengths of substances"	
2021	The NICE tobacco guideline included nicotine-containing e-cigarettes (NVPs) in the "ensure the following are accessible to adults who smoke" list of "stop-smoking interventions". "Advice on nicotine-containing e-cigarettes These recommendations are for people providing stop-smoking support or advice to adults. 1.12.13 Give clear, consistent and up-to-date information about nicotine-containing e-cigarettes to adults who are interested in using them to stop smoking (for example, see the NCSCT e-cigarette guide and Public Health England's information on e-cigarettes and vaping). [2021] 1.12.14 Advise adults how to use nicotine-containing e-cigarettes. This includes explaining that: • e-cigarettes are not licensed medicines but are regulated by the Tobacco and Related Products Regulations (2016) • there is not enough evidence to know whether there are long-term harms from e-cigarette use • use of e-cigarettes is likely to be substantially less harmful than smoking • any smoking is harmful, so people using e-cigarettes should stop smoking tobacco completely. [2021] 1.12.15 Discuss: • how long the person intends to use nicotine-containing e-cigarettes for	[95]

Year	Policy	Citation
	• using them for long enough to prevent a return to smoking and • how to stop using them when they are ready to do so. [2021] 1.12.16 Ask adults using nicotine-containing e-cigarettes about any side effects or safety concerns that they may experience. Report these to the MHRA Yellow Card scheme, and let people know they can report side effects directly. [2021] 1.12.17 Explain to adults who choose to use nicotine-containing e-cigarettes the importance of getting enough nicotine to overcome withdrawal symptoms, and explain how to get enough nicotine. [2021]"	
2022	" 'An offer of treatment' means offering a referral to a local NHS Stop Smoking Service adviser (who might be a member of the practice team) plus pharmacotherapy. Where such treatment is not acceptable to the patient, an alternative form of brief support, such as follow-up appointments with a GP or practice nurse trained in smoking cessation, may be offered. The NICE guidance on tobacco identifies the evidence-based interventions for adults who smoke: • Behavioural support (individual and group) • Very brief advice • Bupropion • Nicotine replacement therapy (NRT) – short and long acting • Varenicline • Nicotine-containing e-cigarettes. For people who smoke and who are using, or are interested in using, a nicotine-containing e-cigarette on general sale to quit smoking, NICE recommend you explain that:	QOF guidelines 2022/23 [190]

Year	Policy	Citation
	• Although these products are not licensed medicines, they are regulated by the Tobacco and Related Products Regulations 2016 • There is not enough evidence to know whether there are long-term harms from e-cigarette use • Use of e-cigarettes is likely to be substantially less harmful than smoking • Any smoking is harmful, so people using e-cigarettes should stop smoking tobacco completely."	
2023	The English government announced in 2023 that people who smoke "will be provided with a vape starter kit alongside behavioural support" ('swap to stop' scheme).	[185]

Summary

While uncertainties exist around NVPs and policy around NVPs varies internationally, NVPs have been shown to improve smoking cessation likelihood and evidence suggests that using NVPs is less harmful than smoking tobacco.

In terms of reducing population smoking prevalence, there are criticisms that the effect of smoking cessation aids (such as, NRT, varenicline, bupropion) on population smoking prevalence is not high enough [192]. Some researchers argue that cessation options with a higher population-level impact are needed [192] and harm reduction options should be considered [193]. NVPs are accessible (have a high reach) and have been shown to be efficacious and effective at achieving smoking cessation; hence, they hence have the potential to have a high population impact given that the population impact of an intervention = effectiveness x reach [194].

Additionally, as aforementioned, effective pharmaceutical options for smoking cessation in the UK are currently limited, as varenicline and bupropion have been unavailable internationally since 2021 [105] and 2022 [106], respectively. Above, Figure 1.2 showed that in England, in 2023, less than 10% of quit attempts used over-the-counter NRT, less than 5% used prescription cessation medications (prescription NRT, varenicline, bupropion), and ~2% used NHS Stop Smoking Services. Approximately 35% of smoking quit attempts used NVPs.

Hence, NVPs should be considered a smoking cessation support option and NVPs should be offered to people who smoke, alongside the other existing cessation options. Based on the evidence currently available, I believe that:

- There is not enough evidence to know whether there are long-term harms from NVP use. It is important to conduct population health surveillance of smoking and NVP use internationally and establish the benefits and harms of using NVPs on health outcomes and other societal outcomes.
- Using NVPs is likely to be substantially less harmful than smoking in the short- to medium-term.
- Those who smoke should quit smoking or switch to using NVPs.

- Those who use NVPs should aim to quit using NVPs if they can, because using NVPs is not risk-free, given the lack of evidence about long-term harms.
- People who do not smoke or use NVPs should not start using NVPs, because using NVPs is not risk-free, given the lack of evidence about long-term harms.
- Health professionals should provide accurate information about NVPs to their patients and recommend NVPs to patients who smoke as a smoking cessation support option.
- Policy-making regarding the regulation and marketing of NVPs should consider the above points.

Role of health professionals

As outlined above, although using cessation support in quit attempts can increase the likelihood of successful smoking cessation, many quit attempts are made without the use of any support. This section introduces the role of health professionals and the primary care setting in smoking cessation.

Primary care

Although all clinicians are advised to offer cessation advice and help to stop smoking – the World Health Organization (WHO) recommends that "cessation support and treatment is provided in all health care settings and by all health care providers" [195] – the primary care setting is often seen as the best place to deliver smoking cessation interventions because primary health care system infrastructure already exists in most countries and has a high population coverage. To exemplify high population coverage, in the UK – where all members of the population are entitled to register with a general practice and care is free-of-charge at the point of access [196] – 98% of the population is registered at a general practice [197]. There were 62,581,556 patients registered at general practices in England on 1 July 2023 [198].

Although the delivery of smoking cessation treatment to individuals who smoke could be considered clinical medicine, an individual-level approach to health [199], interventions delivered by general practitioners (GPs) could also be considered a population-level (public health) approach because of the high number of people GPs have access to. Primary care is regarded as suitable [200,201] for addressing smoking cessation because people who smoke frequently attend, and it is an opportunistic and trustworthy setting [202,203]. People who smoke and have mental health conditions are also in regular contact with their general practice [165], and GPs may be able to play a key role in encouraging and helping patients to stop smoking [164]. A recent study [204] (which is further described in section *VBA – Provision in the 'real world'*, below) demonstrated that smoking cessation treatment provision by GPs in England can have a significant effect on population smoking prevalence.

In the UK, GPs are financially incentivised to perform certain clinical behaviours via the pay-for-performance scheme, Quality and Outcomes Framework (QOF) [201]. The important role of the GP in treating smoking is reflected by the inclusion of smoking indicators in the QOF [201]. Some of the QOF indicators specifically include mental health conditions. See the 2022/23 QOF as an example (Table 1.6).

Table 1.6. Quality and Outcomes Framework 2022/23: Smoking indicators

Indicator	**Points**	**Thresholds**
Records		
SMOK002. The percentage of patients with any or any combination of the following conditions: CHD, PAD, stroke or TIA, hypertension, diabetes, COPD, CKD, asthma, schizophrenia, bipolar affective disorder or other psychoses whose notes record smoking status in the preceding 12 months	25	50-90%
Ongoing management		
SMOK004. The percentage of patients aged 15 or over who are recorded as current smokers who have a record of an offer of support and treatment within the preceding 24 months	12	40-90%
SMOK005. The percentage of patients with any or any combination of the following conditions: CHD, PAD, stroke or TIA, hypertension,	25	56-96%

Indicator	Points	Thresholds
diabetes, COPD, CKD, asthma, schizophrenia, bipolar affective disorder or other psychoses who are recorded as current smokers who have a record of an offer of support and treatment within the preceding 12 months		

Adapted from: [190]

Monitoring smoking and vaping status using electronic health records (EHRs)

Given that smoking is a major risk factor for morbidity and mortality, it is important for governments to monitor population-level smoking prevalence. Monitoring can be achieved using nationally representative surveys or routinely collected patient electronic health record (EHRs).

As mentioned above, in the UK, GPs are financially incentivised to perform certain clinical behaviours via the pay-for-performance scheme, QOF [201]. One of these behaviours is to screen their patients for smoking and record their smoking status. Studies have shown that the QOF has successfully incentivised GPs to increase the recording of smoking status [205,206] (from 2004 onwards) so that by 2008, the prevalence of current smoking recorded in primary care electronic health records was broadly representative of national [196] and regional [207] smoking prevalence (as estimated by national surveys).

However, the situation is different for vaping status. Despite a Royal College of Physicians consultation in 2018 recommending that vaping status (NVP use) is recorded in EHRs [188], GPs are not currently incentivised to record vaping status via the QOF. QOF guidelines (2018/19 [189] – 2022/23 [190]) recommend that NVP users "who have never smoked or given up smoking should be classified as non-smokers or ex-smokers respectively", which may lead to under-recording of NVP use in EHRs. Although vaping status recording is not incentivised, other UK guidance (2020 [191], 2021 [95]) – which was published in response to the EVALI outbreak in 2019 in the US [176] – recommended that health professionals ask about NVP use routinely.

Using EHRs to monitor NVP use trends (prevalence and uptake) amongst adults and adolescents could establish the long-term benefits and harms of NVP use [170]. Currently, there is sparse literature on how health professionals document NVP use in EHRs, and most are from the USA. Existing studies which examined the prevalence of vaping screening (which include documentation of 'never vaping') found low rates. Vaping screening rate in primary care EHRs from the USA was 34.8% in 2021–22 [208]; in an integrated healthcare delivery system in the USA, vaping screening rate was 16% among those aged 18–35 years who never smoked in 2020 [209]; in 2020, 71.4% of 42 Cancer Centres in the USA reported assessing vaping and 14.3% of centres reported assessing vaping at every patient visit [210], and no records documented vaping assessment in 11–17-year-olds in 2016–2017 at four paediatric primary care clinics in Florida, USA [211]). Two of the studies found that patients with documented (current) vaping were more likely to be male, younger (aged 18–44 years), and White [212,213]. Although the prevalence of US patients who have vaping documentation is still low (<1%), it appears to have increased steeply over time: first-time incidence of vaping documentation in an integrated healthcare delivery system in the USA increased from 0.1 per 100,000 patients in 2006 to 95 per 100,000 patients in 2015 [212,214]; and in another integrated healthcare delivery system in the USA, the prevalence of vaping documentation (including 'never vaping') increased from 0.0032% to 0.46% in progress notes (ambulatory and inpatient encounters), and from 0.00071% to 0.22% in tobacco use comments, between 2009–2014 [215].

Similar to population surveys, the rate of current/former vaping was relatively low in non-smoking populations in EHRs; one study found that among patients (aged 18–35 years) who have never smoked who were screened for vaping in 2020, 1.6% were 'current vaping', 1.2% 'former vaping', and 97.2% 'never vaping' [209]. Previous studies also suggest that vaping screening is not currently standardised; patients are more likely to be screened for vaping if they have indicated that they smoke, for example, in primary care EHRs from 2021–2022 in the USA, those documented as currently smoking had 1.32 increased odds of being screened for vaping [208]. Hence, there were high proportions of current smoking and former smoking among those who had vaping documentation: between 2006–2015, of those with any vaping documentation, 57% of patients were currently smoking, 35% formerly smoked, and 8% had never smoked [212,214]; and in another study, among those

with any vaping documentation between 2009–2014 [215], the majority indicated 'current vaping' and 52.4% of progress notes mentioned concurrent smoking.

These findings are similar to the findings of one study from the UK. Gao et al. [216] recently conducted a study investigating the association between smoking, NVP use and severe COVID-19, where they used the QResearch database, which holds anonymised primary care EHRs from ~20% (1,205) general practices in England. They found that among the ≥20-year-old patients who were registered with a GP between January 2020 and April 2020, 69,047 (0.9%) out of the 8,256,161 patients were recorded as using NVPs [216]. Of these patients, 4.7% (n=3,251) were recorded as never smoking, 51.1% (n=35,267) were recorded as formerly smoking, and 44.2% (n=30,529) were recorded as currently smoking [216].

Some of the studies from the USA suggested that some patients are using vaping for smoking cessation. For example, one study found that among those with any vaping documentation between 2009 and 2014 [215], 27.6% of progress notes and 15.0% of tobacco use comments indicated vaping for tobacco cessation. Lastly, two studies from the USA examined transitions between current vaping and smoking status, finding that smoking cessation was more likely among those who received 'current vaping' documentation compared to those who were not vaping: one study [214] using 2012–2015 EHRs from an integrated healthcare delivery system in the USA found that among those who currently smoked, 23% of those currently vaping reported quitting smoking during the following year, compared to 19% who had smoked only; and the other study [213] using EHRs from 2018–2020 from a tertiary care medical centre in the USA found that the proportion of those who both vaped and smoked ranged between 0.8% and 2.3% in their four outpatient cohorts, and among those who smoked, the prevalence of smoking cessation at 12-months was significantly higher among those who had smoked and vaped (20.8%), compared to among those who had smoked only (16.8%) [213].

To our knowledge, there have been no studies specifically investigating health professionals' documentation of vaping in the UK and the extent to which vaping has been recorded over time in UK EHRs is not known. The use of existing medical codes to record vaping is hypothesised to be suboptimal [217].

Very Brief Advice (VBA, 3As) – What is it?

Clinical guidelines recommend that health professionals address their patients' tobacco use by giving 'brief advice' to all patients [218].

The first model for 'brief advice' was initially the '5As' [204,219]:

- 'Ask' about tobacco use,
- 'Advise' to quit,
- 'Assess' willingness to make a quit attempt,
- 'Assist' in quit attempt,
- 'Arrange' follow-up.

However, assessing the willingness/motivation of a person who smokes to quit originated from the transtheoretical (stage of change) model [220]. Studies have since critiqued the model [221]. Aveyard et al. [222] conducted a meta-analysis of RCTs which had minimal (less than 10 minutes) of physician advice as the intervention. In the studies they included, physicians did not assess willingness to quit prior to offering assistance. They found that if 20% of a population of people who smoke attempt a quit attempt in the 6 months following a GP appointment, if the GP offers advice to stop smoking, this would increase to 25%, and if GPs offer assistance to stop as well, this would increase to 35% [222]. Given that willingness to quit was not assessed for these patients, Aveyard et al. [222] argued that 'assess' (Step 3) should not feature in the physician intervention model, because if the 5As model is followed, those patients who are assessed as 'not willing to stop smoking' will not receive assistance to stop smoking. This recommendation was supported by later studies which found that motivation or willingness to stop smoking is not a predictor of cessation success (e.g., [223]). Hence, in some countries now (such as, the UK), the '3As' or 'Very Brief Advice' (VBA) model is recommended [224]. Table 1.7 shows a comparison of the steps involved in the 5As and 3As/Very Brief Advice model for delivering 'brief advice' about smoking cessation to people who smoke.

Table 1.7. 5As and 3As/Very Brief Advice (VBA)

5As	**Very Brief Advice (VBA)**
Ask about tobacco use	Ask about current/past smoking behaviour
Advise to quit	Advise about the consequences of smoking and smoking cessation
Assess willingness to make a quit attempt	
Assist in quit attempt (provide general assistance, prescribe cessation medications, set quit date, provide counselling, provide self-help materials)	Act: offer cessation medication and support wherever it is locally available. Provide options for later/additional support.
Arrange follow-up appointment to address smoking	

VBA – Efficacy in RCTs

RCTs where the intervention was physicians delivering 'brief advice' showed that a higher proportion of participants in the intervention group made a quit attempt and were smoking abstinent at ≥6 months. The 'Physician advice for smoking cessation' Cochrane review [225] has shown that physician advice to promote smoking cessation is efficacious in increasing ≥6-month smoking abstinence, irrespective of initial interest in quitting among participants. RCTs of brief advice vs no advice (or usual care) detected a significant increase in quit rate, RR: 1.66, 95% CI: 1.42–1.94. Stead et al. commented that "assuming an unassisted quit rate of 2 to 3%, a brief advice intervention can increase quitting by a further 1 to 3%" [225].

To examine the different components of the brief advice intervention on quit attempt rate and cessation rate, Aveyard et al. [222] conducted a meta-analysis of the RCTs in the Cochrane review [225]. The majority (10 out of 13) of the RCTs which had minimal (less than 10 minutes of) physician advice as the intervention that Aveyard et al.'s [222] meta-analysis included were set in a primary care (family medicine, general practice) setting. Aveyard et al. [222] found strong evidence that health professionals can trigger patients who smoke to

make a quit attempt. The effect of advice to quit (vs no intervention) increased the frequency of quit attempts (RR: 1.24, 95% CI: 1.16–1.33). The effect of offering assistance to quit (vs no intervention) was examined: offering behavioural assistance to quit doubled attempts to stop (RR: 2.17, 95% CI: 1.52–3.11); offering NRT increased quit attempts (RR: 1.68, 95% CI: 1.48–1.89). When directly comparing offering advice to quit and offering assistance, offering assistance generated more quit attempts than giving advice to quit (RR: 1.69, 95% CI: 1.24–2.31 for behavioural support and 1.39, 95% CI: 1.25–1.54 for offering NRT). Similarly, Aveyard et al.'s [222] meta-analysis found that effect of advice to quit (vs no intervention) increased the ≥6-month smoking abstinence rate, RR: 1.47, 95% CI: 1.24–1.75; and offering NRT (assistance) (vs no intervention) increased smoking abstinence, RR: 1.49, 95% CI: 1.17–1.89; however, offering behavioural assistance (vs no intervention) did not increase smoking abstinence, RR: 5.24, 95% CI: 0.62–44.14.

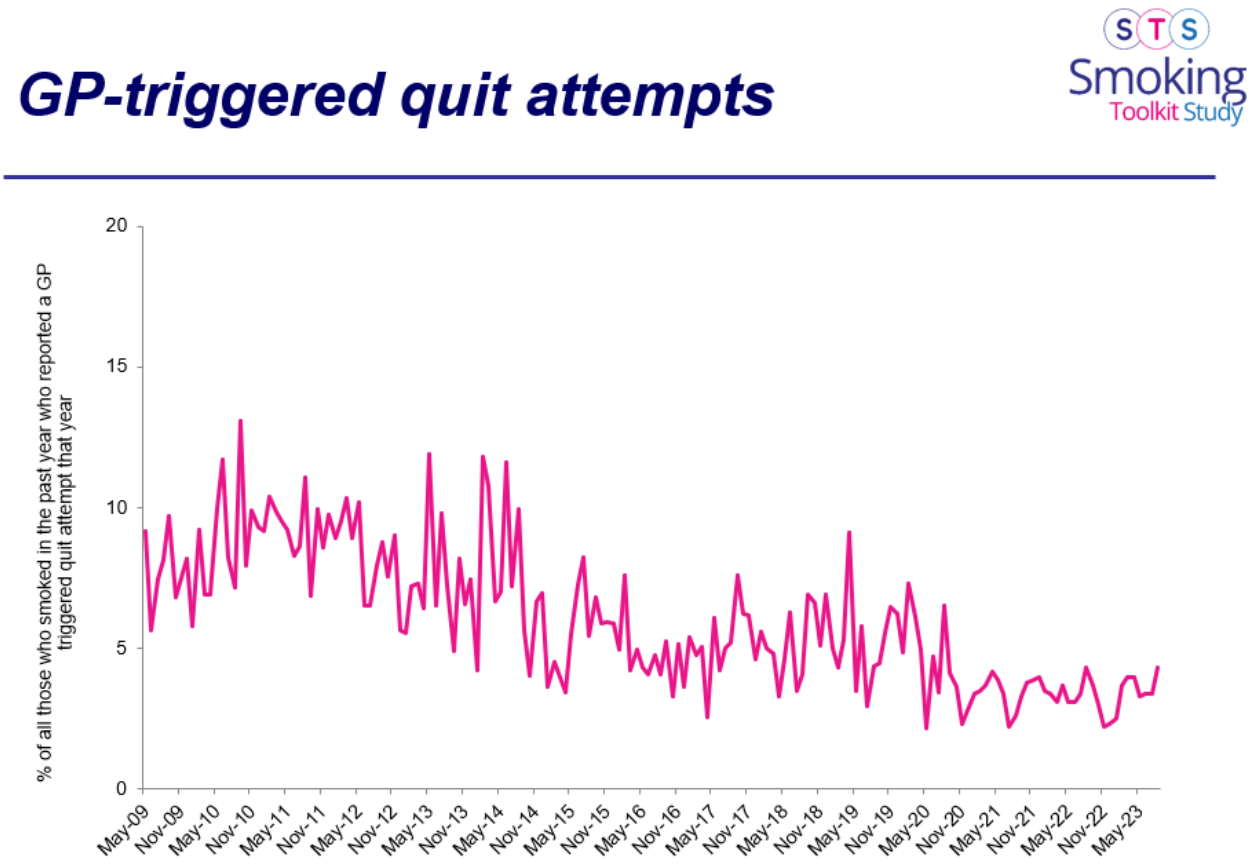
VBA – Effectiveness in the 'real world'

Quit attempts

One of the top four most commonly cited triggers among people who have smoked in the past year and attempted to quit is advice from a health professional [226,227] – the other prevalent prompts were: future health concerns, current health concerns, and the cost of smoking [227]. Ussher et al. [226] found that of ≥16-year-olds who had made at least one smoking quit attempt in the last 12 months between 2009 and 2012, from the Smoking Toolkit Study, almost a quarter (24.5%) reported that advice from a health professional was a contributing prompt to their most recent quit attempt. The Smoking Toolkit Study survey measures the proportion of GP-triggered quit attempts in the last 12 months of ≥16-year-olds who smoke in England [26]. The proportion fluctuates considerably, but between 2009 and 2023, between 2.2 and 13.1% of quit attempts are reported to have been triggered by their GPs [26]; see Figure 1.3. Brose et al. [84], using Smoking Toolkit Study survey data collected between January 2016 and December 2017 from ≥16-year-olds in England, found that among people (aged ≥16 years) who had made a quit attempt in the past year, overall, approximately 13.5% reported that receiving advice from a health professional was a

contributing trigger that prompted their most recent quit attempt, and there was no significant difference between those with and without mental health conditions.

Figure 1.3. Proportion of smoking quit attempts triggered by health professional advice in England



Reproduced from [26]

Using Canadian (Ontario Tobacco Survey) data of ≥18-year-olds collected between 2005–2011, Zhang et al. [228] found that those who received advice to quit smoking from a health professional were more likely to make a quit attempt compared to those who did not receive advice, 28.1% vs 23.8%, $p<0.001$, OR: 1.25, 95% CI: 1.10–1.41.

In England, Jackson et al. [229] used 2016–2019 Smoking Toolkit Study survey responses from ≥16-year-olds to find that of those who smoked and reported having visited their GP in the last 12 months, those who were offered any advice or offer of support were significantly

more likely to report a quit attempt than those who were not – received any advice: OR: 1.95, 95% CI: 1.75–2.17; offered any support: OR: 1.52, 95% CI: 1.30–1.76; offered prescription medication: OR: 2.52, 95% CI: 2.04–3.12; recommended stop smoking service: OR: 1.39, 95% CI: 1.17–1.66; recommended NVP: OR: 1.80, 95% CI: 1.35–2.41.

Using 2009–2013 Global Adult Tobacco Survey from Romania, Turkey, Ukraine, Poland, Greece and Russia, Cakir et al. [230] found that, of those who visited a health professional in the past 12 months and reported that their doctor advised them on stopping smoking, 45.4% had made a smoking quit attempt over the past 12 months, compared to 38.9% of those who received no advice, OR: 1.31, 95% CI: 1.14–1.50.

Cessation option use and quit success

Zhang et al. [228] also found that those who received advice to quit smoking from a health professional (21%) were more likely to use cessation medications, compared to those who did not receive advice (13%), $p<0.001$. They found that those who received advice to quit smoking from a health professional were more likely to be quit smoking over >6 months, compared to those who received no advice, 4.1% vs 3.5%, respectively (adjusted OR: 1.49, 95% CI: 1.10–2.02). However, Zhang et al.'s mediation analyses found that 38% of the impact on long-term quitting was due to using cessation medications.

Similarly, Jackson et al. [229] found that of those who smoked and reported having visited their GP in the last 12 months, due to low cessation prevalence overall (only 5.4% had reported being smoking abstinent at the time of the survey), only the offer of prescription cessation medication was significantly associated with increased odds of cessation, OR: 1.73, 95% CI: 1.13–2.66 – the associations between other forms of advice and smoking cessation were inconclusive.

Ussher et al. [226] also found an effect of health professional advice on using cessation aids during their most recent quit attempt; those who reported health professional advice as a contributing prompt in their most recent quit attempt were more likely to make an assisted quit attempt (adjusted OR: 3.64, 95% CI: 3.14–4.22). However, this study found that health professional advice was not associated with higher quit success.

Summary

Several observational studies found that health professional advice can increase the rate of smoking quit attempts, and some demonstrated that it can increase the likelihood of using cessation aids in quit attempts. However, not all studies demonstrated a significant positive effect on smoking cessation. Some researchers have proposed that the effect of health professional advice may be primarily in prompting quit attempts [133] and increasing the chance that they will involve evidence-based treatment, rather than independently aiding those attempts [226].

Discrepancies between RCT findings and observational studies may be due to the general population of people who smoke in the 'real world' differing from people who participate in RCTs, or due to observational studies measuring the independent variable (health professional advice as a trigger for quit attempts) differently – for example, Ussher et al. [226] asked survey respondents 'Which of the following do you think contributed to you making the most recent quit attempt?' and to select as many options as they considered to be appropriate from the list; while Vangeli et al. [227] asked "What finally triggered your most recent quit attempt?" and respondents could only choose one trigger.

VBA – Provision in the 'real world'

Despite widespread *evidence*-based recommendations and guidelines, internationally, there is an '*evidence-practice gap*' in the rates at which healthcare professionals screen for smoking and offer support (i.e., provide VBA) in clinical *practice* in the 'real world'.

General population

For example, an international systematic review of studies published between 2000 and 2015 which investigated self-reported smoking cessation counselling by primary care

physicians in 17 countries found that the following proportion of primary care physicians reported carrying out each step of the 5As [231]:

- 'Ask': 65% (range: 7–100%),
- 'Advise': 63% (range: 13–99%),
- 'Assess': 36% (range: 11–72%),
- 'Assist': 44% (range: 2–98%),
- 'Arrange': 22% (range: 2–54%).

Using ITC Project survey data from 2016 from eight countries (England, Germany, Greece, Hungary, the Netherlands, Poland, Romania and Spain), Hummel et al. [56] calculated the proportion of ≥18-year-olds who were currently smoking and visited a health professional in the last 12 months and received advice about quitting smoking. The highest proportion was in Romania (56.5%), the lowest (21.8%) in the Netherlands, and in England it was 38.3%. A different study using 2016 ITC Project survey data from Australia, Canada, England and the US by Gravely et al. [232] found that among those who were currently smoking and visited a health professional in the last 12 months, 47.5% reported receiving advice to quit smoking. Receiving advice to quit was most common in the US (58.3%), followed by Australia (50.4%), then Canada (47.1%), then England (39.5%) [232].

Using more recent data (2016–2019 Smoking Toolkit Study survey), Jackson et al. [229] found that among ≥16-year-olds in England who smoked and reported having visited their GP in the last 12 months, 47.2% reported receiving any advice on smoking. Less than a third (30.1%) reported being offered any cessation support: 16.5% were offered referral to a Stop Smoking Service, and 8.1% were prescribed smoking cessation medication (varenicline, bupropion or prescription NRT) [229].

In the UK, the charity Cancer Research UK [204] generated some models which showed that if 2010–2017 VBA rate data (where only 53% of GPs and practice nurses frequently complete all three steps of VBA for smoking cessation) are extrapolated as being 'usual care' in primary care, adult smoking prevalence in the year 2030 is predicted to be 8.7% (+/- 0.1%). However, if GPs were to intervene at least once a year with all patients who smoke who attended an appointment by referring these patients to a Stop Smoking Service and

offering a prescription for a cessation medication, national smoking prevalence in 2030 in England would be 6.2% (+/- 0.1%) in 2030.

The proportion whose health professional talked to people who smoke about NVPs also varies widely. For example, in Hummel et al.'s [56] study using 2016 survey data, among those who smoked currently and visited a health professional in the last 12 months, health professionals discussing NVPs was reported most often in Hungary (9.8%) and least often in Germany (0.6%), while in England it was 6.7%. Among all who visited a health professional in the past year in Gravely et al.'s [232] study (2016 survey of Australia, Canada, England, USA), 6.8% reported discussing NVPs with their health professional – 8.8% in the US, 7.8% in Canada, 6.2% in England, and 4.3% in Canada. Using more recent survey data, Cho et al. [233] used longitudinal ITC Project survey data from Australia, Canada, England and the US to find that the prevalence of health professionals discussing NVPs with their patients remained relatively unchanged between 2016, 2018 and 2020 – in 2020, it was 2.0% in Australia, 3.9% in Canada, 4.1% in England, and 6.2% in the USA.

Some studies have specifically examined whether HPs are positive or negative about using NVPs as a smoking cessation support option. In Gravely et al.'s [232] study, among those who had received smoking cessation advice, 37.8% received advice to use an NVP, 20.9% were advised against NVP use, and 41.3% of health professionals remained neutral. Using more recent data, Cho et al. [233] found that among respondents who discussed NVPs with their HPs, the prevalence of receiving NVP recommendations from HPs between 2016 and 2020 increased significantly in England (55.7% in 2020) but did not change significantly in Australia (20.2% in 2020), Canada (25.7% in 2020), or the US (14.7% in 2020). Similarly, Gallegos-Carrillo et al. [234] used 2018–2019 survey data from Mexican adults (≥18-year-olds) who smoked, finding that 33.7% of those who visited a health professional in the last 4 months reported discussing NVPs with their health professional; and of those who discussed NVPs with their health professional, 46% reported that their health professional recommended their use.

However, it is important to consider that the overall proportion of people who smoke who visit their health professional and subsequently receive a positive recommendation regarding NVPs is quite low. In Gravely et al.'s [232] study, among all who visited a health

professional in the past year, only 2.1% reported receiving a positive recommendation to use NVPs from their HP – 3.2% in the US, 2.4% in Canada, 1.9% in England, and 1.1% in Canada. Similarly, Jackson et al. [229] (using 2016–2019 England survey data) found that only 3.7% of those who smoke who had visited their GP in the last 12 months had been recommended to use an NVP.

People with mental health conditions

In England, NHS Digital leads data collection about physical health checks for people with severe mental illness – they found that in 2021, 59.8% of people with serious mental illness in England had a physical health check that mentioned smoking [235], but there was no information available about whether a smoking cessation intervention was delivered in these health checks. Some research studies have specifically investigated the provision of VBA to people who smoke with and without mental health conditions.

For example, a systematic review by Mitchell et al. [236] included seven studies (published up to 2014) that compared receipt of smoking cessation advice between people with and without a mental illness. They found that overall, people with mental illness (including serious mental illness) and people in the general population were broadly offered comparable rates of smoking cessation advice, RR: 1.02, 95% CI: 0.94–1.11. Subgroup analyses found that people with serious mental illness (schizophrenia, bipolar disorders) were offered comparable rates (RR: 1.10, 95% CI: 0.98–1.23), while people with non-serious mental illness (e.g., depression, anxiety) were offered slightly higher rates of smoking cessation advice rates (RR: 1.16, 95% CI: 1.04–1.30).

The TABS study mentioned above by Morris et al. [66] found that those who reported mental health limitations were more likely to report receiving advice to quit in the last 12 months, compared to those without limitations (81.6% vs 60.3%, $p<0.05$).

A study [165] using 2009–2010 UK primary care electronic health records showed that 33.4% (95% CI: 33.3–33.6%) of ≥16-year-old patients who smoked without a mental health condition had a record of having received cessation advice. In contrast, 50.6% (95% CI: 50.0–51.2%) of those with a diagnosis of one or more mental health conditions had a record of

cessation advice and 49.3% (95% CI: 49.0–49.7%), of those prescribed one or more psychoactive medications had a record of cessation advice. Patients with a diagnosis of mental health conditions or psychoactive medication prescriptions had a higher mean number of consultations per year, 10.00 and 9.80, respectively, than those without these conditions (3.89). However, notably, on average, cessation advice was recorded in 7.90% of consultations in those with a diagnosis of mental health condition, in 8.16% of consultations in those with a psychoactive medication prescription, compared to 12.30% of consultations in those without either indicator of poor mental health. Therefore, although patients who smoke with mental health conditions were more likely to have received cessation advice (compared to those with no mental health condition), given equal opportunity to do so, GPs appear less likely to intervene with people who smoke with indicators of poor mental health compared to those without.

In England, 2012 survey participants who self-reported depression/anxiety were more likely to have seen their GP in the past year than those without (83.4% vs 66.1%) [162]. Of those who had seen their GP in the past year, 28.3% of those who had depression/anxiety were not asked about smoking, compared to 26.3% of those with no depression/anxiety – these proportions were not significantly different between the two groups. However, those with depression/anxiety were more likely to have been asked about smoking, to receive advice and to receive an offer of support (42.2%), compared to 38.2% of those with no depression/anxiety, OR: 1.50, 95% CI: 1.05–2.13; and more likely to have been advised to try a stop smoking advisor/group (20.3% vs 14.7%, OR: 1.69, 95% CI: 1.13–2.54).

In 2007–2014 primary care electronic health record data from England [164], overall, >70% of ≥18-year-old patients who smoked received advice to quit smoking within 6 months of their smoking status being updated, the proportion reaching 80% among those with a history of serious mental illness. The proportion of those with depression and no history of serious mental illness or depression who received cessation advice increased steeply between 2011 and 2012 by nearly 10% points, to 80.6% in those with depression in 2012, and 76.6% in those without mental illness. The proportion of those with a history of serious mental illness who received cessation advice was consistently higher than the other two groups between 2007 and 2014, it being 83.8% in 2012 – however, the gap between the three groups reduced after 2012.

Gravely et al. [232], using 2016 survey data from Australia, Canada, England and the US, found no difference in the proportion of people who smoke with and without self-reported current diagnosis/treatment of depression or anxiety who had discussions with a HP about NVPs – depression: 3.0% of those who visited a HP in the last year talked to their HP about NVPs vs no depression: 2.6% (OR: 1.15, 95% CI: 0.82–1.62); and anxiety: 2.1% of those who visited a HP in the last year talked to their HP about NVPs vs no anxiety: 3.0% (OR: 0.69, 95% CI: 0.48–1.00). However, they found that fewer people who smoke with anxiety (who visited a HP in the last year) (0.2%) were recommended to use an NVP from their HPs, compared to people who smoke without anxiety (0.5%), OR: 0.48, 95% CI: 0.29–0.81. For those with depression, the proportions recommended to use an NVP from their HPs were similar for those with depression (0.5%) and those without depression (0.4%), OR: 1.40, 95% CI: 0.87–2.26.

Summary

For people who smoke in the general population, it appears that health professionals have increased the rate at which they ask about their smoking status and advise them to quit smoking. However, the proportion of health professionals who offer cessation support options, and discuss/recommend NVPs, is low, overall. It must be noted that not many surveys ask about the offer of cessation support to quit smoking.

Although some studies found that the overall proportion of people who smoke and have mental health conditions with cessation advice is higher than people who do not have mental health conditions, the one study [165] which was able to adjust for the number of consultations patients have (in a given time period) found that because the proportion of consultations in which cessation advice was given was lower in patients with mental health conditions, it suggests that given equal opportunity to do so, GPs appear less likely to intervene with people who smoke with indicators of poor mental health compared to those without. The proportion who were offered cessation support options was low in this patient population, too. Again, there were fewer studies which asked about offer of support to quit smoking, and we only identified one study [232] which asked about health professionals recommending NVPs to people who smoke and have mental health conditions.

Increasing the provision of VBA

Given that the rate at which health professionals screen for smoking and offer support (i.e., provide VBA) is suboptimal, it is important to assess if there are any interventions ('implementation strategies' [237,238]) which can increase the provision of VBA in primary care settings.

A recent Cochrane review [239] evaluated randomised and cluster-randomised controlled trials of strategies designed to increase the rate and quality of delivery of the 5As/VBA to adult primary healthcare patients, when delivered in addition to 'standard' cessation support or 'usual care'. They categorised the interventions as single-component and multi-component. Their primary outcome measure was smoking abstinence at long-term follow-up (at least 6 months), and their secondary outcomes were practitioner performance in the 5As and participant quit attempts. The systematic review included 81 studies – all these measured the primary outcomes, but only 25 reported on number of quit attempts made by study participants, and only 21 reported on provider performance outcomes in a way that allowed between-group comparison.

For the single-component interventions, for the primary outcome (smoking abstinence at ≥6-month follow-up), Lindson et al. [239] found moderate-certainty evidence for adjunctive counselling (counselling delivered by a health professional other than the primary care physician) (RR: 1.43, 95% CI: 1.15–1.78, moderate certainty evidence), cost-free medications (RR: 1.36, 95% CI: 1.05–1.76, moderate certainty evidence), and tailored print materials (RR: 1.29, 95% CI: 1.04–1.56, moderate certainty evidence) increasing quit rates.

They found no clear evidence for biomedical feedback (RR: 1.07, 95% CI: 0.81–1.41, low certainty evidence), provider training (RR: 1.10, 95% CI: 0.85–1.41, low certainty evidence), or provider incentives (RR: 1.14, 95% CI: 0.97–1.34, very low certainty evidence) increasing quit rates [239].

For the multi-component interventions, for the primary outcome, Lindson et al. [239] found some evidence that (i) adjunctive counselling combined with cost-free medications (RR: 3.09, 95% CI: 1.13–8.44, 3 RCTs), and (ii) adjunctive counselling combined with provider

training (RR: 2.66, 95% CI: 1.27–5.57, 6 RCTs), and (iii) provider training combined with flow sheets to aid physician decision-making (RR: 1.70, 95% CI: 1.27–2.27, 3 RCTs), improved quit rates. However, they found no clear evidence that (iv) provider training combined with outreach facilitation (RR: 1.55, 95% CI: 0.95–2.52, 2 RCTs) improved quit rates.

For the secondary outcomes (practitioner performance in the 5As and participant quit attempts), for the single-component interventions, Lindson et al. [239] found some evidence that adjunctive counselling increased cessation medication provision, quit attempts, and arranging patient follow-up by physicians, but evidence for cessation advice provision, offering self-help materials or counselling or assisting in setting a quit date were mixed. For cost-free medications, they found that these increased quit attempts. For tailored print materials, they found inconclusive results for increasing quit attempts. For provider training, they found evidence that this increased smoking status recording, cessation advice provision, cessation counselling, and offering self-help materials, but they found mixed results for participants setting a quit date, cessation medication provision, quit attempts, and arranging patient follow-up.

For the secondary outcomes for the multi-component interventions, Lindson et al. [239] found that provider training combined with flow sheets could increase the rate that physicians arranged follow-up for participants, but the evidence for smoking status recording and cessation medication provision was inconclusive. Lastly, provider training combined with outreach facilitation had some beneficial effect on participants setting a quit date, self-help material provision, and arranging patient follow-up, but the evidence was inconclusive for recording smoking status, providing cessation medication, and quit attempts.

It is important to note here that, again, these RCT efficacy estimates may not translate to effectiveness in the ‘real world’. Implementation scientists believe that when an intervention is being tested in a trial setting, because it usually involves “research resources which are separate from the clinical infrastructure and which are externally funded, time-limited, and evanescent at the end of the protocol”, even if that intervention is demonstrated to be efficacious, if that intervention is subsequently implemented in a ‘real world’ setting unassisted (without the research resources), it is not guaranteed to be

effective [240]. (I expand on implementation science concepts in *Chapter 2*.) The Cochrane review [239] did not include observational studies which evaluate implementation strategies enacted without researcher input, in the 'real world', as a national or state-wide policy or change to clinical guidelines.

Thesis aim and objectives

The overarching aim of this thesis is to contribute to the evidence base regarding how the provision and uptake of smoking cessation support options (including NVPs) in the UK could be improved, to further reduce the prevalence of smoking and meet national smoke-free targets (≤5% adult smoking prevalence), including reducing the prevalence of smoking in people with mental health conditions.

Based on gaps in the evidence, four objectives were developed. These four objectives were addressed through four studies presented in *Chapters 3, 4, 5* and *6*.

Objective 1 – Strategies to increase smoking cessation support provision

It is important to assess what interventions can increase the provision of VBA in primary care setting in the 'real world' because this has the potential to significantly increase smoking cessation rates and contribute to a decrease in population-level smoking prevalence.

As identified above (in *Increasing the provision of VBA*), at the time of my PhD, to our knowledge, there was no systematic summary of observational studies which evaluated interventions which were implemented on a national or state-wide scale in the 'real world' without researcher input, which aimed to increase the provision of VBA or smoking cessation treatment in primary care. The study I conducted sought to complement the Cochrane systematic review of RCTs [239].

Objective 1:
Review the evidence for the effectiveness of interventions (implementation strategies),

which were implemented on a national or state-wide scale, aiming to increase the provision of smoking cessation treatment in primary care.

Objective 2 – Vaping recording in electronic health records

It is important to assess the current utility of population-level EHR vaping status data because EHRs could be used to investigate the long-term health effects and smoking cessation outcomes of vaping.

As identified above (in *Monitoring smoking and vaping status using electronic health records*), at the time of my PhD, to our knowledge, there was sparse literature on how health professionals are documenting NVP use in EHRs. We found no studies that specifically investigated how health professionals are documenting NVP use in EHRs in the UK.

Objective 2:
Describe and characterise the extent to which NVP use has been recorded in primary care electronic health records in the UK.

Objective 3 – Mental health and health professional interactions

Given that smoking prevalence is higher in those with mental health conditions compared to those without, it is important to assess whether health professionals are providing VBA to people who smoke with mental health conditions, including discussing NVPs with them as a viable smoking cessation support option.

As identified above (in *VBA – Provision in the 'real world': People with mental health conditions*), at the time of my PhD, to our knowledge, there were no papers published using post-2016 data to examine if there is a difference between people who smoke with and without mental health conditions and their receipt of smoking cessation advice and advice about NVPs.

Objective 3:
Examine interactions between health professionals and people who smoke with and without common mental health conditions (depression and/or anxiety), about smoking cessation and nicotine vaping products.

Objective 4 – Mental health and smoking cessation support option use

Given that smoking prevalence is higher in those who have mental health conditions than those who do not, because using cessation support in quit attempts can increase the likelihood of smoking cessation success, it is important to assess whether people with mental health conditions are using cessation support in their smoking quit attempts.

As identified above (in *Smoking cessation support options – Rate of use in the 'real world': People with mental health conditions*), at the time of my PhD, to our knowledge, there were no papers published using post-2017 data to examine if there is a difference between people who smoke with and without mental health conditions and what cessation support options they use in smoking quit attempts.

Objective 4:
Assess cessation aid utilisation by people who smoke with and without common mental health conditions (depression and/or anxiety) used in their last attempt to quit smoking.

Chapter 2 – Methods

Preface

Chapter 1 identified some evidence gaps from which four objectives were developed. These four objectives were addressed through four studies presented in *Chapters 3*, *4*, *5* and *6*, using various research designs and methods.

As this is a thesis incorporating publications, *Chapters 3* to *6* each present a separate study and their methodology is described in the separate chapters. This chapter, *Chapter 2*, provides a rationale for the methods chosen and some additional detail about the research methods and the datasets that were used for the studies.

Study 1: Systematic Review

Chapter 3 describes a systematic review of 49 studies.

Rationale for study method

As discussed in *Chapter 1*, a recent Cochrane systematic review [239] evaluated randomised and cluster-randomised controlled trials of implementation strategies designed to increase the rate and quality of delivery of the 5As/VBA to adult primary health patients, when delivered in addition to 'standard' cessation support or 'usual care'. However, the Cochrane review did not include observational studies.

Hence, my review sought to focus on studies which evaluated the impact of implementation strategies enacted without researcher input, in the 'real world', as a national or state-wide policy or change to clinical guidelines. My review sought to complement the Cochrane review, and identify any differences in the findings – which may be due to barriers to implementation in the real world – that may help explain the evidence-practice gap.

My supervisors and I concluded that the systematic review methodology was the most appropriate to use for my review, as systematic searching enables the identification of relevant papers, reduces researcher bias, and allows for the critical appraisal of the included studies – the latter was pertinent as observational studies are at risk of more confounders than clinical trials. To develop my systematic review protocol, I consulted the Cochrane Handbook for Systematic Reviews of Interventions [241].

Development of the systematic review protocol

Refining the scope of the systematic review

In order to refine the research questions of my systematic review, I contacted one of the authors of the relevant Cochrane systematic review [239] which was in progress at the time. Dr Nicola Lindson provided information about the scope of their review and clarified that observational studies were not to be included in the Cochrane review. Dr Lindson also provided me with the search strategy they used for the Cochrane systematic review (including appropriate synonyms for tobacco and smoking search terms commonly used in the tobacco control field) and the key terms and keywords they developed for 'primary care'. I also spoke to Prof Tim Coleman (GP and a Professor in Primary Care at the University of Nottingham) to get his general perspective on the provision of smoking cessation treatment in primary care. Lastly, I spoke to Dr Sarah Knowles (Research Fellow in health services research at the University of York, specialising in mental health and implementation science and has worked on studies investigating smoking cessation interventions for service users with serious mental illness) about the issue of introducing new interventions into the clinic and broader implementation science concepts. These discussions led to me focussing my review on observational studies which evaluated an intervention ('implementation strategy') which was enacted on a national or state-wide scale and aimed to increase smoking cessation treatment provision in the primary care setting (e.g. a national policy or a clinical guideline change), in order to: identify what strategies have been implemented in a 'real world' setting; which were effective; which were cost-effective; and to examine the explanations proposed about why they were effective or not.

Implementation science concepts

Very Brief Advice (VBA) is a clinical intervention or practice which is evidence-based, hence, it can be considered an evidence-based practice (EBP). Implementation science argues that focused efforts are required to facilitate the movement of EBPs (i.e., VBA) into clinical practice because the contexts that the EBP aims to enter are complex and variable [240]. Implementation research "investigates how best to help people or places do the EBP" [238].

'Implementation strategies' are "methods or techniques used to enhance the adoption, implementation, and sustainability of a clinical program or practice" [237,238]. Two examples of an implementation strategy are: "remind clinicians" and "fund and contract for the clinical innovation" [242]. The Expert Recommendations for Implementing Change (ERIC) programme defined 73 distinct 'implementation strategy' categories, grouped into nine implementation strategy domains [242,243]. The nine domains are:

- Domain 1. Use of evaluative and iterative strategies
- Domain 2. Provide interactive assistance
- Domain 3. Adapt and tailor to context
- Domain 4. Develop stakeholder inter-relationships
- Domain 5. Train and educate stakeholders
- Domain 6. Support clinicians
- Domain 7. Engage consumers
- Domain 8. Utilize financial strategies
- Domain 9. Change infrastructure

Implementation outcomes are usually "how much and how well people or places do the EBP" [238]. The outcomes of implementation studies may be on the level of the "patient, provider, clinic, facility, or system" [240]. For example, implementation studies may have practitioner-level outcomes that measure the rate at which clinicians perform a particular clinical behaviour; and they may have patient-level outcomes that relate to a particular behaviour which can lead to the health outcome, or the health outcome itself. For example,

in the field of smoking cessation, practitioner-level outcomes may be around the performance of the 5As/3As/VBA – for example, a clinician recording the smoking status of a patient (measured, for example, by clinicians logging in patient files the smoking status of a patient) would be the rate of compliance with the 'Ask' aspect of the EBP (5As/3As/VBA). In smoking cessation, patient-level outcomes may be a behaviour: whether a patient has made a smoking quit attempt, filled a prescription for smoking cessation medication, or attended smoking cessation behavioural counselling sessions. The outcome may be on the health outcome level: patient smoking abstinence defined over a period of time (usually 3-, 6-, or 12-months).

For my systematic review, I used some concepts and frameworks from the field of implementation science:

- Interventions in the studies included in my review were mapped to the key 'implementation strategy' they involved (Appendix B.2).

- The quantitative outcome measures (practitioner-level and patient-level) were linked to the possible 'implementation outcomes' outlined above.

- Explanations for and against effectiveness in the included studies were mapped to determinants in the Consolidated Framework for Implementation Research (CFIR) [244] – which is a framework which can be used alongside ERIC programme's implementation strategy categories (Appendix B.7).

Developing the search strategy

For my review, I chose to search a variety of databases in order to capture as much of the existing literature as possible. My search included medical-focussed databases, social policy/social science-focussed databases, and grey literature sources.

When developing my search strategy, I trialled various iterations to see if the search output would include key papers previously identified which were relevant to include in my review, such as [245,246]. The key search concepts were: 'smoking' and 'smoking cessation' and

'primary care'. Keywords and subject headings (where available) were used. It is challenging to identify observational study designs in literature databases because studies included in databases are indexed by study type and may be inaccurate [247]; when iterating my search strategy, I trialled using the 'observational study' filter that was available in some of the databases but the search output did not include my key papers of interest. Therefore, I decided not to use a 'study type' filter and instead decided to manually exclude studies that were not observational studies during the screening stage.

Study 2: CPRD Primary Care Electronic Health Records

Chapter 4 describes findings from a secondary analysis of electronic health record data from general practices in the UK which contribute to the Clinical Practice Research Datalink (CPRD) [248]. All patients (aged ≥18 years at index date) who received a medical code related to vaping at any point ('incidence') from 1 September 2006 to 31 March 2022 were extracted from the CPRD GOLD April 2023 build and the CPRD Aurum March 2023 build.

Rationale for study method

As discussed in *Chapter 1*, there is not enough evidence to know whether there are long-term harms from NVP use. If high-quality population health surveillance of smoking and NVP use existed, such a dataset might be employed to establish the benefits and harms of using NVPs on health outcomes. Although population surveys can generate NVP use prevalence estimates [172,249,250], these are often cross-sectional, under-sample vulnerable populations, have short-term follow-up, or do not enquire extensively about health outcomes. EHRs could help identify the long-term wider health benefits and harms of NVP use, pending NVP use data completeness. EHRs have several advantages, such as: large samples; long-term longitudinal routine data collection; detailed demographic, clinical and therapeutic information about each patient; and linkage to additional sources, including death and disease registries, and hospital data [251].

Currently, there is sparse literature on how health professionals are documenting NVP use in EHRs and all are from the USA. We found no studies that specifically investigated how health professionals are documenting NVP use in EHRs in the UK. Hence, I aimed to conduct a descriptive analysis of patients aged ≥18 years in Clinical Practice Research Datalink (CPRD), which contains primary care electronic health records of 25% of the UK population. Using descriptive statistics, I sought to report the frequency of vaping codes; their distribution by patient age, gender, and ethnicity; trends over time in first-time incidence of vaping codes between 2006–2022; and transitions in patient smoking status.

Development of the study design

Study protocol

I did not pre-register an analysis plan for this study because this was an exploratory study of CPRD using descriptive statistics, and I did not propose to perform any hypothesis testing.

King's College London holds a Multi-Study Licence for access to CPRD data, and the licence is managed by Professor Martin Gulliford and Dr Alexandru Dregan. I completed a study protocol to obtain ethical approval from the organisation that manages CPRD data. Further discussion of the roles of my collaborators is provided in *Chapter 4*.

Electronic health records training

In order to familiarise myself with the CPRD dataset, I completed the online CPRD GOLD training module [252] (https://cprd.com/using-cprd-primary-care-data) and I read the Data Specification documentation about the relevant build of CPRD GOLD [253] and CPRD Aurum [254] and the data checking/cleaning procedure CPRD undertake internally.

Additional methodological detail to the publication

Recording vaping product use

GPs record information in patient consultations using their primary care patient management IT software system, and GPs can record vaping in two ways [252]:

1. Using medical codes: During consultations with patients, certain medical conditions (e.g., symptoms, vaping) are defined via specific SNOMED or Read medical codes. GPs can type in keywords to obtain the term associated with medical codes and add this medical code to the patient consultation record. Note: When a GP adds a vaping medical code to a patient consultation record, this medical code is not carried forward automatically to future consultation records.
2. Using free text comments: GPs can also enter free text comments which describe symptoms or events into the patient consultation record. Free text information is not accessible for research purposes.

Clinical Practice Research Datalink (CPRD)

The CPRD is one of the world's largest electronic primary care databases that includes prospectively collected, anonymised medical records from UK general practices from 1990 to the present [251,252]. Data collection began in 1987, and the primary care dataset became the General Practice Research Database (GPRD) in 1993 [255]. The dataset expanded to form the CPRD in 2012 [255]. CPRD GOLD was the original dataset, and CPRD Aurum was launched in October 2017 [197]. There are four principal GP IT systems (primary care patient management software system) suppliers in England, and the largest coverage is provided by EMIS Health [197]. CPRD GOLD contains data contributed by practices using Vision software [248]. CPRD Aurum contains routinely collected data from practices using EMIS Web electronic patient record system software [248].

CPRD typically collects data from a GP practice on a monthly basis (not a set day each month) [252]. The monthly collection includes detailed diagnostic, therapeutic, laboratory, referral, and demographic data and includes: information on consultations that have

occurred since the last collection; corrections to consultations and information that were recorded previously; information on patients that have newly registered at the GP practice; information on patients that have left the GP practice or died; and notification of patients who have decided to opt out of contributing their data to CPRD. Hence, a new version of the CPRD database is created each month, "taking a snapshot of the data in time" – the new version of the database contains all of the data from the previous version of the database plus all of the collections that have been processed since the previous version was created.

CPRD GOLD includes practices from England, Wales, Scotland and Northern Ireland [255], while CPRD Aurum only includes practices from England and Northern Ireland currently [248]. In 2020, the two CPRD datasets (GOLD and Aurum) contained 14.9 million current patients (22.5% of the UK population) from 1,642 practices (18.3% of the UK practices) [251]. In 2022, the CPRD included detailed medical data for approximately 16 million active patients (25% of the UK population) and 60 million historical patients from around 2,000 UK practices (26% of UK practices). As 98% of the UK population is registered at a general practice, CPRD data is considered to be population-based [197]. The dataset is considered to be representative of the UK population in terms of geography, relative social deprivation, age and gender [197]. In a recent CPRD dataset (linked with Hospital Episode Statistics), over 80% of currently registered patients had their ethnicity recorded and the distribution was broadly representative of the UK population [256]. Also, prevalence estimates from 2007–2011 CPRD data for current smoking and non-smoking were found to be similar to those from nationally representative surveys [257].

For this study, pooled data from the CPRD GOLD April 2023 build and the CPRD Aurum March 2023 build were used, with a cut-off event date of 31 March 2022, because CPRD was experiencing temporary issues with data quality after this date [254]. Dr Dregan informed me that the time periods covered by CPRD GOLD and CPRD Aurum are the same, and when they are pooled, all four countries of the United Kingdom (England, Wales, Scotland and Northern Ireland) are deemed to be represented.

Obtaining the patient population

All patients who received a medical code related to vaping at any point ('incidence') from 1 September 2006 to 31 March 2022 were extracted from the CPRD GOLD April 2023 build and the CPRD Aurum March 2023 build.

The study included all patients aged 18 years of age and older at the time of first vaping medical code record (index date).

Patient acceptability: In every iteration of CPRD, CPRD check whether an individual patient's data are 'acceptable'. To be 'acceptable', patients must have: a valid gender and birth date; logically consistent and valid registration dates; a valid transferred-out-date and reason (more information available in the glossary of terms/data definitions documents [248]). Only observations which were 'acceptable' were extracted.

Practice up-to-standard (UTS) date: Individual practices are given this date, which indicates from when data in a practice are considered to be of research quality: where practice mortality rates lie within an expected range, where dead patients have not been deleted from the system; and where there is continuity in data recording (more information available in glossary of terms/data definitions documents [248]). Practice UTS date is currently only in use in CPRD GOLD [248,254]. All CPRD GOLD observations in my dataset had a UTS.

Valid event date: The event date is the date a consultation occurred. All observations had a valid event date. Additionally, there were no observations where the last collection date (LCD, date of the most recent CPRD data collection for the practice) preceded the event date of the vaping medical code observation.

Patients aged under 18 years old on the vaping code event date were removed. In CPRD GOLD, there were n=4 observations, and in CPRD Aurum there were n=112 observations.

Duplication of practices in CPRD Aurum: The data specification [254] noted that there are 29 GP practices in CPRD Aurum where one practice has been absorbed by another practice. CPRD recommended that records with the following practice IDs are excluded from research studies: 20024, 20036, 20091, 20202, 20254, 20389, 20430, 20469, 20487, 20552, 20554,

20734, 20790, 20803, 20868, 20996, 21001, 21078, 21118, 21172, 21173, 21277, 21334, 21390, 21444, 21451, 21553, 21558, 21585. In CPRD Aurum there were n=1,156 observations which involved these practices.

Duplication within CPRD GOLD and CPRD Aurum: Before merging CPRD GOLD and CPRD Aurum, the datasets were individually checked for duplicated observations based on: event date, year of birth, patient ID, gender, and medical code. In CPRD GOLD, there were n=39 duplicated observations, and in CPRD Aurum there were n=2,412 duplicated observations.

Duplication between CPRD GOLD and CPRD Aurum: After checking for duplicates within CPRD GOLD and CPRD Aurum separately (previous step), I merged the two datasets together. Some GP practices that previously contributed data to CPRD GOLD when using Vision software, are now supported by EMIS software and now contribute data to CPRD Aurum [254]. In these cases, CPRD holds duplicate historical data for these practices. The 'VisionToEmisMigrators.txt' file supplied by CPRD [254] was used, and observations concerning these practice IDs were excluded from the CPRD GOLD dataset (Table 2.1). In CPRD GOLD, there were n=896 observations which involved these practices.

Table 2.1. Practice IDs excluded due to duplication of data between CPRD GOLD and CPRD Aurum

Practice IDs excluded									
10001	10010	10020	10022	10023	10025	10027	10028	10032	10036
10037	10040	10043	10047	10054	10055	10056	10058	10070	10071
10074	10075	10076	10080	10087	10088	10091	10092	10098	10101
10107	10108	10109	10110	10111	10112	10118	10123	10125	10127
10128	10129	10131	10132	10138	10140	10141	10145	10147	10149
10155	10162	10165	10167	10168	10169	10171	10172	10173	10175
10184	10187	10190	10191	10192	10196	10198	10204	10209	10218
10224	10226	10227	10228	10229	10231	10237	10238	10239	10243
10247	10250	10251	10252	10255	10257	10258	10267	10269	10270
10273	10275	10279	10287	10290	10294	10295	10299	10300	10302
10303	10304	10306	10307	10310	10319	10330	10331	10335	10336
10339	10344	10345	10349	10351	10353	10356	10357	10359	10361
10364	10365	10367	10368	10370	10371	10372	10379	10380	10382
10383	10384	10388	10389	10396	10400	10401	10415	10420	10421
10424	10426	10430	10431	10435	10438	10441	10443	10446	10455
10460	10465	10466	10473	10474	10481	10482	10483	10488	10489
10493	10503	10506	10508	10517	10519	10520	10524	10525	10527
10528	10532	10533	10536	10539	10541	10544	10549	10551	10552
10553	10555	10567	10573	10578	10586	10588	10591	10593	10597
10599	10601	10602	10620	10622	10624	10625	10627	10630	10631
10633	10634	10635	10638	10640	10644	10647	10653	10659	10664
10667	10669	10670	10672	10676	10678	10681	10682	10685	10688
10691	10692	10696	10697	10699	10700	10718	10721	10722	10723
10724	10727	10729	10735	10750	10757	10762	10789	10794	10800
10811	10829	10856	10866	10868	10869	10894	10901	10909	10920
10943									

Denominators

The number of GP practices contributing data to CPRD has increased since the inception of CPRD because, over time, new practices join and contribute their (historical and ongoing) patient data. The CPRD GOLD April 2023 build and the CPRD Aurum March 2023 build denominator files were obtained from CPRD, containing records of all the 'acceptable' patients in the databases. These files can be used to calculate the number of patients who were contributing to CPRD at specific time periods [258] – hence can be used as denominators to calculate measures such as point prevalence or incidence rate.

From the CPRD Aurum denominator file, observations with practice IDs of the 29 GP practices recommended for exclusion were removed. From the CPRD GOLD denominator file, observations with practice IDs belonging to those practices which are now contributing data to CPRD Aurum were removed from CPRD GOLD. The two denominator files were then merged. Using the merged file, a new dataset was derived, which indicated the number of patients (aged ≥18 years at the specific time period) contributing data to CPRD in each month from September 2011 to March 2022. I defined the 'start date' and 'end date' of a patient contributing to CPRD conservatively, following the recommendation from CPRD [258]: the 'start date' for each patient contributing to CPRD was the chronologically latest of 'registration start date' and 'current registration date'; the 'end date' for each patient contributing to CPRD was the chronologically earliest of the 'registration end date', 'death date', 'transfer out date', or 'last collection date' of the practice.

Investigation of pre- and post-EVALI outbreak effects

In my original study, which I wrote up as a manuscript, I initially did not perform any statistical analyses to test if EVALI had a statistically significant effect on our outcome variable, I only visually inspected the data.

During peer review of the manuscript, I provided access to cleaned and prepared data to my co-author (Sol Richardson). He conducted interrupted time series analyses to assess the effect of EVALI using statistical methods (as per one of the peer reviewer

recommendations). The final publication in *Chapter 4* contains the methodological description of these analyses and the results, but I do not discuss it further here as I did not perform these analyses.

Study 3 and 4: ITC Project Surveys

Chapter 5 and *Chapter 6* contain findings from secondary analysis of cross-sectional Wave 2 (March–June 2018) International Tobacco Control (ITC) Four Country Smoking and Vaping (4CV) Survey data of adults ≥18 years who smoke, vape or those who recently quit smoking from Australia, Canada, England, and the US.

The analytical study samples I used for the two studies differed. In *Chapter 5*: the study sample consisted of n=11,040 adult respondents who were either currently smoking cigarettes (daily/weekly/monthly) or had recently quit (quit smoking in the last 18 months AND had smoked >100 cigarettes in their lifetime), at the time of the 2018 survey. In *Chapter 6*: the study sample consisted of 5,177 respondents classified as adults who had made at least one attempt to quit smoking in the past 18 months and who were currently smoking cigarettes (daily/weekly/monthly) or had recently quit (quit smoking in the last 18 months AND had smoked >100 cigarettes in their lifetime), at the time of the 2018 survey.

Rationale for study method

As discussed in *Chapter 1*, given that smoking prevalence is higher in those who have mental health conditions than those who do not, it is important to: (a) assess whether health professionals are providing VBA to people who smoke with mental health conditions, including discussing NVPs with them as a potential smoking cessation support option; and (b) it is important to assess whether these people are using cessation support in their smoking quit attempts, because using cessation support in quit attempts can increase the likelihood of smoking cessation success.

In order to answer these quantitative research questions, one could potentially use routinely collected EHR data or population surveys. I briefly discuss these two sources of data here.

First, I consider EHRs. Regarding the provision of smoking cessation advice, EHRs may contain data relevant to this, if health professionals believe this is important to record or if clinical guidelines specify that this should be regularly recorded (for example, in the UK, general practitioners were financially incentivised to record when they have delivered cessation advice to their patients), however, as far as we were aware, this is not standardised across time and in countries other than the UK. Regarding discussing NVPs as a smoking cessation support option, again, as far as we were aware and considering my *Study 2*, this is not a clinical behaviour that health professionals are explicitly required to record in EHRs. Regarding cessation support option use, data on this may be present in EHRs using medical codes, especially referral to Stop Smoking Services (in the UK) and prescriptions for cessation medications. However, the use of over-the-counter NRT or NVPs would likely not be recorded in individual patient EHRs. Additionally, it is possible that patients are referred to behavioural support or are prescribed cessation medication but opt not to adhere (attend, or take the medication, respectively).

Second, I consider population surveys. Regarding cessation advice, past research [246], which compared patient recall of receiving cessation advice to the recording of cessation advice provision in EHRs, found that more patients had cessation advice recorded in their medical records than recalled receiving advice – the discrepancy could be attributed to health professionals not adequately communicating cessation advice to patients, or that health professionals misrepresented the provision of cessation advice due to financial incentives. One could argue that, even if recall of cessation advice is affected by recall bias (i.e., a patient may have received adequate cessation advice, and merely forgot this when they were answering the survey questions), the most impactful outcome measure is whether patients are able to recall receiving cessation advice in the long-term. Hence, it can be argued that the method best suited to assess the 'true' proportion of patients who have received cessation advice is by asking patients in surveys. I argue this also for discussing NVPs as a smoking cessation support option. Lastly, regarding cessation support option use, survey participants should hopefully be able to accurately recall if they have used any

cessation support option in their last quit attempt, whether they received the cessation aid via their health professional, over the counter, or the internet.

Considering these two potential data sources, I decided to use the second. I then decided on using the International Tobacco Control (ITC) Project survey data, as this contains nationally representative cohorts of adults who smoke or vape or recently quit smoking in multiple countries. The survey enables the comparison of countries which have differing guidelines and policies related to smoking cessation support options (including NVPs). The ITC Project survey uniquely contains very detailed information on smoking and nicotine use behaviours, quitting behaviours, and smoking cessation methods, which is unparalleled in other similar surveys.

I aimed to generate multivariate logistic regression models, using cross-sectional survey data from 2018, to investigate if there were differences in the odds between adults ≥18 years with and without self-reported depression/anxiety in terms of various outcomes concerning:

- *Chapter 5*: their interactions with healthcare professionals (HPs) about smoking cessation and nicotine vaping products; and
- *Chapter 6*: the cessation support option they used in their last attempt to quit smoking.

Development of the study design

Registered study protocol

My secondary supervisor (Prof Ann McNeill) is a co-Principal Investigator on the ITC Project. I used the publicly available survey questionnaire and derived variables documents to identify my variables of interest [259,260]. I completed the ITC Project data usage agreement form in order to get approval to carry out my proposed analyses. I registered an analysis plan on the Open Science Framework (OSF) website before I received the data and conducted the analyses: https://osf.io/y72cj (Appendix A.1).

Further discussion of the roles of my collaborators is provided in *Chapter 5* and *Chapter 6*.

Additional methodological detail to the publications

ITC Project

The ITC Project was established in 2002 to measure the psychosocial and behavioural impact of key national-level policies that are implemented in countries that are signatories to the WHO Framework Convention on Tobacco Control (FCTC), the international public health treaty [250]. The ITC Project conducts longitudinal surveys in nationally representative cohorts in 31 countries [250]. The *ITC Four Country Smoking and Vaping (4CV) Survey* was also designed to investigate the relationship between the use of nicotine vaping products and tobacco use, and to inform emerging policies on NVPs in Australia, Canada, England, and the US [261]. It uses nationally representative cohorts (adults ≥18 years) who smoke or vape or recently quit smoking [261].

The Wave 2 (2018) survey data was the most recent data available at the time of my PhD, where survey respondents were asked about having depression and/or anxiety.

The Wave 2 survey data collection took place between March and June 2018 [261]. Market research organisations, such as Ipsos, were utilised to recruit respondents [261]. The survey was offered by web only in all four countries, but respondents had the option to complete a phone-assisted web-interview [261]. The Wave 2 survey sample included those who were re-contacted from the previous wave (Wave 1, 2016) and new participants who were recruited to address attrition and maintain sample size over time. The sample comprised the following subsamples: (1) recontact people who smoke and people who formerly smoked who had participated in the Wave 1 (2016) Survey, (2) newly recruited people who currently smoke and people who recently formerly smoked (i.e., quit smoking in the previous 24 months) from country-specific panels, regardless of vaping status, (3) recontact people who vape who had participated in the Wave 1 (2016) Survey, and (4) newly recruited people who currently vape (using a vaping device at least weekly) from country-specific panels, regardless of smoking status. The newly recruited smoking and vaping (adults ≥18 years) samples in each country were designed to be representative of people who smoke, or vape

at least weekly, in each country, and used either probability-based sampling frames or non-probability opt-in sampling frames, or a combination of these methods. Full methodological details are available online (https://itcproject.org/methods) [261,262].

Weighting

The ITC Project Analysts calculate various weightings for the respondents [259]. After consulting the ITC Project Analysts regarding my studies, I was advised to derive a new weighting variable, using two of the cross-sectional survey weights derived by the ITC Project Analysts [259]: adult respondents who were either currently smoking cigarettes daily, weekly or monthly were weighted using the variable lWTS201v (wave 2 cross-sectional weights for the respondents who smoked cigarettes at the time of wave 2 data collection, rescaled to sum to the sample size in each country); and respondents who had recently quit weighted using the variable lWTS501v (wave 2 cross-sectional weights for those respondents who had quit smoking at the time of wave 2 data collection, rescaled to sum to the sample size in each country).

A cross-sectional weight was not assigned by the ITC Project Analysts to some of the respondents from Australia; those who were recruited via the Australian Dedicated Vapers (and hence were not representative of people who smoke or vape in Australia). I was advised by the ITC Project Analysts to exclude these respondents from my analytical samples.

Deviation from pre-registered analysis plan

There were some slight deviations to my pre-registered analysis plan (Appendix A.1).

My pre-registered analysis plan included both of these studies, but after writing up the results, it made sense to divide them into two separate manuscripts because they concerned two separate topics: (*Chapter 5*) health professional interactions and (*Chapter 6*) cessation aid use; and they had two differing analytical samples.

Change to proposed variables

The proposed outcome variables of *Chapter 5* were: 'Visiting a health professional', 'Advice to quit smoking from a health professional', and 'Positive recommendation to use NVPs'. After dividing the studies, my co-authors and I considered that it would improve my study if I added a fourth outcome variable: 'Discussion about NVPs'. This was in order to provide a fuller picture of the health professional interaction outcomes, and because the respondents who were asked the survey question about 'Positive recommendation to use NVPs' had to answer 'yes' that their health professional discussed NVPs with them ('Discussion about NVPs').

The proposed outcome variables of *Chapter 6* were: 'Used NVPs', 'Used NRT', 'Used varenicline or bupropion', 'Used behavioural support'. My co-authors and I considered that it would improve my study if I added a fifth outcome variable: 'Used any cessation aids', an aggregate outcome, derived from the original four outcomes. This was done to provide a fuller picture of people who smoke with and without depression and/or anxiety using cessation aids in their smoking quit attempts.

Change to statistical analysis

For both *Chapter 5* and *Chapter 6*, in addition to the unadjusted (Model 1) and adjusted logistic regression models (Model 2 and 3) proposed in the analysis plan, to assess whether the association between mental health condition and each outcome varies by country, for each outcome, I performed a likelihood-ratio test to assess whether there was a significant difference between Model 3 and a fourth model which contained interaction terms between mental health condition and country (Model 4).

For both *Chapter 5* and *Chapter 6*, in addition to reporting 95% confidence intervals and exact p-values, I received further statistical advice which recommended that I adjust for

multiple comparisons to increase the robustness of my findings. Hence, I evaluated the statistical significance level, alpha, at:

- *Chapter 5*: 0.0125 level, as per the Bonferroni correction (α=0.05/4 outcomes= 0.0125), and
- *Chapter 6*: 0.01 level, as per the Bonferroni correction (α=0.05/5 outcomes= 0.01).

Reflexivity

As a researcher, it is important to be reflexive about one's positionality and assumptions.

I personally do not smoke nor vape, nor use any other nicotine product. My grandparents on my father's side smoked heavily but quit smoking when they developed cardiovascular disease after middle age. My parents were very anti-tobacco. As a teenager in England, I remember seeing Stoptober adverts on the television. I felt like the health harms of smoking were clearly communicated to me during my childhood and adolescence, and a large majority of my friends did not smoke or experiment with smoking, so I personally never felt peer pressured as a youth.

I studied biomedical science for my undergraduate degree. In my third year, we had some teaching in the Royal Brompton Hospital – patients who had COPD and were receiving oxygen were asked to tell us about their stories and their quality of life. I carried out various laboratory projects which looked at the effect of smoking on microRNA and neutrophils and learnt a lot about airway mucus. Although having an understanding of the molecular mechanisms involved in tobacco-related health issues has been useful to underpin my research, upon reflection, basic science research does not always evaluate the exposure under investigation using realistic 'real world' methods of administration or consider the broader context in which the exposure is administered (such as the possibility that it may be a substitute for another exposure).

In 2016, I briefly worked with Prof Nick Hopkinson, who is the current Chair of Action on Smoking and Health, to deliver the SmokeFreeArts campaign. The campaign aimed to raise awareness about the tobacco industry's involvement in funding UK arts institutions. The

campaign resulted in media coverage and >1,000 healthcare professionals signed the campaign letter. Following the campaign, the Royal Academy, Southbank Centre, National Theatre, London Symphony Orchestra terminated sponsorship from various tobacco companies. The campaign was mentioned in the Royal College of Physicians 'Smoking and Health 2021' report [6] under the 'Tobacco advertising and promotion' section (page 61). Nick gave me an insight into political activism and the history of Big Tobacco.

Before I started the PhD, I read the Public Health England-commissioned vaping evidence reviews that my supervisors co-authored. I saw the value of NVPs as a form of tobacco harm reduction but my biomedical science background made me wary of the potential health harms of vaping. During my Medicine, Health and Public Policy Master's degree, I got the opportunity to read about the commercial determinants of health, Prof Anna Gilmore's work on tobacco industry internal documents and policy-manipulation tactics, and Global Tobacco Control by Prof Paul Cairney et al. Also, I conducted interviews with vape shop managers for my dissertation, asking them about their experiences of helping their clients stop smoking. These experiences gave me a better understanding into why some tobacco control researchers are so opposed to vaping.

Joining the Addictions Department gave me an eye-opening look at addiction itself as a phenomenon – I had not previously considered the non-health impacts to society that addiction can cause nor about the distinction between 'smoke-free' and 'nicotine-free' goals for society.

I think it is important to be wary of industry tactics regarding consumer products, especially those which are addictive, and keep a watchful eye for societal unintended consequences. However, it is also important to be mindful of the very real health harms of smoking combustible cigarettes and remain open to approaches which mitigate these harms.

Chapter 3 – Strategies to increase smoking cessation support provision: a systematic review of observational studies

Preface

The objective of this chapter was to review the evidence for the effectiveness of interventions (implementation strategies) that were implemented on a national or state-wide scale, internationally, aiming to increase the [quality and quantity of] provision of smoking cessation treatment in primary care, via a systematic review.

This chapter presents the systematic review I conducted and published as a peer-reviewed publication [1]:

> Tildy, B. E., McNeill, A., Perman-Howe, P. R., & Brose, L. S. (2023). Implementation strategies to increase smoking cessation treatment provision in primary care: a systematic review of observational studies. *BMC Primary Care*, *24*(1), 1–61. https://doi.org/10.1186/s12875-023-01981-2

The supplementary materials referred to in the publication are available in **Appendix B** of this thesis.

In this chapter, the Author's Accepted Manuscript version of the publication [1] is included, rather than the publisher's typeset PDF of the manuscript, which allowed me to edit the format (font type and size, line spacing) to ease reading. For the references cited in the manuscript, I have retained their original in-text citation number (but have made these superscript numbers to distinguish them from the in-text citations in the thesis), and a reference list for this manuscript is provided at the end of this chapter.

Declaration of roles

I developed this publication in collaboration with Dr Leonie Brose, Professor Ann McNeill and Dr Parvati Perman-Howe (King's College London). LB, AM and I developed and refined the review questions and the search strategy. I ran all the searches. PP-H and I screened the search records and refined the inclusion and exclusion criteria, with oversight from LB. I performed the data extraction; where there were uncertainties about the outcomes, I consulted LB. I completed risk of bias assessments; after the first five studies were assessed, LB also assessed these, and LB and I compared ratings. I analysed and interpreted the data, with supervision from LB and AM. I wrote the initial manuscript. LB, AM and I were involved with reviewing and editing subsequent drafts. I handled the manuscript submission and responded to peer reviews. All authors read and approved the final manuscript.

Publication

Implementation strategies to increase smoking cessation treatment provision in primary care: a systematic review of observational studies

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Abstract

Background: Internationally, there is an 'evidence-practice gap' in the rate healthcare professionals assess tobacco use and offer cessation support in clinical practice, including primary care. Evidence is needed for implementation strategies enacted in the 'real-world'. Aim: To identify implementation strategies aiming to increase smoking cessation treatment provision in primary care, their effectiveness, cost-effectiveness and any perceived facilitators and barriers for effectiveness.

Methods: 'Embase', 'Medline', 'PsycINFO', 'CINAHL', 'Global Health', 'Social Policy & Practice', 'ASSIA Applied Social Sciences Index and Abstracts' databases, and grey literature sources were searched from inception to April 2021. Studies were included if they evaluated an implementation strategy implemented on a nation-/state-wide scale, targeting any type of healthcare professional within the primary care setting, aiming to increase smoking cessation treatment provision. Primary outcome measures: implementation strategy identification, and effectiveness (practitioner-/patient-level). Secondary outcome measures: perceived facilitators and barriers to effectiveness, and cost-effectiveness. Studies were assessed using the Risk Of Bias In Non-randomized Studies of Interventions (ROBINS-I) tool. A narrative synthesis was conducted using the Expert Recommendations for Implementing Change (ERIC) compilation and the Consolidated Framework for Implementation Research (CFIR).

Results: Of 49 included papers, half were of moderate/low risk of bias. The implementation strategy domains identified involved utilizing financial strategies, changing infrastructure, training and educating stakeholders, and engaging consumers. The first three increased practitioner-level smoking status recording and cessation advice provision. Interventions in the utilizing financial strategies domain also appeared to increase smoking cessation (patient-level). Key facilitator: external policies/incentives (tobacco control measures and funding for public health and cessation clinics). Key barriers: time and financial constraints, lack of free cessation medications and follow-up, deprioritisation and unclear targets in

primary care, lack of knowledge of healthcare professionals, and unclear messaging to patients about available cessation support options. No studies assessed cost-effectiveness.

Conclusions: Some implementation strategy categories increased the rate of smoking status recording and cessation advice provision in primary care. We found some evidence for interventions utilizing financial strategies having a beneficial impact on cessation. Identified barriers to effectiveness should be reduced. More pragmatic approaches are recommended, such as hybrid effectiveness-implementation designs and utilising Multiphase Optimization Strategy methodology.

Registration: PROSPERO:CRD42021246683

Keywords: Systematic literature review, smoking, smoking cessation, tobacco, substance use, primary care, general practice, implementation strategy, 5As, Very Brief Advice

Background

Smoking remains one of the leading preventable causes of illness and premature death in the UK [1] and worldwide [2]. Most adult smokers want to quit smoking [3–5] but quit attempts have a low success rate because fewer than a third use evidence-based treatment [3,5]. For example, the current stop-smoking interventions recommended in the UK are: behavioural support, nicotine replacement therapy (NRT), bupropion, varenicline, and nicotine-containing electronic cigarettes [6]. Healthcare practitioners can trigger and aid quit attempts, increasing cessation likelihood by up to three times [7]. Primary care is suitable for addressing cessation because smokers frequently attend, and it is an opportunistic and trustworthy setting [8]. The World Health Organization (WHO) recommends that "cessation support and treatment is provided in all health care settings and by all health care providers" [9], especially in primary health care systems as this infrastructure already exists in most countries and has a high population coverage. Clinical guidelines recommend addressing patients' tobacco use by giving "brief advice" to all patients [10]. The first model for this was the '5As' [11,12] and in some countries now, the '3As' or 'Very Brief Advice' (VBA) is recommended [13] (Appendix 1).

Cancer Research UK recently modelled that if GPs intervened at least once a year with all smokers who attended an appointment (referring smokers to a stop smoking service (SSS) and prescribing a cessation medication), national smoking prevalence in 2030 in England would be 2.5% lower than if current rates of brief advice were continued [11]. Despite evidence-based recommendations and guidelines, internationally there is an 'evidence-practice gap' in the rates at which healthcare professionals assess tobacco use and offer support in clinical practice in the real-world [14]. A systematic review of primary care physicians in 17 countries found the following average rates: "65% for 'Ask', 63% for 'Advise', 36% for 'Assess', 44% for 'Assist', and 22% for 'Arrange' [14].

Integrating smoking cessation treatment into routine clinical care and infrastructures is difficult [5]. Implementation science argues that focused efforts are required to facilitate the movement of evidence-based practices (EBP) (e.g., 5As/VBA) into clinical practice because the contexts that the EBP aims to enter are complex and variable [15]. 'Implementation strategies' are "methods or techniques used to enhance the adoption, implementation, and sustainability of a clinical program or practice" [16,17], e.g., "remind clinicians", "fund and contract for the clinical innovation" [18]. The Expert Recommendations for Implementing Change (ERIC) programme defined 73 distinct 'implementation strategy' categories organised into nine implementation strategy domains [18,19] (Appendix 2).

A recent Cochrane review [20] evaluated randomised and cluster-randomised controlled trials of implementation strategies designed to increase the rate and quality of delivery of the 5As/VBA to adult primary healthcare patients, when delivered in addition to 'standard' cessation support or 'usual care'. Their primary outcome measure was smoking abstinence at long-term follow-up (at least 6 months) and their secondary outcomes were practitioner performance in the 5As and quit attempts. They found moderate-certainty evidence for adjunctive counselling (counselling delivered by a health professional other than the primary care physician), free stop-smoking medications, and tailored print materials increasing quit rates. They found no clear evidence for biomedical feedback, provider training, or provider incentives increasing quit rates. For secondary outcomes, they found some evidence that adjunctive counselling increased cessation medication provision, quit attempts, and arranging patient follow-up by physicians; free stop-smoking medications

increased quit attempts; and mixed results for tailored print-materials regarding quit attempts. They found evidence that provider training increased smoking status recording, cessation advice provision, cessation counselling, and providing self-help materials, but mixed results for participants setting a quit date, cessation medication provision, quit attempts, and arranging patient follow-up. For multi-component interventions, adjunctive counselling combined with free stop-smoking medications, and adjunctive counselling combined with provider smoking cessation training increased quit rates. Combining provider training with flow sheets to aid physician decision-making also increased quit rates; but the results for secondary outcomes for smoking status recording, cessation medication provision, and physicians arranging patient follow-up were mixed. Lastly, combining provider training with outreach facilitation had no effect on quit rate, recording smoking status, providing cessation medication, or quit attempts; but had some beneficial effect on participants setting a quit date, providing self-help materials, and arranging patient follow-up.

The Cochrane review did not include observational studies; hence the current review focuses on studies which evaluated the impact of implementation strategies enacted without researcher input, in the 'real-world', as a national or state-wide policy or change to clinical guidelines. This review complements the Cochrane review and sought to identify differences in the findings which may be due to barriers to implementation in the real-world, to help explain the evidence-practice gap.

Review questions

The aim of this systematic review was to identify implementation, effectiveness and cost-effectiveness of implementation strategies aiming to increase smoking cessation treatment provision in the primary care setting. Given the evidence-practice-gap, it is important to identify potential facilitators and barriers to implementation. As a secondary outcome, we therefore extracted the proposed facilitators and barriers to effectiveness (qualitative outcomes) from the studies which assessed the effectiveness of implementation strategies on quantitative outcomes.

RQ1 (Primary): What implementation strategies aiming to increase smoking cessation treatment provision in the primary care setting have been implemented on a national or state-wide scale?

RQ2 (Primary): Which implementation strategies were effective (practitioner-level and patient-level outcomes) in increasing smoking cessation treatment provision in the primary care setting?

RQ3 (Secondary): What explanations (perceived facilitators and barriers) have been proposed to explain why certain implementation strategies to increase the provision of smoking cessation treatment in primary care settings were/were not effective?

RQ4 (Secondary): What is the cost-effectiveness of effective implementation strategies to increase the provision of smoking cessation treatment in primary care settings?

Methods

Protocol and registration

The systematic review protocol was registered on PROSPERO on 1 April 2021 (ID: CRD42021246683), it follows the PRISMA statement [21] (Appendix 3).

Amendments made after protocol registration were: interventions were only included if they involved an implementation strategy enacted on a national/state-wide scale; PhD theses were excluded; key contacts and organisations were not contacted to identify publications not retrieved by the search strategy.

Search strategy

The searches were carried out on 7 April 2021. ‘Smoking’, ‘smoking cessation’ and ‘primary care’ subject headings and key words were used. MEDLINE, EMBASE, CINAHL, PsycINFO,

ASSIA Applied Social Sciences Index and Abstracts, Global Health, and Social Policy & Practice were searched for published journal articles. OpenGrey, Social Care Online, and Healthcare Management Information Consortium (HMIC) Database were searched for grey literature. The King's College London library service and the authors of the related Cochrane review [20] were consulted in developing the search strategy. (Full search strategy: Appendix 4.)

Forward and backward direct citation tracking was conducted using Web of Science [22]: studies published before 7 April 2021 which cited the included studies, and studies referenced by the included studies, were screened against the inclusion/exclusion criteria.

Article selection

Inclusion/exclusion criteria

Participants/population: The target of the intervention(s) was any type of healthcare professional within the primary care setting. 'Primary care setting' was defined as family medicine or general medical practice [20]. Excluded are public health interventions delivered outside primary care practices and interventions delivered in dental settings or pharmacies. Studies including the whole practice patient population were included, as well as those which included specific sub-populations in primary care settings (e.g., people with chronic obstructive pulmonary disease (COPD), diabetes, adolescents, pregnant women). Studies were excluded if outcome data could not be extracted exclusively for the primary care setting.

Intervention/exposure: Articles were included if they evaluated an 'implementation strategy' [16–18] aiming to increase smoking cessation treatment provision in the primary care setting which was implemented on a national or state-wide scale. The focus of this review was specifically on implementation strategies which were implemented nation-wide or state-wide because we were interested in the scalability of implementation strategies. Articles

which assessed local-scale (i.e.: 'non-national' or 'non-state-wide') implementation strategies were excluded.

Control: Control could be usual care, any other intervention, or before and after designs. Cross-sectional studies without a comparison/control were excluded.

Outcome measures: Articles that assessed any of the primary outcome measures were included in the review.

Primary outcome measures:

1. Implementation strategy identification: Description of the implementation strategy was extracted from the article.

2. Implementation strategy effectiveness:

   2.a. Practitioner-level:

   Practitioner performance in 5As/VBA – definitions used by the original studies were accepted:

   - Ask (ask patients about smoking at every visit)
   - Advise (advise all tobacco users to quit)
   - Assess (assess smokers' willingness to try to quit)
   - Assist (assist smokers' efforts with treatment and referrals, e.g.: 'discuss medications', 'prescribe medications', 'set a quit date', 'provide counselling')
   - Arrange (arrange follow-up contacts to support cessation efforts)

   2.b. Patient-level:

   - Smokers entering into cessation programmes, facilitated by healthcare professionals in primary care (e.g.: attending smoking cessation clinic or behavioural support appointments; filling prescriptions; calling quit telephone helpline)
   - Smokers setting a quit date or quit attempts
   - Smoking cessation

Secondary outcome measures:

1. Facilitators and barriers to effectiveness: Explanations (perceived facilitators and barriers) offered by the original study authors to explain why certain implementation strategies aiming to increase the provision of smoking cessation treatment in primary care settings were/were not effective.

2. Implementation strategy cost-effectiveness: Any measures relating to cost-effectiveness or economic indicators of the intervention in the study (which may have involved one or multiple implementation strategy categories).

Date: Date restrictions regarding publication were not applied.

Study design: Non-randomised designs, including comparative observational study designs such as cohort (prospective and retrospective) studies, case-control studies, interrupted time series studies.

Language: English.

Publication type: Published studies and reports were included. PhD theses, conference abstracts, protocols, reviews, systematic reviews, letters, editorials, commentaries, and studies with only qualitative outcomes were excluded.

Screening process

The search results were imported into www.cadima.info and duplicates were removed. Articles were screened by BT at two stages (title/abstract, and full text). Reasons for exclusion were documented at the full text level. The PICO checklist used during screening was piloted between BT and a second screener (PP-H). The second screener (PP-H) screened 200 records at the title/abstract screening stage, and 30 records at the full text screening stage. Inconsistencies were discussed and the inclusion and exclusion criteria were clarified by the two screeners and a third reviewer (LB).

Data extraction

Data from included studies were extracted into a pre-piloted form (Appendix 5). BT performed the data extraction for the 49 included studies, where there were uncertainties about the outcomes, BT consulted LB. Authors were contacted to provide missing data. Where these data were not provided, they are reported as "missing".

Risk of bias assessment

The ROBINS-I (Risk Of Bias In Non-randomized Studies of Interventions) tool was used to evaluate the risk of bias in non-randomised observational studies [23–25]. BT performed the risk of bias assessments. After the first five studies were assessed, LB also assessed these, and BT and LB compared ratings. The risk of bias assessment ratings and justifications are included in Appendix 6.

The tool assesses risk of bias in seven domains [23]:

- Pre-intervention: (1) confounding, (2) selection of participants into the study.
- At intervention: (3) classification of interventions.
- Post-intervention: (4) deviations from intended interventions, (5) missing data, (6) measurement of outcomes, (7) selection of the reported result.

Then an overall risk of bias rating is decided for each study: low, moderate, serious, or critical risk of bias, or no information available [23].

Synthesis methods

Due to heterogeneity in study populations and outcome measures, a narrative synthesis was used.

Based on the descriptions provided in the included studies, the key aspects of the interventions under investigation were coded to the nine implementation strategy domains and 73 categories developed by the ERIC program [18,19] (Appendix 2).

Perceived facilitators and barriers, extracted from the studies, were mapped to the determinants in the Consolidated Framework for Implementation Research (CFIR) [26] (Appendix 7).

Results

Study selection

The database search strategy yielded 12,527 records. After de-duplication and screening, 42 studies met the inclusion criteria. Forward and backward direct citation tracking identified an additional seven papers, resulting in 49 papers being included in this review (Figure 3.1).

Study characteristics

Table 3.1 shows the characteristics of the 49 included studies. Studies were set in the UK (n=23) [27–49], USA (n=13) [50–62], Ireland (n=4) [63–66], the Netherlands (n=3) [67–69], Australia (n=2) [70,71], Turkey (n=1) [72], Poland (n=1) [73], Finland (n=1) [74], and one [75] compared different policies in the Germany and the UK.

Thirteen were cohort studies [31,40,44,48,54,56,60,62,65,66,68,71,73]. One was a controlled before-and-after study [69]. Three were cross-sectional with a comparator [58,59,75]. The other 32 studies were repeated cross-sectional studies. Ten of these used advanced analytical techniques: interrupted time series design [27,33,37,46,67], segmented regression design [34–36], regression discontinuity design [45], difference-in-differences and triple differences design [57]. Thirteen of the repeated cross-sectional studies tested for statistical significance between pre- and post-intervention measurements [32,42,43,47,49–51,53,55,70,72,74], and nine only described the pre- and post-intervention measures [28–30,38,39,41,61,63,64].

Risk of bias

One study [71] had 'critical' risk of bias and was not included in the narrative synthesis as per Cochrane guidance [25]. Twenty-four studies [28–30,32,36,38,39,41–44,49,51,52,55,61,63,64,66,69,70,72,74,75] had 'serious' risk of bias, predominantly due to receiving a poor rating for the 'bias due to confounding' domain. Twenty studies [27,33–35,37,45–47,50,53,54,56–60,65,67,68,73] had 'moderate' risk of bias; these had more sophisticated study designs which controlled for time-varying confounders but did not have a pre-specified/pre-registered analysis plan, scoring a poor rating for the 'bias in selection of reported result' domain. Four studies [31,40,48,62] were at 'low' risk of bias – these were cohort studies which controlled for various confounders and had pre-specified analysis plans (Appendix 6).

RQ1: Implementation strategies that were implemented

Interventions in six studies [37,50,51,56,67,72] used multiple implementation strategies; interventions in the other 42 studies used one key implementation strategy category only (Figure 3.2). We did not identify studies for all possible implementation strategy domains and categories which are outlined in the list developed by the ERIC program [18,19] (Appendix 2). The domains in which implementation strategies were identified were 'Utilize financial strategies' (Domain 8., 34 studies), 'Change infrastructure' (Domain 9., 14 studies), 'Train and educate stakeholders' (Domain 5., three studies), and 'Engage consumers' (Domain 7., three studies). More details of the implementation strategy domains and categories are given in Table 3.2 and summarised below when discussing outcomes for RQ2 and RQ3.

RQ2: Effectiveness & RQ3: Perceived Facilitators and Barriers

For conciseness and clarity, we present the effectiveness findings and the key facilitators and barriers proposed by the included studies' authors together in this section, organised by implementation strategy domain and category. Details can be found in Table 3.2 and a summary of the facilitators and barriers in Table 3.3. The extracted quantitative outcomes

are included in Appendix 8.

Utilize financial strategies (Domain 8)

Thirty-four studies [27–32,37–40,42–45,47–50,54,56–58,60–67,69,72,73,75] evaluated interventions using an implementation strategy that increased funding towards the provision of smoking cessation treatment in primary care.

Fund and contract for the clinical innovation (Category 57)

The six studies in this category investigated policies where primary care practices received funding to deliver national cardiovascular disease prevention programs (including health checks). Two studies were at low risk of bias [31,48], two moderate [65,73], and two serious [66,69].

Effectiveness. For practitioner-level outcomes: two studies showed an increase in smoking status recording [48,73]; two indicated an increase [31,69] and one no effect [73] on the provision of cessation advice; and one increased [31] and one had no effect [73] on cessation medication prescribing. For patient-level outcomes, three studies indicated an increase [31,65,66] in cessation while one showed no effect [73].

Facilitators/barriers. A perceived barrier was that health check programs focused on the 'risk factor identification' and not the 'intervention' aspects of cessation treatment [31,73]. Another barrier was time constraints and insufficient financial recompense for physicians to deliver cessation treatment [31,66,69,73]. Authors noted that there was selection bias in the type of patients who respond to an invitation for a health check [31,48], but that the value of opportunistic health checks should not be underplayed [31]. A proposed facilitator to increase effectiveness was improved linkages to community-based programmes and support [65,69] or improved mechanisms for follow-up/monitoring of cardiovascular risk factors in primary care [31,66].

Place innovation on fee for service lists/formularies (Category 59)

The 10 studies in this category examined changes in insurance schemes which included aspects of smoking cessation treatment [54,57,58,60–62,67] or the introduction of a new smoking cessation medication [37,63,64]. One study was at low risk of bias [62], six moderate [37,54,57,58,60,67], and three serious [61,63,64].

Effectiveness. For practitioner-level outcomes, the introduction of a new cessation medication onto a country's prescription scheme – NRT in Ireland in 2001 [63,64], and varenicline in England in 2006 [37] – increased the prescription of the new medication, but did not change overall prescribing of smoking cessation medications. For practitioner-level outcomes, in the USA, increasing access to health insurance coverage which included smoking cessation treatment, increased smoking status recording (multi-state, Oregon) [61,62], cessation advice provision (Colorado) [58] and cessation medication prescribing (Oregon, multi-state) [54,60]. In the Netherlands [67], increasing health insurance coverage for smoking cessation also increased cessation medication prescribing. For patient-level outcomes, in the USA, one study (Massachusetts) found no difference in quit attempts [57] but two studies (Oregon, and multi-state) found a positive effect on smoking cessation following the increases in medication prescribing [54,60]. The Dutch study [67] indicated increased cessation, but evidence for this was less robust. Patient-level outcomes were not measured in the studies assessing the introduction of new medications.

Facilitators/barriers. Perceived barriers were that physician confidence in, and patients' awareness of, cessation medications was too low [37]. A proposed facilitator of increasing access to health insurance coverage was that this increases access to medications and primary care services [54,60], which in turn increase the odds that services like smoking status assessment would be performed [62]. Other proposed facilitators included structural characteristics, such as providing sufficient education/training about the 5As/VBA [63], delivering 5As/VBA as an organisational priority and allocating sufficient physician time for it [57,58,63].

Alter incentive/allowance structures (Category 60)

Of the 16 studies in this category, two studies in the USA (Oregon, and multi-state) [50,56] investigated the 'Meaningful use' (MU) scheme, which included the introduction of incentive payment for physicians to record their patients' smoking status and offer cessation assistance alongside other measures (such as changing recording systems) from 2011. The other 14 studies examined various amendments of the Quality and Outcomes Framework (QOF), a pay-for-performance scheme in the UK which financially incentivised GPs to perform certain interventions.

- 13 studies [28–30,32,38–40,42–45,47,49] investigated the 2004 QOF, which set the following targets: every 15 months record smoking status for patients who have coronary heart disease, diabetes mellitus, COPD, transient ischaemic attack or stroke, asthma, or hypertension; and every 15 months offer cessation advice or referral to a cessation service for these co-morbid patients who smoke.
- One study [30] investigated the 2004, 2006 and 2008 QOF. 2006 amendment: record smoking status in patients without smoking-related morbidity every 27 months rather than 'ever'. 2008 amendment: chronic kidney disease, schizophrenia, bipolar disorder, and other psychoses were added to the list of smoking-related conditions which required recording of smoking status and cessation advice every 15 months.
- One study [27] investigated the 2012 QOF amendment: offer referral to the National Health Service Stop Smoking Services (NHS SSS) and prescribe pharmacotherapy to all people who smoke, regardless of their smoking-related medical history.

In this category, one study [40] was at low risk of bias, five moderate [27,45,47,50,56], and ten serious [28–30,32,38,39,42–44,49]; most of the latter did not account for underlying secular trends.

Effectiveness. For practitioner-level outcomes, several studies in the UK for the 2004 QOF found increased smoking status [29,30,32,38,40,42–44,47,49] and cessation advice recording [30,32,40,42–44,49] in primary care for all patients and those who had a QOF-targeted-morbidity. However, one study of survey participants with a QOF-targeted-morbidity found that the recall of receiving cessation advice by patients did not increase significantly [45]; one study found that there was an increase in cessation advice provision to pregnant women who smoked [not

direct targets of this policy] but this increase was not sustained long term [39]; and one study which compared the rate of cessation advice recording in primary care electronic health records with the rate of patient recall of receiving cessation advice found mixed results (increase in the former, no effect on the latter) [28]. Two studies found that there was no effect of the 2004 QOF on cessation medication prescribing [an indirect target of the policy] [32,45], while one found an increase in cessation medication prescribing [40]. The study which assessed the 2006 and 2008 revisions of the QOF only examined practitioner-level outcomes and found no significant effect on smoking status recording or cessation advice provision (but the outcome for the 2008 QOF is less robust) [30]. The one study investigating the 2012 QOF amendment also only examined practitioner-level outcomes and found an increase in the provision of cessation advice and referrals to NHS SSS, but no increase in cessation medication prescribing [27]. In the USA, the two studies (Oregon, and multi-state) [50,56] examined the introduction of incentive payments via the 'Meaningful Use' scheme, however as this intervention included several measures from multiple implementation strategy domains, it is not possible to disentangle individual effects. These studies found an increase for practitioner-level outcomes: an increase in smoking status recording [50,56], cessation counselling [50] and cessation medication prescribing [50]. For patient-level outcomes, one study indicated an increase in cessation too [50]. In contrast, the only study assessing a patient-level outcome of the QOF 2004 found no effect on cessation [40].

Facilitators/barriers. A suggested barrier to effectiveness on the cessation medication prescribing outcome was incorrect wording/electronic coding of clinical targets [27,30,32] – authors recommended that the clinical behaviours and outcome measures targeted are made clearer [27]. Another proposed barrier to effectiveness was the way the implementation outcomes are measured: some authors suggested that any observed increase in cessation advice-giving may not reflect an increase in 'real life', but rather more complete recording of advice GPs were already giving [28,32]. Alternatively, GPs may have increased their provision of cessation advice, but patients were not recognising it as 'advice' [28,39], perhaps due to improper practitioner training on smoking cessation and the delivery of the 5As/VBA [39]. Hence, uncertainty regarding real-world cessation advice provision may be the reason for the mixed effect observed for the cessation medication prescribing outcome. A proposed facilitator was to combine financial incentives with other quality improvement initiatives,

such as active dissemination of cessation guidelines and ongoing training [39] and support for front-line staff, within a comprehensive tobacco control strategy [44].

Use capitated payments (Category 65)

The two studies [72,75] in this category assessed capitated payments (where providers of care are given a set amount of money per patient for delivering clinical care). One [72] (described in more detail in Category 66 below) assessed other measures in addition to capitated payments so it is not possible to disentangle individual effects there. Both studies in this category were at serious risk of bias.

Effectiveness. The two studies [72,75] found no effect on cessation advice provision, and one [75] found no effect on cessation medication prescribing. No patient-level outcomes were measured.

Facilitators/barriers. A proposed barrier was regarding cultural factors within health infrastructures, one study suggested that physicians did not consider cessation treatment to fit with the "traditional curative model of medicine" and that physicians assume they know the barriers which prevent their patients from quitting [75].

Change infrastructure (Domain 9)

Fourteen studies [34–37,41,50,52,53,55,56,59,67,68,72] evaluated an intervention using an implementation strategy that involved infrastructure change aiming to increase the provision of smoking cessation treatment in primary care.

Mandate change (Category 66)

The two studies [36,72] assessed aspects of wider infrastructure change which aimed to increase smoking cessation treatment provision in primary care. One study [72] investigated a broad national health infrastructure change occurring between 2003–2010 in Turkey ('Health Transformation Program') alongside other measures, the other study [36] investigated

a change in 2013 to the public health commissioning infrastructure in England (where responsibility for commissioning cessation services was transferred to regional budgets). Both studies were at serious risk of bias.

Effectiveness. Only practitioner-level outcomes were measured. The Turkish study [72] found no effect on the provision of cessation counselling. The English study [36] found a negative effect on the prescribing of any and dual NRT to pregnant women who smoke.

Facilitators/barriers. A proposed barrier for effectiveness was that external policies which indirectly result in the decommissioning of cessation services decrease the stimulus for GPs to discuss smoking cessation and directly prescribe NRT in primary care [36].

Change record systems (Category 67)

The two studies in this category both assessed multiple implementation strategy domains, so it is not possible to disentangle individual effects for this category. Both studies have been described earlier: one examined the 'Meaningful use' (MU) scheme in Oregon, USA which included changing recording systems alongside other measures [50], and the other was the broad health infrastructure change in Turkey which included changing recording systems as one of its measures [72]. One study was at serious risk of bias [72] and one moderate [50].

Effectiveness. For practitioner-level outcomes, the Turkish study found no effect on the provision of cessation counselling [72]. The Oregon study [50] found increased smoking status recording, cessation counselling and prescribing of cessation medications. Patient-level outcomes were only assessed in the Oregon study which also indicated an increase in cessation [50].

Facilitators/barriers. A proposed facilitator from the Oregon study which indicated effectiveness was that the change to the recording system aligned well with an existing practice in the clinic (having smoking status as a 'vital sign') [50].

Create or change credentialing and/or licensure standards (Category 69)

The seven studies in this category investigated either an expansion to the indications for NRT to new patient populations in primary care [34,35,41] or the publication of new/updated national guidelines regarding smoking cessation treatment [37,53,55,67]. Five studies were at moderate risk of bias [34,35,37,53,67], two serious [41,55].

Effectiveness. Most of the effects were measured for practitioner-level outcomes. In the UK, the expansion of indications for NRT in 2005 did not increase prescribing of NRT to pregnant women who smoke [41], to adolescents who smoke [34], or to patients who have cardiovascular disease who smoke [35]. Publication of the national guideline related to varenicline in 2007 in the UK increased prescribing of varenicline but had no effect on the overall prescribing rate for cessation medications [37]. In the USA (multi-state), the release (1996) and update (2000) of the national guidelines for the treatment of tobacco use had no impact on the recording of smoking status or cessation advice [53]. In the USA (multi-state), the 2013 national guideline recommendation to provide low-dose computed tomography for lung cancer screening for certain patients who smoke led to an increase in cessation counselling recording and referral to smoking cessation programs, and increased smoking cessation medication prescribing [55] – however the outcome measure for this study may have been confounded by the re-released 2015 national guideline recommendation for clinicians to offer cessation support to smokers. In the Netherlands, the introduction of the first national tobacco treatment guideline in 2007 did not have any significant immediate or long-term trend impact on primary care prescriptions of smoking cessation medications or dispensed prescriptions [67]. The only study to assess a patient-level outcome was the Dutch study, which found no significant effect of this intervention on cessation [67].

Facilitators/barriers. A proposed barrier for the lack of increase on NRT prescribing to patients who have cardiovascular disease who smoke was that external factors – perhaps even the increase in the prescription of varenicline – led to a widespread decrease in prescribing for NRT [35]. Regarding guideline publications, a proposed facilitator to achieve effectiveness was that future guideline changes should be accompanied by other measures which target the time barriers that clinicians face, such as systems-level interventions that

can identify patients' smoking status and support clinicians' efforts by facilitating referral to resources outside the physician's office [53].

Change accreditation or membership requirements (Category 71)

Of the five studies in this category, two studies [52,72] investigated accreditation programs for primary care *physicians* and were at serious risk of bias. The other three [56,59,68] investigated changing accreditation standards for primary care *practices* and were at moderate risk of bias.

Effectiveness. For the accreditation programs for physicians [52,72], only practitioner-level outcomes were measured. The program in Turkey (already described) found no effect on the provision of smoking cessation counselling [72]. The other study in the USA (multi-state) [52] found that patient-recalled cessation advice increased significantly post-intervention. For the accreditation standards for practices [56,59,68], most of the effects were measured for practitioner-level outcomes. In the two multi-state studies in the USA, there was an increase in the recording of smoking status [56,59] and provision of cessation interventions [59] following the change of standards which applied to community health centres. However, in one of the studies [56] (described above), incentive payments were also introduced as the change to standards occurred so the effects of individual implementation strategies cannot be disentangled. In the Netherlands [68], the accreditation program for primary care in 2005 had a mixed effect on smoking status recording (no effect for COPD patients, but positive effect for cardiovascular patients) and an uncertain effect on cessation advice provision. This study had no effect on the patient-level outcome: cessation [68].

Facilitators/barriers. A proposed facilitator was that quality improvement interventions may be effective if they are compatible with and integrated into the clinics' usual culture and systems of care [52]. These may be attractive to physicians because they can take ownership of the tailored improvement plans, but the intervention should be simple [68].

Engage consumers (Domain 7)

Three studies [33,46,51] evaluated an intervention which used an implementation strategy that involved engaging people who smoke to raise awareness about the availability of cessation treatment in primary care. The facilitators and barriers are discussed for the domain.

Prepare patients/consumers to be active participants (Category 54)

Of the two studies in this category, one examined the introduction of smoke-free legislation in England [33] because an indirect target was to increase smoking cessation treatment in primary care. The other study in Delaware, USA was the 'Ask and Act' program which displayed patient materials in primary care clinics designed to engage patients who smoked, alongside other measures [51]. One study was at moderate risk of bias [33] and one serious [51].

Effectiveness. One study found that prescribing of all smoking cessation medications increased in the months leading up to the introduction of smoke-free legislation, but this increase was not sustained [33]. The other study found an increase in cessation advice recording (practitioner-level outcome) and an increase in cessation (patient-level outcome) following the program which engaged patients who smoked [51], but the authors implied the effect was more likely due to the other 'educating healthcare professionals' components of the intervention (Domain 5, below).

Use mass media (Category 56)

The only study [46] in this category evaluated the impact of anti-tobacco mass media advertising and pharmaceutical company-funded smoking cessation medication advertising in England, and was at moderate risk of bias.

Effectiveness. The only relevant finding was that neither intervention had a significant effect on NRT prescribing in primary care (practitioner-level outcome) [46].

Facilitators/barriers: A proposed facilitator was that when engaging consumers, the intervention needs to be sustained for longer durations [33,46] or that consumers need to be engaged in multiple ways, considering other contextual factors and social norms around tobacco use [33].

Train and educate stakeholders (Domain 5)

Three studies in this domain [51,70,74] evaluated an intervention which used an implementation strategy that involved training and educating healthcare professionals in primary care who deliver cessation treatment. The facilitators and barriers are discussed for the domain.

Distribute educational materials (Category 40)

Of the two studies in this category, one examined the 'Ask and Act' program in Delaware, USA (mentioned above) which included a measure where cessation materials were distributed to physicians [51]. The other study evaluated an intervention where an educational pack designed to prompt the delivery of smoking status assessment and cessation advice was distributed to GPs in Victoria, Australia [70]. Both studies [51,70] were at serious risk of bias.

Effectiveness. For practitioner-level outcomes, one study [70] found no effect on smoking status recording but both studies found an increase in cessation advice provision [51,70]. For patient-level outcomes, one study [51] indicated increased cessation – however, the intervention also involved 'Conduct educational meetings' (Category 42) and 'Prepare patients/consumers to be active participants' (Domain 7, Category 54), but the authors implied that the effect can likely be attributed to Domain 5.

Conduct educational meetings (Category 42)

Of the two studies in this category, one examined the 'Ask and Act' program in Delaware, USA (mentioned above) which included a measure which delivered continuing medical

education programs for physicians [51]. The other study evaluated the Finnish 'National Programme for Chronic Bronchitis and COPD 1998-2007' where training events were organised for primary healthcare personnel [74]. Both studies [51,74] were at serious risk of bias.

Effectiveness. For practitioner-level outcomes, one study [74] found a positive effect on smoking status recording and the other study [51] found increased cessation advice recording. The Delaware study [51] also found an increase in cessation (patient-level outcome), but, as aforementioned, this intervention covered multiple implementation strategy categories.

Facilitators/barriers: For this domain, proposed facilitators were the simplicity of the educational material the physicians received [70] and it was suggested that educating physicians in smoking cessation treatment can lead to physicians feeling more comfortable with delivering and billing for cessation counselling [51].

RQ4: Cost-effectiveness of implementation strategies

Some studies [28,30,32,38,43,45,47,66,69] included the cost of the interventions but none investigated cost-effectiveness.

Discussion

Summary of evidence

This systematic review aimed to find evidence for the adoption of implementation strategies on a national/state-wide scale, and effectiveness and cost-effectiveness regarding smoking cessation treatment provision and patient smoking outcomes in real-world primary care settings. The 49 included studies assessed only four out of nine implementation strategy domains. The majority of studies identified in this review did not measure patient-level outcomes. We found some evidence for interventions which utilized financial strategies having a beneficial impact on cessation. There were 34 studies which investigated interventions **utilizing financial strategies**, with only four being at low risk of bias. These

appeared to increase the recording of smoking status and cessation advice, but the effect on cessation medication prescribing was mixed. Only one study assessed quit attempts and it found no effect, but seven out of nine studies which assessed smoking cessation found an increase. There were 14 studies which investigated interventions **changing infrastructure**, none at low risk of bias. These had mixed results for smoking status recording, cessation advice provision and cessation medication prescribing. No studies measured quit attempts, and one out of three studies which assessed smoking cessation found an increase. Only three studies, all at serious risk of bias, investigated interventions which **trained and educated stakeholders.** These indicated a beneficial impact on smoking status and cessation advice recording, and smoking cessation, but should be interpreted with caution because the evidence was low-quality. There were three studies which investigated interventions **engaging consumers**, none at low risk of bias. Two studies showed no effect on cessation medication prescribing in primary care. One study assessed cessation advice provision and cessation (both increased), but the intervention also involved implementation strategy categories which involved training and educating stakeholders and the effectiveness was attributed to this latter domain by the study authors. No studies assessed cost-effectiveness.

Authors of the included studies suggested a range of barriers and facilitators. Some key facilitators were the simplicity of the intervention and external policies/incentives which were complementary to the smoking cessation aims of the intervention (such as, wider tobacco control measures and funding for public health and cessation clinics) and having the ability for physicians to refer smokers to cessation programs or community-based support. Some of the key barriers included time and financial constraints, lack of free cessation medications and follow-up, deprioritisation and unclear targets in primary care, lack of knowledge of healthcare professionals, and insufficient messaging to patients about available cessation support options. Some of the key barriers identified were similar to those identified recently by the UK Royal College of Physicians [76].

This review complements the findings of a recent Cochrane review [20] which evaluated randomised and cluster-randomised trials of similar interventions but in controlled environments. There appears to be a 'gap' between the implementation strategies that

have been enacted on a national/state-wide scale (identified by this review) and those demonstrating efficacy in trials [20]. While trials indicated efficacy of adjunctive counselling and tailored print materials on quit rate [20], no studies have assessed these interventions in national implementation.

Trials found a beneficial impact of adding cost-free medications to standard cessation support on smoking quit rates and quit attempts [20]. Regarding real-world implementation, this review found some evidence that increasing access to health insurance which included coverage for smoking cessation treatment had a beneficial impact on the recording of smoking status, the provision of cessation advice and cessation medications, and cessation. The only study which assessed quit attempts found no effect [57]. Where new free cessation medications were introduced, prescribing of the new medication increased but there was no change in overall prescribing for cessation medications (other outcomes were not assessed).

Trials found no clear evidence that provider incentives could increase smoking cessation [20]. In real-world implementation of financial incentives studied in this review, cessation outcomes were only assessed in two out of 16 studies (one showed an increase [50], one no effect [40]). We found evidence that a nationally implemented financial incentive for GPs was effective in increasing the recording of smoking status and cessation advice, and (in one study [27]) referral to cessation services; however, there was a mixed effect on cessation medication prescribing and smoking cessation. We also identified studies where primary care practices received funding to deliver national cardiovascular disease prevention programs (including health checks); these overall indicated increased smoking status recording, cessation advice and cessation medication provision, and cessation. There was no robust evidence regarding capitated payments.

Trials found some evidence for provider training, either individually or in combination with other interventions: the former having some beneficial impact on smoking status recording, cessation advice provision, cessation counselling, and providing self-help materials; the latter, a beneficial impact on quit rates and some outcomes of cessation assistance (setting a quit date, providing self-help materials, and arranging patient follow-up) [20]. We identified some low-quality evidence of provider training as a 'real-world' intervention (three studies,

all at serious risk of bias), having a beneficial impact on smoking status recording, cessation advice recording, and cessation.

Strengths and limitations

A robust approach was used to identify and synthesise relevant literature using a pre-registered protocol and a comprehensive search strategy. However, the search strategy may not have identified all relevant papers, because different terminology exists internationally for 'primary care setting' and no effective observational study filter exists [77]. To mitigate against this, the search terms from a recent Cochrane review [20] were used, the search strategy was piloted, and backward and forward citation tracking of included studies was conducted. A limitation is that only articles in English were included.

This systematic review investigated the scalability of national and state-wide policies, where policies were implemented without researcher input over large geographical areas, potentially diverse in patient and provider characteristics. This review evaluated observational studies which, whilst at risk of bias and unable to demonstrate causality, can provide evidence of real-world implementation. A large number of studies were included in the evidence synthesis, however, only half were at moderate or low risk of bias. Despite an international scope, most studies were set in the UK and the USA. In six studies, the intervention involved multiple implementation strategy categories and it was challenging to disentangle their individual effects.

Implications and recommendations

Our findings indicate that during the development of future implementation strategies, a significant consideration should be given to the current demands of the primary care setting, such as existing time constraints and clinical priorities; future implementation strategies should better align with existing technologies and the routine systems in place; and the clinical outcomes which are targeted should be clearly communicated. We

recommend profiling, both in the clinic and in government papers, that smoking cessation is a key priority and that various cessation support is available.

Future research could investigate the five implementation strategy domains not identified by this review ('Use of evaluative and iterative strategies', 'Provide interactive assistance', 'Adapt and tailor to context', 'Develop stakeholder inter-relationships', 'Support clinicians') and the strategies that were efficacious in the controlled-trial setting [20]: adjunctive counselling and tailored print materials. However, we recommend that the perceived facilitators and barriers identified by this review are considered when designing interventions.

We advise that hybrid effectiveness-implementation designs [15] are used, where studies robustly assess both the effectiveness of implementation strategies on (practitioner-level) provider performance as well as (patient-level) smoking outcomes. Additionally, we recommend measuring 'advice provision about e-cigarettes' as an additional outcome – due to the relative novelty of e-cigarettes being recommended as harm reduction tools in clinical guidelines (in 2021 in the UK [6] and Australia [78]), none of the studies in this review investigated this. Lastly, we recommend using methods such as Multiphase Optimization Strategy (MOST) [79], which consider the time and resource constraints of clinical settings, and verify that all the components of the 5As/VBA or the proposed implementation strategy interventions are optimised and cost-effective.

Conclusions

This systematic review aimed to find evidence for the adoption, on a national or state-wide scale, of implementation strategies aiming to increase smoking cessation treatment provision in real-world primary care settings. The implementation strategies identified involved utilizing financial strategies, changing infrastructure, training and educating stakeholders, and engaging consumers. The first three strategies appeared to increase the rate of smoking status recording and cessation advice provision in primary care. The most amount of evidence was identified for the utilizing financial strategies domain, which also appeared to increase smoking cessation.

Availability of data and materials

The systematic review protocol (ID: CRD42021246683) is available at https://www.crd.york.ac.uk/prospero/display_record.php?RecordID=246683. As not all the included studies are available Open Access, the completed data extraction form and PDFs of the 49 included studies are available from the corresponding author on reasonable request.

Competing interests

AM is a National Institute for Health Research (NIHR) Senior Investigator. The views expressed in this article are those of the authors and not necessarily those of the NIHR. The other authors (BT, PP-H and LB) declare no conflicts of interest.

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Abbreviations

CFIR – Consolidated Framework for Implementation Research

COPD – Chronic Obstructive Pulmonary Disease

ERIC – Expert Recommendations for Implementing Change

GP – General Practitioner

MOST – Multiphase Optimization Strategy

NHS – National Health Service

NRT – Nicotine Replacement Therapy

QOF – Quality and Outcomes Framework

ROBINS-I – Risk Of Bias In Non-Randomized Studies of Interventions

SSS – Stop Smoking Service

UK – United Kingdom

USA – United States of America

VBA – Very Brief Advice

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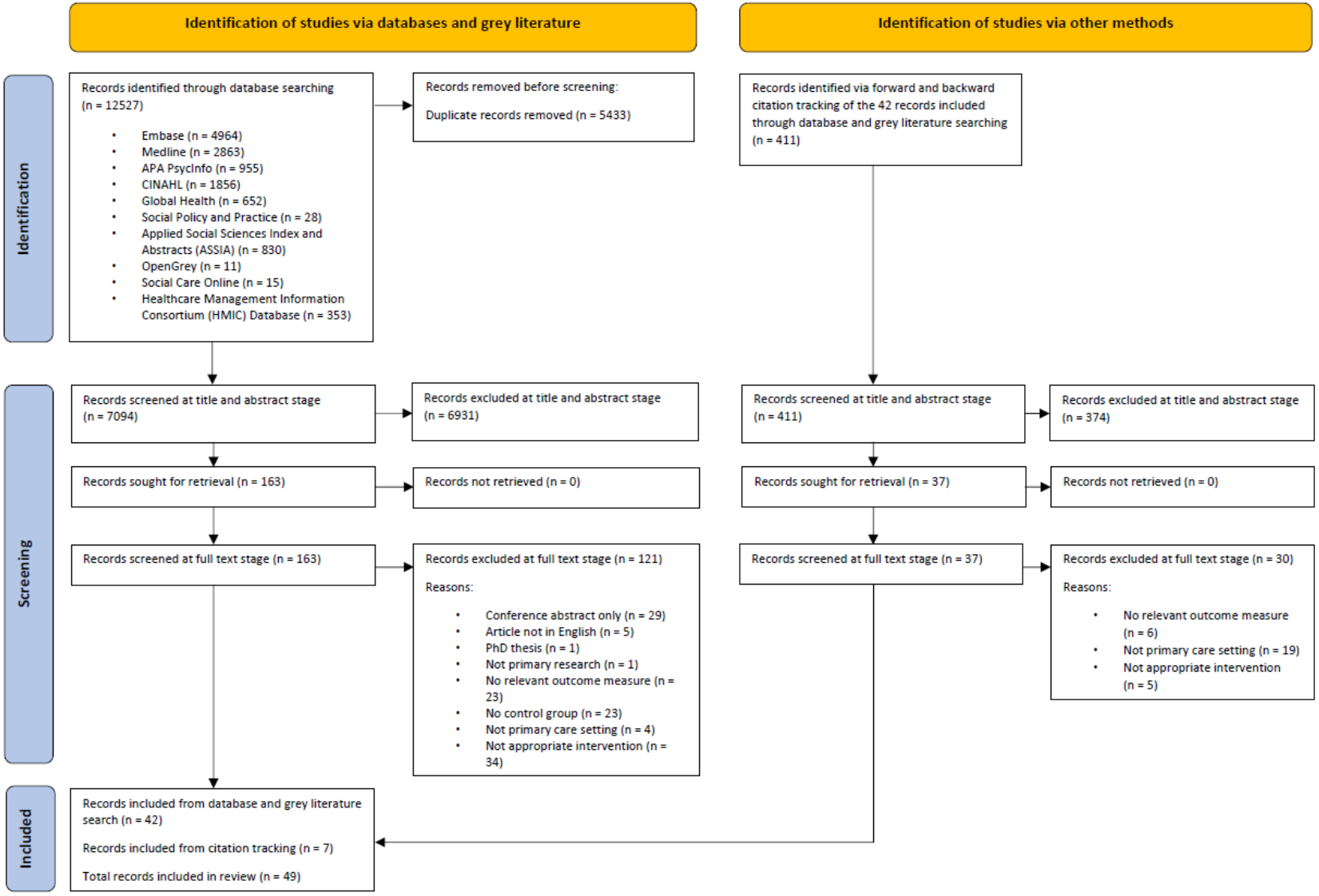
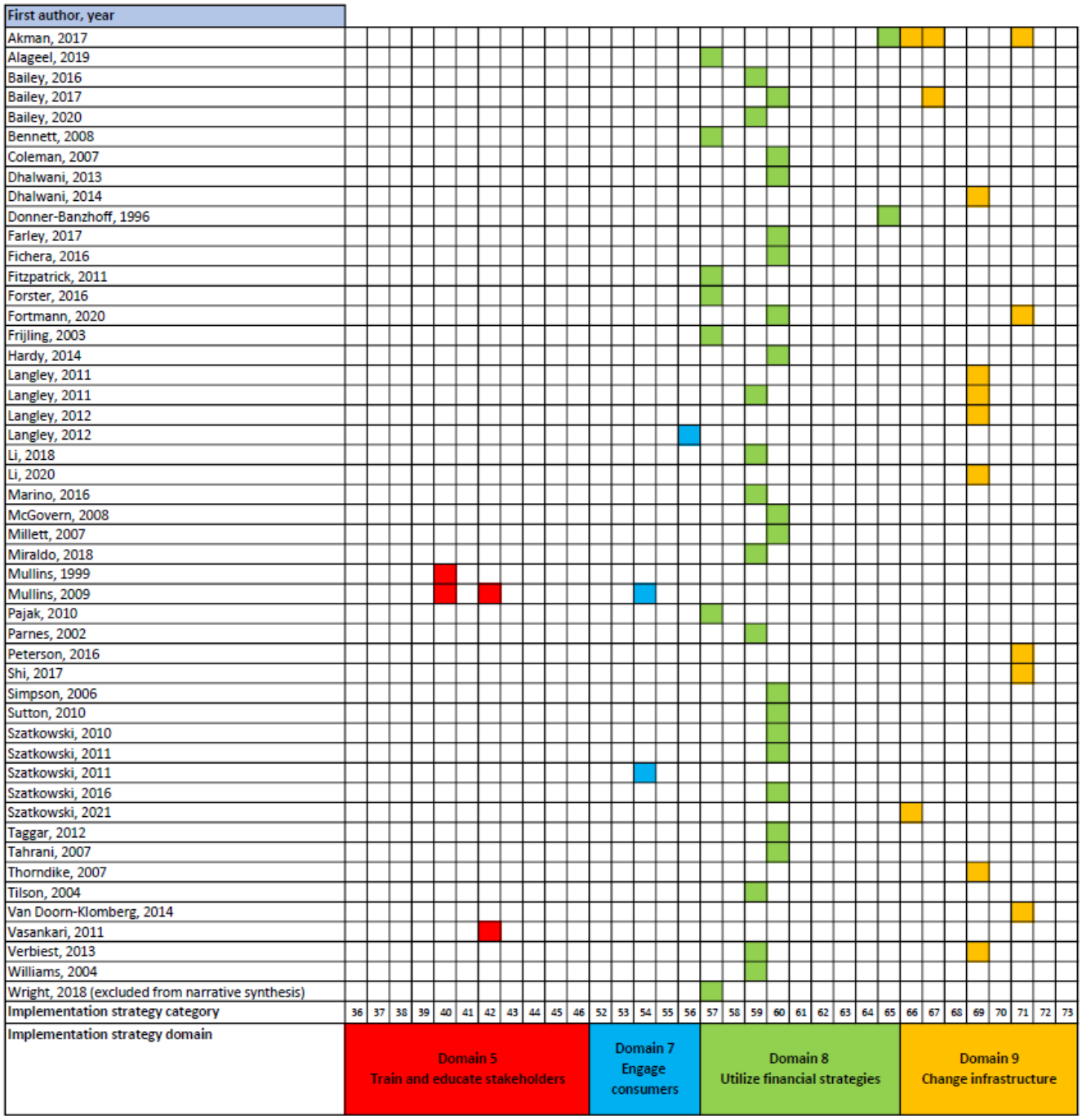
Figures and tables

Figure 3.1. PRISMA flow diagram



PRISMA flow chart showing the number of papers identified through the search strategy and the study selection process.

Figure 3.2. Implementation strategy categories identified in the included studies



Implementation strategy categories identified in the included studies. The interventions in the 49 included studies were coded to the implementation strategy domains (1 to 9) and categories (1 to 73) developed by the Expert Recommendations for Implementing Change (ERIC) program [18, 19]. Each column represents one of the 73 implementation strategy categories. A shaded cell indicates the specific strategy that the intervention under investigation in the study involved. Only the four domains that were identified are displayed in this figure. The other domains were not included in any of the studies: Use of evaluative and iterative strategies (Domain 1), Provide interactive assistance (Domain 2), Adapt and tailor to context (Domain 3), Develop stakeholder inter-relationships (Domain 4), Support clinicians (Domain 6). (Wright, 2018) [71] was excluded from narrative synthesis as it was at critical risk of bias.

Table 3.1. Study characteristics

First author, year	Location	Implementation strategy category	Study design	Patient population (within primary care setting)	Data source and outcome measure definition
Domain 5. Train and educate stakeholders					
Mullins, 1999 [70]	Victoria, Australia	40. Distribute educational materials	Repeated cross-sectional study Analytical	Aged 16 years and over, smokers 1990: *n* = 624 1992: *n* = 596 1994: *n* = 609 1996: *n* = 563	Data source: Population-based survey of adults in Victoria Outcome measure: Practitioner-level: Each year, smokers were shown a card, and asked, "Which of any of those things has your GP ever said to you?". Mutually exclusive categories were created by developing a hierarchy of response, and each respondent was coded according to the most appropriate advice he or she had ever been given
Vasankari, 2011 [74]	Finland	42. Conduct educational meetings	Repeated cross-sectional study Analytical	Aged 16 years and over, respiratory symptoms 1997: *n* = 1,072 patients 2002: *n* = 1,645 patients	Data source: Electronic patient record system of one "medium-sized primary healthcare center in south-west Finland with computerized patient records" Outcome measure: Practitioner-level: "history of smoking", "data on smoking status available"
Domain 7. Engage consumers					
Szatkowski, 2011 [33]	England	54. Prepare patients/consumers to be active participants	Repeated cross-sectional study Interrupted time series analysis (no control)	Aged 16 years and over, smokers 2000 to 2009: *n* = missing	Data source: UK-representative primary care electronic healthcare records, THIN Outcome measure: Practitioner-level: British National Formulary drug codes were used to identify smokers with one or more prescriptions for NRT, bupropion or varenicline recorded in their notes each month. Not

First author, year	Location	Implementation strategy category	Study design	Patient population (within primary care setting)	Data source and outcome measure definition
					enough data to model trends in prescribing of varenicline
Langley, 2012 [46]	England (and Wales)	56. Use mass media	Repeated cross-sectional study Interrupted time series analysis (no control)	Unspecified January 2002 to June 2009: *n* = missing "Some of the outcome data cover England only, but due to the make-up of the United Kingdom's TV regions, TVRs for Wales cannot be separated from those for England."	Data source: UK-representative primary care electronic healthcare records, THIN Outcome measure: Practitioner-level: "prescribing of NRT"
Domain 8. Utilize financial strategies					
Alageel, 2019 [31]	England	57. Fund and contract for the clinical innovation	Cohort study Interrupted time series analysis (with control)	Aged between 40–74 years Intervention group: had a health check recorded between 1 April 2010 and 31 December 2013 (Read medical codes indicating that a health check or CVD risk assessment was completed) (*n* = 127,891 participants, from 431 general practices in England) "Consistent with the eligibility criteria for the NHS Heath Check, health check participants were excluded if they had diagnoses of ischaemic heart disease, stroke or diabetes, or were treated	Data source: UK-representative primary care electronic healthcare records, CPRD Outcome measure: Practitioner-level and patient-level: "Read codes relating to smoking and smoking advice." "Product codes indicating prescription of smoking cessation therapy." "Smoking cessation interventions were divided into two categories: referrals to a smoking-cessation advisor or stop smoking clinic and medication (nicotine replacement therapy)."

First author, year	Location	Implementation strategy category	Study design	Patient population (within primary care setting)	Data source and outcome measure definition
				with antihypertensive drugs or statins before the date of the health check." Matched cohort: matched for age, sex, and general practice, participants who did not receive the check with follow-up data available up to the latest date of 31 March 2017 (*n* = 322,910)	
Bennett, 2008 [65]	Ireland	57. Fund and contract for the clinical innovation	Cohort study	Patients with diagnosis of coronary heart disease ("patients attending primary care from February 2003 after an acute myocardial infarction (AMI) or coronary intervention, such as percutaneous coronary intervention or coronary artery bypass grafting, which may have been recent or some time ago." 2004, 1-year follow-up cohort: *n* = 7,099 patients, 84.4% had four or five visits over the year 2005, 2-year follow-up cohort: *n* = 4,011 patients, 60.5% had at least eight or nine visits over 2 years	Data source: Primary care electronic medical records. 470 (20%) of all Irish GPs were selected to participate in the programme Outcome measure: Patient-level: "the percentage smoking prevalence was calculated based on an individual having at least one of the following recorded: smoker of one or more cigarettes per day, cigar or pipe smoker." "Absolute change in risk factors between baseline and the 1-year or 2-year follow-up visit was calculated."

First author, year	Location	Implementation strategy category	Study design	Patient population (within primary care setting)	Data source and outcome measure definition
Fitzpatrick, 2011 [66]	Ireland	57. Fund and contract for the clinical innovation	Cohort study	Patients with diagnosis of coronary heart disease (significant proven coronary heart disease (CHD); a history of myocardial infarction (MI), percutaneous coronary intervention or coronary artery bypass graft surgery) 2004, 1-year cohort: *n* = 8,309 patients 2005, 2-year cohort: *n* = 5,431 patients 2006, 3-year cohort: *n* = 3,470 patients 2007, 3.5-year cohort: *n* = 2,078 patients	Data source: Primary care electronic medical records. The programme involved 480 (20%) of general practices Outcome measure: Patient-level: "The percentage smoking was calculated based on an individual having one or more of the following recorded — smoker of one or more cigarettes per day, cigar or pipe." "Absolute changes in risk factors between baseline and follow-up were calculated." "medication prescription" **raw figures not available for smoking cessation medication prescription
Forster, 2016 [48]	England	57. Fund and contract for the clinical innovation	Cohort study	Aged between 40–74 years Intervention group: had a health check recorded between 1 April 2010 and 31 March 2013, never treated with antihypertensive drugs or statins, and not diagnosed with diabetes, stroke or coronary heart disease before the check (*n* = 91,618 patients) Control group: (n = 182,245 patients), matched controls were identified for 75,123 (82%) of the intervention group	Data source: UK-representative primary care electronic healthcare records, CPRD Outcome measure: Practitioner-level: "The date of each risk factor record was evaluated with reference to the date of the Health Check (the date of the check was the reference date for the cases and their matched controls were also assigned this date of the check). We evaluated risk factor detection, including … the proportion with current smoking recorded…"

First author, year	Location	Implementation strategy category	Study design	Patient population (within primary care setting)	Data source and outcome measure definition
Frijling, 2003 [69]	Netherlands	57. Fund and contract for the clinical innovation	Controlled before-and-after trial	Aged 60 years and over, with high cardiovascular risk (diagnosed with diabetes, hypertension, hypercholesterolaemia, have cardiovascular disease history or family history of coronary heart disease) Intervention group: 420 practices randomly invited from the 800 practices participating in the nationwide project. Response to baseline (October 1998) and post-intervention (September 2000) questionnaire: 316 GPs (84.0%)—returned the shortened version of the post-intervention questionnaires: 37 GPs (11.7%) Control group: 600 practices randomly invited from the 4000 practices which did not participate in the nationwide project. Response to baseline (October 1998) and post-intervention (September 2000) questionnaire: 301 GPs (77.2%)—returned the shortened version of the post-	Data source: GP postal questionnaire Outcome measure: Practitioner-level: "The information was provided by one GP per practice and the same GP for both measurement points." "Assessment of … the following risk factors: … smoking habits." "the GPs were asked whether the minimal contact intervention (MCI) for smoking cessation was used in their practices"

First author, year	Location	Implementation strategy category	Study design	Patient population (within primary care setting)	Data source and outcome measure definition
				intervention questionnaires: 74 GPs (24.6%)	
Pajak, 2010 [73]	Poland	57. Fund and contract for the clinical innovation	Cohort study	Aged between 35–55 years. "Free of cardiovascular disease and with medical documentation going back to at least 1 January 2005". The final examination was conducted in 2007 Active clinics: 33 clinics, *n* = 3,940 patients. *n* = 1,244 patients (31.6%) participated in the PCVDP. Participated in final examination: n = 2,314 patients (58.7%) Control clinics: 33 clinics, *n* = 3,162 patients. Participated in final examination: *n* = 2,107 patients (66.6%)	Data source: Patient healthcare records, patient questionnaire Outcome measure: Practitioner-level: "Information on risk factors (smoking)" in patient healthcare records Patients were interviewed by a trainer interviewer, current smoker patients were asked whether they received "verbal advice or leaflets" regarding tobacco cessation, whether they were "referred to a specialist clinic", whether they received "pharmacotherapy", and whether they discussed "other methods" regarding tobacco cessation Patient-level: Patients reaching "prevention targets" ("not smoking"), but this seems to be 'non-smoking prevalence at final examination'
Wright, 2018 [71]	Australia	57. Fund and contract for the clinical innovation	Cohort study	Aboriginal and Torres Strait Islander people, aged 15 years and over, "has attended the health service [at least] three times in the past 2 years", 2014–2016 65% of all services that provide national key performance indicator (nKPI) data (152/233)	Data source: Aggregate service-level patient electronic health records; national key performance indicator (nKPI) data Outcome measure: "(1) the number (and proportion) of clients with a smoking status recorded in the health service records; and (2) the number (and proportion) of clients with smoking status recorded as current, ex- and non-smoker."

First author, year	Location	Implementation strategy category	Study design	Patient population (within primary care setting)	Data source and outcome measure definition
				were included: 44 TIS currently funded services and 108 non-TIS-funded services 'Exposure' was defined as an organisation that was funded (*n* = 44/152) either directly or indirectly (via consortium arrangements) by the Australian Government's TIS program 2016: *n* = 81,187 clients accessed TIS-funded services, *n* = 85,098 clients accessed non-TIS-funded services	**Timeline of intervention is unclear. TIS program started in 2016. This study uses 2014 as the pre-intervention timepoint, and 6-months into 2016 as the post-intervention/during intervention timepoint
Bailey, 2016 [54]	Oregon, USA	59. Place innovation on fee for service lists/formularies	Cohort study	Aged between 19–64 years, smokers. "Low-income adults". Pregnant women excluded Intervention group: *n* = 5,935 patients gained Oregon Medicaid coverage between 2008 and 2011 after being uninsured for ≥ 6 months and who maintained this insurance for ≥ 6 months Control group: *n* = 9,371 patients who did not gain Medicaid, patients who were continuously uninsured throughout the 24-month	Data source: Primary care electronic healthcare records (Oregon Community Health Information Network, "OCHIN, Inc.") Outcome measure: Patient-level: "…discrete data field for smoking status, and the OCHIN workflow requires review of tobacco use status at each primary care encounter." "smoking status (i.e., current every day, current some day, former, or never smoker) can be confirmed or modified, and the reviewed or changed date is saved in the EHR. Tobacco cessation medications were abstracted from EHR medication order data." "Our primary outcome was 'quit' smoking status after the baseline assessment, coded as a binary yes/no variable. A person was

First author, year	Location	Implementation strategy category	Study design	Patient population (within primary care setting)	Data source and outcome measure definition
				follow-up period and met the current smoker criteria Final study sample included 4,140 matched pairs (*n* = 8,280 patients)	identified as 'quit' if baseline smoking status was 'current every day' or 'some day' and status changed to 'former smoker' at a subsequent visit." Practitioner-level: "We also assessed prevalence of having a smoking cessation medication ordered (yes/no), and analyzed quit smoking status stratified by whether medication was ordered. Medications included bupropion, varenicline, and all nicotine replacement products."
Bailey, 2020 [60]	United States (multi-state)	59. Place innovation on fee for service lists/formularies	Cohort study	Aged between 19–64 years. Tobacco user. Pregnant women excluded Intervention group: Medicaid-expansion states from 1 January 2014 (California, Hawaii, Maryland, Minnesota, New Mexico, Ohio, Oregon, Rhode Island, Washington, and Wisconsin), *n* = 219 primary care community health centres (CHCs). *n* = 62,164 patients Control group: non-Medicaid-expansion states (Florida, Kansas, Missouri, North Carolina, Texas, and Montana). n = 108 primary care CHCs. n = 31,881 patients States had electronic health records from 1 January 2013. Outcomes assessed 24-months	Data source: Electronic medical records (from primary care community health centres (CHCs)… This study used CHC data from the OCHIN network and the Health Choice Network (HCN)." Outcome measure: Patient-level: "The EHR presents a discrete data field for tobacco use status at each primary care encounter, which can be confirmed, updated, or not reviewed. If confirmed or updated, the date is saved. Our primary outcome was tobacco cessation ("quit") during the post-period, coded as a binary yes/no variable. … a person was identified as "quit" if the last recorded tobacco-use status during the pre-period indicated that the patient was a current user, and if there was at least one subsequent measurement documented in the post-period that indicated the patient's status was a "nonuser" (eg, former user, not a current user)." Practitioner-level: "tobacco cessation medications from EHR medication orders: bupropion, varenicline, and all nicotine replacement products"

First author, year	Location	Implementation strategy category	Study design	Patient population (within primary care setting)	Data source and outcome measure definition
				post-expansion: 31 December 2015 Propensity score matched comparison sample: expansion states (*n* = 27,670 patients), non-expansion states (*n* = 27,670 patients)	
Li, 2018 [61]	United States (multi-state)	59. Place innovation on fee for service lists/formularies	Repeated cross-sectional study Descriptive	Aged between 55–80 years. No evidence of lung cancer. Had at least one office visit to a Family Medicine or Internal Medicine provider between 1st January 2010 and 31st December 2016 2010 to 2016: *n* = 1,572,538 patient years	Data source: "Electronic health records (EHR) data from patients in a large community healthcare system located in northern California" Outcome measure: Practitioner-level: "Annual rate of documentation of smoking history is the proportion of patients who had documented smoking history among those with at least one visit in the year."
Marino, 2016 [62]	Oregon, USA	59. Place innovation on fee for service lists/formularies	Cohort study	Aged between 19–64 years "From a "reservation list" of > 100,000 entries, approximately 30,000 people were randomly selected to apply, and approximately 10,000 gained health insurance (Medicaid) coverage in 2008." In the study, the authors attempted to identify people who gained coverage and patients who were on the reservation list but were not selected to gain coverage. Outcomes assessed 36-months	Data source: Primary care electronic healthcare record (EHR) data from 49 community health centres (CHCs), OCHIN community health information network (OCHIN, Inc.), in Oregon state Outcome measure: Practitioner-level: "The primary outcomes were whether or not the patient received preventive care services in the post-period: … smoking. Codes were used based on EHR Meaningful Use Stage 1 measures." "Screening for smoking", "assessment of smoking status"

First author, year	Location	Implementation strategy category	Study design	Patient population (within primary care setting)	Data source and outcome measure definition
				after the selection date (~ 2011) Intervention group: Randomly selected to apply for health insurance coverage: *n* = 4,049 people. Gained health insurance coverage: n = 1,718 people (44% of n = 4,049 actually gained coverage) Control group: Not selected to apply for health insurance coverage: *n* = 6,594 people	
Miraldo, 2018 [57]	Massachusetts, USA	59. Place innovation on fee for service lists/formularies	Repeated cross-sectional study with control Difference-in-differences (DD) and triple differences (DDD) design	Aged between 18–64 years. Had low income (income below 300% of the federal poverty level) Intervention group: Massachusetts Control group: other New England States (ONES) (Connecticut, New Hampshire, Rhode Island, Maine and Vermont), and higher income groups in Massachusetts who were unaffected by the reform Differences-in-differences (DD) method: Massachusetts vs ONES. "The total sample used for the difference-in-differences (DD) analysis	Data source: Population-based survey of adults in multiple states within the USA. (Behavioural Risk Factor Surveillance System (BRFSS)). "The BRFSS is a state-based survey … involves random-digit dialling (between 2001 and 2010 only landline numbers were included) and a random selection of one adult within that household to participate in a telephone survey." Outcome measure: Patient-level: self-reported: "Current smokers that tried to quit smoking in the past year"

First author, year	Location	Implementation strategy category	Study design	Patient population (within primary care setting)	Data source and outcome measure definition
				consisted of 131,002 individuals; 39,745 from Massachusetts and 91,257 from ONES." Triple differences (DDD) method: low income and high income patients in Massachusetts vs low income and high income patients in ONES "Massachusetts had the lowest response rate from 2001 to 2007 and for 2010, ranging from 34.6% to 47.7%." In 2008 and 2009, Connecticut had the lowest response rate at 39.8% and 44.23% respectively "The highest response rate was for Vermont in 2001 and from 2003 to 2010, ranging from 52.1% to 60.5%." "In 2002 Maine had the highest response rate at 59.4%."	
Parnes, 2002 [58]	Colorado, USA	59. Place innovation on fee for service lists/formularies	Cross-sectional study (with control group) Analytical	Aged between 13–65 years "Colorado Research Network (CaReNet) is a state-wide primary care, practice-based research network founded in 1997 with a particular focus on disadvantaged populations,	Data source: Physician survey (modified version of the 1994 National Ambulatory Medical Care Survey (NAMCS)). "The NAMCS instrument is a physician survey that collects information about an ambulatory visit." "Each CaReNet practice collected data on a total of 400 patient visits in 1-week cycles (100 patients per cycle), quarterly, for 1 year. We

First author, year	Location	Implementation strategy category	Study design	Patient population (within primary care setting)	Data source and outcome measure definition
				including rural people, minorities, and the urban poor." *n* = 7 primacy care practices in CaReNet in 1998 and 1999. (*n* = 4 family medicine residency sites, *n* = 2 federally-funded community health centers, n = 1 was clinic for the medically indigent.) CaReNet providers completed NAMCS forms on 2,773 patient encounters of 2,800 eligible visits (99% completion rate) in 1998–1999. n = 1,443 patient visit records remained after excludions. "351 patients in the study sample (24%) were identified as smokers."	used the typical NAMCS protocol of collecting data on every second patient presenting for medical care during the study period." Outcome measure: "the key modification was the addition of "uninsured" in the Expected Source of Payment category. This category included patients who were in 1 of several programs that discount charges on the basis of income, thus covering some of the costs of care." "To identify patients with private insurance, the options "Private/commercial" and "HMO/other prepaid" were combined ("Private/HMO")." Practitioner-level: "we examined the impact of patient insurance on 2 primary outcomes: (1) patient smoking status, and (2) whether smokers received smoking cessation counseling. Each provider coded smoking status as "Yes," "No," or "Unknown." Only patients with a known smoking status (90% of sample) were included in the present analysis. For those patients coded as smokers, we determined whether providers checked the "Smoking Cessation" box."
Tilson, 2004 [63]	Ireland	59. Place innovation on fee for service lists/formularies	Repeated cross-sectional study Descriptive	Medical cardholders in Ireland, who are entitled to free prescriptions of certain medicines via the General Medical Services (GMS) scheme In 2002: 29.84% of the population, *n* = 1,168,745 patients	Data source: National prescription database, General Medical Services (GMS) Payments Board prescription database Outcome measure: Practitioner-level: "Using the GMS Payments Board prescription database we conducted a detailed analysis of NRT prescribing (ATC code N07BA)" "the number of monthly prescriptions for each NRT

First author, year	Location	Implementation strategy category	Study design	Patient population (within primary care setting)	Data source and outcome measure definition
					preparation (ATC code N07BA01) and bupropion (ATC code N07BA02)" "Mean dosage, duration of therapy and age/gender distribution of NRT treatment was also obtained." "NRT therapy formulations include gum, patches and inhaled medication."
Williams, 2004 [64]	Ireland	59. Place innovation on fee for service lists/formularies	Repeated cross-sectional study Descriptive	Medical cardholders in Ireland, who are entitled to free prescriptions of certain medicines via the General Medical Services (GMS) scheme, aged 16 years and over January to December 2001: 31% of the Irish population, *n* = 919,326 patients *n* = 8,166 patients were prescribed Buproprion, *n* = 18,450 patients were prescribed NRT	Data source: National prescription database, General Medical Services (GMS) Payments Board prescription database. the GMS population "cannot be regarded as representative of the general population as socially disadvantaged persons, children and the elderly are over represented, however, they receive about 70% of all medicines prescribed in Irish general practice." Outcome measure: Practitioner-level: "identified those patients who were prescribed Buproprion or NRT"
Coleman, 2007 [32]	UK	60. Alter incentive/allowance structures	Repeated cross-sectional study Analytical	Aged between 15–75 years. 1990 to 2005 1990: *n* = 776,302 patients 2000: *n* = 1,569,177 patients 2004: *n* = 1,607,782 patients	Data source: UK-representative primary care electronic healthcare records, THIN Outcome measure: Practitioner-level: "smoking status, recorded advice given to stop smoking and prescriptions for nicotine replacement therapy (NRT) or bupropion."

First author, year	Location	Implementation strategy category	Study design	Patient population (within primary care setting)	Data source and outcome measure definition
Dhalwani, 2013 [38]	UK	60. Alter incentive/allowance structures	Repeated cross-sectional study Descriptive	Pregnant women January 2000 to December 2009: *n* = 277,552 pregnancies, *n* = 215,703 women with pregnancies resulting in live births or stillbirths	Data source: UK-representative primary care electronic healthcare records, THIN Outcome measure: Practitioner-level: "Records of maternal smoking status during pregnancy were identified using Read codes. These included codes for current, never, and ex-smoking, codes indicating the type or number of cigarettes smoked, and codes indicating smoking cessation interventions delivered to patients. Women were also considered to be smokers if they had a prescription for a smoking cessation drug (nicotine replacement therapy, bupropion or varenicline) in their medical records during pregnancy." "The prevalence of smoking status recording during pregnancy was calculated for each year from 2000 to 2009 as the number of pregnancies with at least one recording of smoking status during the gestational period divided by the total number of pregnancies delivered in that year." "Since April 2006 the QOF has not required GPs to record the smoking status of patients after the age of 25 years if they have been a never smoker until that age. After 2008, if a patient who once smoked has been recorded as an ex-smoker for three years, GPs need no longer check and update the patient's smoking status records. Therefore, we recalculated the proportion of pregnancies with missing gestational smoking status data to take these rules into account. For women who only had records of being a never smoker up to age 25 and who did not

First author, year	Location	Implementation strategy category	Study design	Patient population (within primary care setting)	Data source and outcome measure definition
					have a record of smoking during a subsequent pregnancy we imputed a never smoking record during gestation. Similarly, for women who had no smoking status records during gestation but who were recorded as ex-smokers for three consecutive years before the conception we imputed an ex-smoking record during gestation. We then recalculated the annual proportion of pregnancies with a recording of smoking status during the gestational period."
Farley, 2017 [40]	UK	60. Alter incentive/allowance structures	Cohort study	Intervention group: Patients diagnosed with lung, bladder, or upper aerodigestive tract cancer between 1999–2013, had a record of smoking at diagnosis or within 3 years of diagnosis. *n* = 42,112 patients, *n* = 13,449 (32.0%) smoked at diagnosis, *n* = 3,092 (7.3%) had stopped smoking within 3 years of diagnosis Control group: Matched patients with incident CHD diagnosed during the same period as control cases based on year of diagnosis, general practice, and smoking status. *n* = 159,182 patients, *n* = 28,987 (18.2%) smoked at diagnosis, *n* = 6,301	Data source: UK-representative primary care electronic healthcare records, CPRD Outcome measure: Practitioner-level and patient-level: "the proportion of current smokers and recent ex-smokers for whom their general practitioners updated smoking status, advised patients to stop or provided advice on how to do so, and prescribed cessation medication, as well as of patients who quit smoking during the year after diagnosis." "We defined smoking at diagnosis as smoking on the last occasion smoking status was recorded in the 3 years before diagnosis. A recent ex-smoker was defined as someone recorded as smoking within 3 years of diagnosis and subsequently recorded as not smoking on the last occasion before diagnosis."

First author, year	Location	Implementation strategy category	Study design	Patient population (within primary care setting)	Data source and outcome measure definition
				(4.0%) had stopped smoking within 3 years of diagnosis Of these groups, *n* = 12,393 cancer patients were matched to *n* = 12,393 CHD control patients. (*n* = 9,347 patients with lung cancer (86% current smokers), n = 2,050 patients with bladder cancer (90% current smokers), *n* = 996 patients with upper aerodigestive tract cancers (91% current smokers).)	
Fichera, 2016 [45]	England	60. Alter incentive/allowance structures	Repeated cross-sectional study Regression discontinuity design (with control)	"Sample of individuals reporting at least one condition incentivised by the QOF." 1997 to 2009 "The health conditions recorded in the HSE related to the seven disease areas targeted by the QOF are: cancer, diabetes, other endocrine problems, mental health, stroke, heart attack/angina, hypertension/high blood pressure, bronchitis, asthma, and other respiratory problems." *n* = missing	Data source: Population-based survey of adults in England, "Health Survey for England (HSE) (1997–2009)." "The HSE comprises annual cross-sectional surveys beginning in 1991…. nationally representative of the English adult population with regard to age, gender, geographic area and socio-demographic circumstances. … use 12 years of data from 1997, after which income information was collected." Outcome measure: Practitioner-level: "Smokers are asked whether they have been given smoking cessation advice by a medical practitioner and if so, whether such advice was delivered within the past 12 months. As the smoking cessation variable was not recorded in 2000, 2001 and 2002,

First author, year	Location	Implementation strategy category	Study design	Patient population (within primary care setting)	Data source and outcome measure definition
					we use a multiple imputation procedure to account for missing observations." "The HSE contains information on the medicines that individuals have been prescribed." Patient-level: "In each wave of the survey, respondents are asked whether they smoke and, if so, the average number of cigarettes smoked in a day. Non-smokers are coded as having zero consumption of cigarettes per day."
Hardy, 2014 [39]	UK	60. Alter incentive/allowance structures	Repeated cross-sectional study Descriptive	Pregnant women, aged 15–49 years at time of giving birth, smokers during pregnancy 2000 to 2009: *n* = 45,296 pregnancies, *n* = 39,781 women (classified as smokers during pregnancy) with pregnancies resulting in live births or stillbirths *n* = 4,826 patients had NRT prescribed during pregnancy for smoking cessation	Data source: UK-representative primary care electronic healthcare records, THIN Outcome measure: Practitioner-level: "Women were defined as smokers if they had a Read code indicating smoking recorded in their medical records or a drug code for nicotine replacement therapy (NRT) during their pregnancy, or, in the absence of recording during pregnancy, if their last recorded Read code in the 27 months prior to pregnancy indicated smoking as defined in more detail previously." "Across the whole study period, annual proportions of pregnant smokers with records of smoking cessation advice were calculated as the number of pregnancies among smokers with recorded smoking cessation advice divided by the total number of pregnancies among smokers who gave birth in that year."
McGovern, 2008 [43]	Scotland	60. Alter incentive/allowance structures	Repeated cross-sectional study Analytical	Patients with diagnosis of coronary heart disease (CHD), aged 16 years and over	Data source: Primary care electronic healthcare records: "Anonymized retrospective data from all 310 of the 850 Scottish practices who use the

First author, year	Location	Implementation strategy category	Study design	Patient population (within primary care setting)	Data source and outcome measure definition
				Pre-contract (31 March 2004): *n* = 58,406 patients over 16 years had a computer record of CHD, 3.7% of the 1,578,902 registered individuals. n = 48 patients had a computer record of an exception code Post-contract (31 March 2005): *n* = 75,495 of patients over 16 years had a computer record of CHD, 4.9% of the 1,533,802 registered individuals. n = 3,083 patients had a computer record of an exception code	general practice administrative software system (GPASS) and who participate in Scottish Programme for Improving Clinical Effectiveness (SPICE) were obtained in November 2005." "previously been shown to be representative of the Scottish population." Outcome measure: Practitioner-level: "recording of smoking status and (where appropriate) provision of smoking cessation advice"
Millett, 2007 [44]	UK	60. Alter incentive/allowance structures	Cohort study	Patients with diagnosis of Type 1 or Type 2 diabetes (had Read codes for diagnoses of diabetes (C10) or diabetes care (66A)), received repeat prescriptions for diabetic medications or had glycosylated hemoglobin level was greater than 7.5%, aged 18 years and over. Women with gestational diabetes or who received treatment for polycystic ovarian syndrome	Data source: Primary care electronic healthcare records: "Wandsworth Primary Care Trust, located in southwest London, England, has established comprehensive primary care-based diabetes registers." Outcome measure: Practitioner-level: "We examined smoking status and cessation advice based on information recorded on practice computers during the 2003 and 2005 study periods."

First author, year	Location	Implementation strategy category	Study design	Patient population (within primary care setting)	Data source and outcome measure definition
				rather than diabetes were excluded *n* = 32 practices out of 36 practices in the study area agreed to participate *n* = 4,284 patients registered with the 32 practices in both the 2003 and 2005 study periods	
Simpson, 2006 [49]	Scotland	60. Alter incentive/allowance structures	Repeated cross-sectional study Analytical	Patients with diagnosis of transient ischaemic attack or stroke Pre-contract (31 March 2004): *n* = 21,901 patients had a computer record of any stroke or TIA (1.2% of everyone registered with the practices). n = 46 patients had a computer record of an exception code Post-contract (31 March 2005): *n* = 32,401 patients had a computer record of any stroke or TIA (1.8% of everyone registered with the practices). n = 2,565 had a computer record of an exception code	Data source: Primary care electronic healthcare records: "Anonymous retrospective data from all 310 of the 850 Scottish practices that use the General Practice Administrative Software System and that participate in SPICE were obtained in November 2005. These 310 practices were self-selected; however, they have been shown to be representative of all Scottish practices." Outcome measure: "From the accumulated data, we identified everyone who had a computer record of a TIA (read codes G65 to G654, G656 to G65zz) or stroke (including cerebral hemorrhagic; read codes G61 below but not G617, G66, and below) and nonhemorrhagic stroke (read codes G63y0-1, G6760, G6w, G6x, G64, and below) on March 31, 2004 (1 year before introduction of the new contract in April 2004, the "precontract" period in this article) and March 31, 2005 (1 year after introduction of the new contract in April 2004; the "postcontract" period). All

First author, year	Location	Implementation strategy category	Study design	Patient population (within primary care setting)	Data source and outcome measure definition
					registered patients with a recording of stroke before the 2 time points were included in the analyses." Practitioner-level: "… smoking habits (current, ex-smoker, or never smoked) and (where appropriate) provision of smoking cessation advice…"
Sutton, 2010 [47]	Scotland	60. Alter incentive/allowance structures	Repeated cross-sectional study Analytical	Aged 45 years and over Unit of analysis: each risk factor for each patient in each year. Within a year therefore, there are five observations for each patient. … Patients that are registered with a practice throughout all 6 years appear 30 (5 risk factors * 6 observation years) times." 2000 to 2005: *n* = 9,416,130 observations on 5 five risk factors for *n* = 391,323 individuals in each of up to 6 years	Data source: Primary care electronic healthcare records: Scottish Programme for Improving Clinical Effectiveness in Primary Care (SPICE-PC) data from 315 Scottish practices. "Participation in SPICE-PC is voluntary" "Participation in SPICE-PC was less likely in the most deprived areas and showed some geographical concentration. Compared with non-participants, participating practices had more patients in total (but fewer patients per GP), were more likely to also participate in other voluntary initiatives and achieved 1% more points on average on the 2005/6 QOF. This suggests some caution in extrapolating the results to all Scottish practices. However the differences on each variable are relatively small." Outcome measure: Practitioner-level: recording of risk factor: smoking status. "Practices could also earn additional points for recording that they had offered cessation advice to patients whose current smoking status had been established."
Szatkowski, 2010 [29]	UK	60. Alter incentive/allowance structures	Repeated cross-sectional study Descriptive	Aged 16 years and over. 1990 to 2006 1990: *n* = 56,595 patients across 103 practices	Data source: UK-representative primary care electronic healthcare records, THIN Outcome measure:

First author, year	Location	Implementation strategy category	Study design	Patient population (within primary care setting)	Data source and outcome measure definition
				2006: *n* = 155,359 patients across 399 practices	Practitioner-level: "We used the proportion of patients having their smoking status recorded within 90 days of registration as a proxy for smoking status being recorded at patient registration."
Szatkowski, 2011 [28]	England	60. Alter incentive/allowance structures	Repeated cross-sectional study Descriptive	Aged 16 years and over THIN: July 2000: *n* = 1.8 million patients aged 16 + registered with a THIN practice in England July 2009: *n* = 2.0 million patients aged 16 + registered with a THIN practice in England PCT Patient Survey, in England: 2004: *n* = 122,113 completed patient questionnaires, response rate: 47.4% 2005: *n* = 116,939 completed patient questionnaires, response rate: 45.4% 2008: *n* = 69,470 completed patient questionnaires, response rate: 38.3%	(a) Data source: UK-representative primary care electronic healthcare records, THIN (a) Outcome measure: Practitioner-level: "…Read codes documenting the delivery of smoking cessation advice to that patient, and, for each year, the proportion of patients with a recording of cessation advice in the 12 months prior to the index date was calculated." (b) Data source: Representative survey of primary care patients in England (PCT Patient Survey) (b) Outcome measure: Practitioner-level: "postal questionnaire asked whether the respondent had 'definitely' or 'to some extent' received cessation advice from a health professional (GP or nurse) at their GP surgery within the last 12 months"
Szatkowski, 2016 [27]	England	60. Alter incentive/allowance structures	Repeated cross-sectional study Interrupted time series analysis (no control)	Aged 16 years and over. 2004 to 2013 *n* = 3,337,881 (SD 81,110) patients aged > 16 years registered in THIN each month, on average	Data source: UK-representative primary care electronic healthcare records, THIN Outcome measure: Practitioner-level: "For each patient, Read Codes were used to identify whether they were advised to quit or referred to the NHS Stop Smoking Service in that month. Multilex drug codes were used to identify whether patients were prescribed a smoking

First author, year	Location	Implementation strategy category	Study design	Patient population (within primary care setting)	Data source and outcome measure definition
				n = 41,649 (SD 9,082) patients had a record of advice to quit each month, on average *n* = 1,001 (SD 371) patients had a record of referral to the NHS Stop Smoking Service each month, on average *n* = 9,921 (SD 1,851) patients had a prescription for a smoking cessation medication each month, on average	cessation medication (NRT, bupropion, or varenicline) each month."
Taggar, 2012 [30]	UK	60. Alter incentive/allowance structures	Repeated cross-sectional study Descriptive	Aged over 15 years. 2000 to 2008 2002 (before QOF): *n* = 1,998,631 patients 2004 (at introduction of QOF): *n* = 2,053,840 patients 2008 (after QOF): *n* = 2,149,026 patients	Data source: UK-representative primary care electronic healthcare records, THIN Outcome measure: Practitioner-level: "…patients with a record of smoking status in the last 27 months and patients recorded as smokers with documented cessation advice in the last 15 months; patients were excluded from analysis if they had registered with a practice within the last three months, corresponding to the grace period GPs have to update the records of new patients (which includes the recording of smoking status)."
Tahrani, 2007 [42]	England	60. Alter incentive/allowance structures	Repeated cross-sectional study Analytical	Patients "on the diabetes register" *n* = 2 Primary Care Trusts (PCTs) in Shropshire, England; made up of 66 practices April 2004: *n* = 15,628 patients on the diabetes register	Data source: Primary care electronic healthcare records: Pre-intervention measures: National Diabetes Audit, data generated by 65 of the 66 Shropshire GP practices

First author, year	Location	Implementation strategy category	Study design	Patient population (within primary care setting)	Data source and outcome measure definition
				March 2005: *n* = 16,121 patients on the diabetes register March 2006: *n* = 16,867 patients on the diabetes register	Post-intervention measures: data collected from 66 GP practices in Shropshire at March 2005 and March 2006 Outcome measure: Practitioner-level: "the proportion of patients achieving each quality indicator ("smoking record", "smoking cessation advice") in each practice out of the total number of patients on the diabetes register in that practice"
Donner-Banzhoff, 1996 [75]	Germany vs UK	65. Use capitated payments	Cross-sectional study (comparing two groups) Analytical	Unspecified. Year unknown *n* = 778 consecutive patients attending for a consultation. "8% of the patients approached declined to take part in the study."	Data source: Patient survey and subsequent patient interview. "A total of 15 family practitioners' surgeries in Germany and the UK that were matched for rural–urban location were included in a cross-sectional survey." Outcome measure: Practitioner-level: Consecutive patients attending for consultation were asked to complete a questionnaire. "They filled in a questionnnaire on sociodemographic data, medication, diagnoses, risk factor concepts, and remembered intervention against smoking. In the following interview, queries arising from the questionnaire could be addressed so as to keep the proportion of missing data low. Patients' records were analyzed for medication, laboratory tests, and previous contacts. During this study, interviews and examinations were performed by one researcher (NDB) in both countries." "Whether a given patient could remember an intervention by his/her physician (or related staff) was defined as the main endpoint of the

First author, year	Location	Implementation strategy category	Study design	Patient population (within primary care setting)	Data source and outcome measure definition
					comparison. An intervention was assumed if the question "Has your family doctor ever talked to you about your smoking?" was answered by "yes" or if questions about possible interventions by doctor or nursing staff were answered in the affirmative. The questionnaire was developed simultaneously in German and English. It was then translated from English into German to correct linguistic ambiguities." Categorisation of 'cessation interventions': 'None' or 'Advice once' or 'Advice several times' or 'Nicotine patch/gum' or 'Other'
Domain 9. Change infrastructure					
Szatkowski, 2021 [36]	England	66. Mandate change	Repeated cross-sectional study Segmented regression analysis, no control	Pregnant women, aged 15–49 years at time of giving birth, smokers during pregnancy 2005 to 2017: *n* = 84,539 pregnancies where the mother was recorded as smoking, this was 24.9% of n = 339,875 all pregnancies	Data source: UK-representative primary care electronic healthcare records, CPRD Outcome measure: "Women were identified as smoking in pregnancy if they had a diagnostic code indicating current smoking, or a prescription for a smoking cessation medication, recorded at least once during gestation." Practitioner-level: "Prescriptions for NRT were identified using relevant Multilex drug codes. Dual NRT was defined as prescription of a long-acting transdermal nicotine patch and a short-acting formulation (eg, gum, lozenge, inhalator, tablet, or spray) on the same day."
Dhalwani, 2014 [41]	UK	69. Create or change	Repeated cross-sectional study	Pregnant women, aged 15–49 years at time of giving birth	Data source: UK-representative primary care electronic healthcare records, THIN

First author, year	Location	Implementation strategy category	Study design	Patient population (within primary care setting)	Data source and outcome measure definition
		credentialing and/or licensure standards	Descriptive	2001 to 2012: *n* = 71,685 pregnancies which resulted in live births or still births, where the mother was classified as a smoker during pregnancy, this was 18.5% of *n* = 388,142 of all pregnancies which resulted in live births or stillbirths	Outcome measure: Practitioner-level: "The smoking status of females was determined using Read Codes recorded from 27 months before conception up to the end of pregnancy, based on the recording rules in the GP contract." "Multilex Drug Codes for all NRT formulations available in the UK according to the British National Formulary (BNF) were used for NRT prescriptions." "The use of different forms of NRT (patches, gum, nasal spray, lozenges, sublingual tablets, inhalator cartridges, and combination) was assessed."
Langley, 2011 [34]	England	69. Create or change credentialing and/or licensure standards	Repeated cross-sectional study Segmented regression analysis (no control)	Aged between 12–17 years. 2002 to 2009 *n* = missing	Data source: UK-representative primary care electronic healthcare records, THIN Outcome measure: Practitioner-level: "rates of prescribing of all NRT products per 100,000 adolescents registered with a THIN practice per month."
Langley, 2012 [35]	England	69. Create or change credentialing and/or licensure standards	Repeated cross-sectional study Segmented regression analysis (no control)	Aged over 16 years, had diagnosis of cardiovascular disease or stroke. 2002 to 2009 *n* = 88,000 coronary heart disease (CHD) patients each month *n* = 39,000 stroke patients each month	Data source: UK-representative primary care electronic healthcare records, THIN Outcome measure: Practitioner-level: "the number of patients per 100,000 with CHD and stroke who received a prescription for NRT each month." Extracted data on prescribing of NRT, varenicline and bupropion to CHD and stroke patients
Li, 2020 [55]	United States (multi-state)	69. Create or change credentialing	Repeated cross-sectional study Analytical	Aged between 55–80 years, smokers, no evidence of lung cancer. 2010 to 2017	Data source: Electronic healthcare records: from a "large healthcare system in northern California" Outcome measure:

First author, year	Location	Implementation strategy category	Study design	Patient population (within primary care setting)	Data source and outcome measure definition
		and/or licensure standards		*n* = 12,678 (63.8% of *n* = 19,862) current smokers were included in the analysis, whose eligibility for LDCT-LCS could be determined	Practitioner-level: "Three types of smoking-cessation interventions (i.e., formal in-visit smoking-cessation counseling, informal smoking-cessation counseling or referrals to smoking-cessation programs, and medication orders for pharmacotherapy) were considered. … Keyword searches included but were not limited to, smoking cessation and tobacco counseling in the procedure description. Sessions of 3 – 10 min or > 10 min (e.g., billing codes: 99,406, G0375, G0376; 99,407, G0436, G0437, etc.) were classified as formal in-visit smoking-cessation counseling. Smoking-cessation counseling < 3 min is not separately billed; such unbilled in-visit smoking-cessation counseling, along with referrals for internal free smoking-cessation programs, are categorized as informal smoking-cessation counseling or referrals to smoking-cessation programs. Pharmacotherapy using smoking deterrents was identified by a prescription order for smoking-cessation medication, (e.g., bupropion HCl, varenicline tartrate, nicotine polacrilex, etc.)." "cigarettes smoked per day"
Thorndike, 2007 [53]	United States (multi-state)	69. Create or change credentialing and/or licensure standards	Repeated cross-sectional study Analytical	Aged 18 years and over 1994 to 1996: *n* = 84,104 adult patient visits to 4,118 physicians. Physician response rate: 71% 2001 to 2003: *n* = 58,991 adult patient visits to 2,902	Data source: Physician survey, "The National Ambulatory Medical Care Survey (NAMCS) is an ongoing annual survey of US office-based physicians conducted by the National Center for Health Statistics." "We compared pooled data from the 1994–1996 NAMCSs with data from the 2001–2003 surveys. …

First author, year	Location	Implementation strategy category	Study design	Patient population (within primary care setting)	Data source and outcome measure definition
				physicians. Physician response rate: 67% Difference between physician response rate is statistically significant (p = 0.001)	We were unable to examine these outcomes for the years 1997–2000 because the smoking status item was not included on the NAMCS in those years." "Each participating physician completes a 1-page encounter form for each systematically sampled ambulatory care visit during a randomly assigned week." Outcome measure: Practitioner-level: "(1) Physicians identified a patient's smoking status by answering the question, "Does patient use tobacco?" Smoking status was considered identified if the answer was "yes" or "no"; responses of "unknown" or left blank were considered not identified. (2) Physicians recorded smoking counseling by checking the "Tobacco use/exposure" box under "Counseling/Education." (3) Prescription and nonprescription medications were recorded on the survey form under "Medications." All adult patient visits were included in the analysis of smoking status. Analyses of smoking counseling and smoking medications were restricted to visits by patients identified was smokers Because bupropion is also used to treat depression, we excluded bupropion prescriptions prior to 1997, the year it was approved for smoking cessation."
Peterson, 2016 [52]	United States (multi-state)	71. Change accreditation or membership requirements	Repeated cross-sectional study Analytical	Patients "with hypertension" n = 7,319 completed hypertension Performance in Practice Modules (PPMs)	Data source: "We analyzed data from all hypertension Performance in Practice Modules (PPMs) completed from July 2006 to 2013." Patient health records: "diplomates gather quality measures

First author, year	Location	Implementation strategy category	Study design	Patient population (within primary care setting)	Data source and outcome measure definition
				completed between 2006 and 2013, reflecting quality measures for between 80,000 and 160,000 patients, completed by eligible physicians (residing in the United States). "In 7.8% of the PPMs, physicians selected smoking cessation for improvement."	from at least 10 patients with hypertension". Patient questionnaire: "patients complete a questionnaire" Outcome measure: "The PPM structure is based on a Plan-Do- Study-Act (PDSA) cycle. First, the physician, or assigned clinical staff, gathers data on 10 patients with hypertension from the chart and the corresponding patient survey data, and enters them on templates in the web-based PPM. [quality improvement exercise]…. After the physician implements their chosen interventions, collection of chart and survey data from the next 10 patients they see with a diagnosis of hypertension is repeated. After completion of data entry for this set of patients, the physician is provided with pre- and post-intervention comparisons as well as comparisons to the mean quality scores for all physicians who have previously completed the PPM." Practitioner-level: Patient records (physician-reported): Whether "smoking cessation counseling" was provided Patients complete a questionnaire that includes: "(6) for smokers, whether your doctor asked about quitting"
Shi, 2017 [59]	United States (multi-state)	71. Change accreditation or membership requirements	Cross-sectional study (with control group) Analytical	Unspecified, aged 18 years and over, low income. 2012 *n* = 539 health centres (HCs) achieved 'Patient-centered medical home' (PCMH) recognition status	Data source: Provider survey/electronic records (Health Resources and Services Administration [HRSA] 2012 Uniform Data System (UDS) + HRSA's Patient-Centered Medical/Health Home Initiative) Outcome measure:

First author, year	Location	Implementation strategy category	Study design	Patient population (within primary care setting)	Data source and outcome measure definition
				n = 548 HCs did not achieve PCMH recognition status	Practitioner-level: "percent of adults (18 years or older) assessed for tobacco use". "percent of adults (18 years or older) who were known tobacco users that received tobacco cessation counseling and/or pharmacologic intervention."
Van Doorn-Klomberg, 2014 [68]	Netherlands	71. Change accreditation or membership requirements	Cohort study	Patients with diagnosis of diabetes mellitus, chronic obstructive pulmonary disease (COPD) or cardiovascular disease (CVD). 2006 to 2011 Matched sample: 1st cohort: *n* = 69 practices. 2006–2008: *n* = 4,629 average number of patients per practice. 2009–2011: *n* = 4,808 average number of patients per practice Matched sample: 2nd cohort: *n* = 69 practices. 2009–2011: *n* = 4,830 average number of patients per practice	Data source: Primary care electronic healthcare records from Dutch primary care practices that participated in the accreditation program of the Dutch College of General Practitioners between 2006 and 2011 Outcome measure: Patient-level: Patients with COPD and Patients with CVD: "Percentage of patients that smoke" Practitioner-level: "Percentage of patients with a known smoke status", "Percentage of patients that smoke with a stop smoking advice"
Multiple domains					
Akman, 2017 [72]	Turkey	Domain 8 65. Use capitated payments AND Domain 9 66. Mandate change, 67. Change	Repeated cross-sectional study Analytical	Unspecified patient population 1993: *n* = 199 primary care doctors (response rate: 50%), "doctors working in inner city and urban areas were over-represented"	Data source: 1993: Primary care doctor survey: 1993 European GP Task Profile study. "In 1993, the study sample included a random sample of PCDs in 10 preselected provinces out of all 74 provinces in Turkey"

First author, year	Location	Implementation strategy category	Study design	Patient population (within primary care setting)	Data source and outcome measure definition
		record systems, 71. Change accreditation or membership requirements		2012: *n* = 299 primary care doctors (response rate: 42.9%)	2012: Primary care doctor survey: 2012 Quality and Costs of Primary Care in Europe (QUALICOPC) study. "In 2012, data was collected from seven provinces of Turkey. Selection of provinces was based on the year the FD scheme was introduced, and the geographical distribution within the country. A quota of 10% per region was applied for all PCDs with family medicine specialist qualifications working in the region." Outcome measure: Practitioner-level: self-reported proportion of "primary care doctors who are usually or almost always involved in given preventive care service (smoking counselling during outpatient clinic)". "The questions in the 1993 survey on GP service profiles were repeated in 2012 with the purpose of comparing general practice between the two time points."
Bailey, 2017 [50]	Oregon, USA	Domain 8 60. Alter incentive/allowance structures AND Domain 9 67. Change record systems	Repeated cross-sectional study Analytical	Aged 18 years and over, excludes pregnant patients. "Most are uninsured or Medicaid recipients and have disproportionately high rate of smoking compared with patients seen in private primary care clinics". 2010 to 2014 2010: *n* = 55,398 patients 2012: *n* = 60,610 patients 2014: *n* = 66,712 patients	Data source: Primary care electronic healthcare records (Oregon Community Health Information Network, "OCHIN, Inc."): 26 Oregon community health centers (CHCs))(federally qualified heath centers that are subsidized to serve low-income and vulnerable populations) that were using OCHIN's EHR before 1 July 2009 were extracted Outcome measure: Practitioner-level and patient-level: "The denominator for smoking status assessment included all study patients within a measurement year; the denominator for all other outcomes

First author, year	Location	Implementation strategy category	Study design	Patient population (within primary care setting)	Data source and outcome measure definition
					included patients identified as smokers within a measurement year." (1) "Smoking status was considered to be assessed if changes were made to the discrete data field with drop-down options for smoking status (located in both the vital signs and social history in all study years), if the button was selected to confirm that smoking status was reviewed, or if a status was captured via NLP in the free-text notes within the measurement year (2) A patient was identified as a current smoker if smoking status in the discrete data field was "current every day," "current some day," "smoker, current status unknown," "heavy tobacco smoker," or "light tobacco smoker."" (3) "Receipt of counseling was deemed "yes" if the discrete field, "counseling given," was coded as "yes," if identified by standard procedure codes for smoking-cessation counseling or an internal OCHIN Epic code for counseling referral, or if any statements in the free-text fields about smoking and cessation (e.g., goals, triggers, efforts) were identified." (4) "Smoking-cessation medication orders (bupropion, varenicline, and all nicotine-replacement therapy products) were extracted from the medication orders list (5) "medications ordered or discussed": included orders or any discussion of cessation medications as captured in the free text via NLP

First author, year	Location	Implementation strategy category	Study design	Patient population (within primary care setting)	Data source and outcome measure definition
Fortmann, 2020 [56]	United States (multi-state)	Domain 8 60. Alter incentive/allowance structures AND Domain 9 71. Change accreditation or membership requirements	Cohort study Interrupted time series analysis (no control)	Aged 18 years and over. "72% of patients were members of ethnic and racial minority groups and 73% reported incomes below the Federal Poverty Level (FPL)." 2006–2013 *n* = 9 US states, 15 community health centres (CHCs), 706,840 patients. (Average CHC size: 4,700 to 67,000 patients.)	Data source: Electronic healthcare records (Community Health Applied Research Network (CHARN)—data from 15 community health centres, across 9 US states) Outcome measure: Practitioner-level: "structured EMR data (not free text) on smoking status and patient characteristics from the 15 CHCs with smoking data beginning either in 2006 or in the earliest year in which data were recorded." "Overall rates of documentation were assessed for each year from 2006 to 2013 at the clinic level (the denominator increased as clinics were added to the database)." "Smoking status was recorded as current, former, never, or unknown/missing. The EMRs in this study carried forward smoking status from previous visits to inform clinical staff of prior smoking status, which could then be reviewed and changed if necessary. If the smoking status was unchanged, this was often not specifically noted. …if no smoking status was recorded in a given year, status was set as that of the last recorded value. Thus, missing/unknown smoking status indicated that providers had never recorded smoking status for a given individual."
Langley, 2011 [37]	England	Domain 8 59. Place innovation on fee for service lists/formularies AND	Repeated cross-sectional study Interrupted time series analysis (no control)	Unspecified, "all primary care patients registered". 2000–2009 *n* = missing. "Prescribing of varenicline increased most markedly in July 2007, growing to around 100 prescriptions per	Data source: UK-representative primary care electronic healthcare records, THIN Outcome measure: Practitioner-level: "monthly rates of general practice prescribing for each of NRT, bupropion and

First author, year	Location	Implementation strategy category	Study design	Patient population (within primary care setting)	Data source and outcome measure definition
		Domain 9 69. Create or change credentialing and/or licensure standards		100,000 population, and remained around this higher rate for the rest of the study period."	varenicline and all smoking cessation medications combined."
Mullins, 2009 [51]	Delaware, USA	Domain 5 40. Distribute educational materials 42. Conduct educational meetings AND Domain 7 54. Prepare patients/consumers to be active participants	Repeated cross-sectional study Analytical	Unspecified, "all [primary care] patients". "Patients without a recorded smoking history were excluded." 2006 to 2008 Pre-intervention group (office visit between 1 July 2006 and 1 January 2007): *n* = 922 patients Post-intervention group (office visit between 1 July 2007 and 1 January 2008): *n* = 3,154 patients	Data source: Primary care electronic healthcare records from Family Medicine Center of Christiana Care Health System. "… suburban outpatient office in Wilmington, Delaware", USA Outcome measure: Practitioner-level and patient-level: "The number of patients recorded as current smokers and the number of patients counseled to quit by their physician…" "Smokers were defined as patients who had an EMR flow sheet value for “smoking status” that read “current.” Patients were defined as nonsmokers if smoking status flow sheet values were “quit,” “never,” or if no value was recorded "Tobacco cessation counselling", "patient had at some time been counseled to quit smoking by their provider": Patients were defined as having been counseled to quit smoking if the flow sheet value for “advised to quit” was ever recorded as “yes.”" "The inquiry to determine the preintervention group was “Find Patients where Home Location is 'FMC' AND Date of Last Office Visit is on or after '07/01/2006' AND Date of Last Office Visit is before '01/01/2007' AND SMOK STATUS (any entry)

First author, year	Location	Implementation strategy category	Study design	Patient population (within primary care setting)	Data source and outcome measure definition
					contains 'current' AND SMOK ADVICE (last entry) contains 'yes'." The inquiry to determine the postintervention group was the same, with visits on or after July 1, 2007, and before January 1, 2008."
Verbiest, 2013 [67]	Netherlands	Domain 8 59. Place innovation on fee for service lists/formularies AND Domain 9 69. Create or change credentialing and/or licensure standards	Repeated cross-sectional study Interrupted time series analysis (no control) (of three nation-wide representative databases)	Unspecified, adults (aged 15 years and over) Netherlands Information Network of Primary Care (LINH): representative sample of 84 general practices with approximately 350,000 listed patients. 2001 to 2011 Dutch Foundation for Pharmaceutical Statistics (SFK): representative panel of 95% of Dutch community pharmacies. 2001 to 2012 Dutch Continuous Survey of Smoking Habits (DCSSH): representative of Dutch adult population (15 years and older). 2001 to 2012	(a) Data source: Nation-wide general practice electronic health records (Netherlands Information Network of Primary Care (LINH)). "The characteristics of the study population (GPs and patients) are comparable with the general Dutch population in terms of age and gender." (a) Outcome measure: Practitioner-level: "number of quarterly prescribed stop-smoking medications in general practice… "prescriptions of NRT, varenicline and bupropion in the period 2001–2011 and calculated prescription rates per 1000 smokers. …. The number of smokers was based on the total population and smoking prevalence." (b) Data source: Nation-wide prescription database (Dutch Foundation for Pharmaceutical Statistics (SFK)). "The SFK gathers data from a representative panel of 95% of Dutch community pharmacies. Data were extrapolated to nation-wide figures." (b) Outcome measure: Practitioner-level: "prescriptions of stop-smoking medication dispensed in out-patient pharmacies". "dispensations of NRT, varenicline and bupropion in the period 2001–2012 and calculated dispensed rates per 1000 smokers."

First author, year	Location	Implementation strategy category	Study design	Patient population (within primary care setting)	Data source and outcome measure definition
					For bupropion: **"primary care prescriptions (a) in this study represent the total number of prescriptions for both depression and quit smoking and the dispensed items (b) represent only stop-smoking medication" For varenicline: "We did not assess the impact of the GP guideline introduction on the number of primary care prescriptions and dispensed prescriptions of varenicline because this pharmaceutical was introduced in the Netherlands around the same time as the GP guideline (December 2006)." "we only assessed the immediate effect of the introduction and abolition of the insurance coverage in (dispensed) prescriptions and smoking prevalence, as we lacked sufficient time-points to estimate a change in trend." (c) Data source: Population-based survey of adults in the Netherlands (Dutch Continuous Survey of Smoking Habits (DCSSH)). "The DCSSH assesses smoking behaviour of the Dutch adult population (15 years and older)." Representative; weightings based on gender, age, education level, socioeconomic status, the province in which they lived, and their family and community size (c) Outcome measure: Patient-level: "Smoking prevalence (2001–2012) was assessed by asking participants 'Do you (ever) smoke?'."

Table summarising the characteristics of the studies included in this systematic review. The included studies are ordered by implementation strategy domain (5, 7, 8 and 9 and 'Multiple domains'). Within the domains, the studies are ordered by implementation strategy category then alphabetically by first author surname. (Wright, 2018) [71] was excluded from narrative synthesis as it was at critical risk, but it is included in this table.

Table 3.2. Results

First author, year	Location	Implementation strategy category	Intervention	Practitioner-level outcomes			Patient-level outcomes		Perceived facilitators and barriers	Risk of bias
				Recording smoking status	Providing cessation advice	Prescribing cessation medication	Quit attempts	Cessation		
Domain 5. Train and educate stakeholders										
Mullins, 1999 [70]	Victoria, Australia	40. Distribute educational materials	Simple intervention: GPs mailed a pack containing: information letter for GPs, self-help booklet ('The Can Quit Book') to give to patients, plastic stand for GPs' office/waiting room	**0**	**+**				**Facilitators:** Intervention characteristics: complexity (the intervention was simple and acceptable: survey found that 95% of primary care physicians could recall receiving copies of The Can Quit Book and most physicians reported giving them to patients) Outer setting: external policies and incentives (GPs may have been affected by smoking cessation articles in medical journals and medical magazines, the RACGP's Guidelines for Preventive Activities in General Practice, societal changes of	Serious

First author, year	Location	Implementation strategy category	Intervention	Practitioner-level outcomes			Patient-level outcomes		Perceived facilitators and barriers	Risk of bias
				Recording smoking status	Providing cessation advice	Prescribing cessation medication	Quit attempts	Cessation		
									embracing anti-smoking advice) **Barriers:** Outer setting: cosmopolitanism (lack of appropriate/easy referral system to effective cessation programs or products)	
Mullins, 2009 [51]	Delaware, USA	Domain 5 40. Distribute educational materials 42. Conduct educational meetings AND Domain 7 54. Prepare patients/consumers to be active participants	'Ask and Act program' Program contains: (i) educational component for physicians (free patient materials for offices, continuing medical education programs for physicians and allied health professionals, and information on evidence-based interventions), and		+			+	**Facilitators:** Inner setting: readiness for implementation: (iii) access to knowledge and information (physicians reported that they felt more comfortable with smoking cessation counselling and billing for this intervention, and that they were more likely to counsel their patients after hearing the presentation)	Serious

First author, year	Location	Implementation strategy category	Intervention	Practitioner-level outcomes			Patient-level outcomes		Perceived facilitators and barriers	Risk of bias
				Recording smoking status	Providing cessation advice	Prescribing cessation medication	Quit attempts	Cessation		
			(ii) free patient materials which engage patients (patient materials include pre-printed prescription pads with tips on how to quit, brochures, and laminated quitline referral cards. Metal lapel pins and wall posters act as visual cues to encourage patients to ask their family physician for help, and a guide to tobacco cessation group visits details how practices can organize and bill for counselling sessions)							

First author, year	Location	Implementation strategy category	Intervention	Practitioner-level outcomes			Patient-level outcomes		Perceived facilitators and barriers	Risk of bias
				Recording smoking status	Providing cessation advice	Prescribing cessation medication	Quit attempts	Cessation		
Vasankari, 2011 [74]	Finland	42. Conduct educational meetings	Finnish 'National Programme for Chronic Bronchitis and COPD 1998–2007': training events organised in hospitals and primary health care centres, covering topics: COPD as a disease, diagnosis of COPD (spirometry), smoking cessation and treatment of COPD	+					**Facilitators:** Outer setting: external policies and incentives (anti-smoking work and legislation on the national level, increased improvements in the national level of spirometry and knowledge of smoking habits of COPD patients)	Serious
Domain 7. Engage consumers										
Mullins, 2009 [51]	Delaware, USA	Domain 5 40. Distribute educational materials 42. Conduct educational meetings AND	'Ask and Act program' Program contains: (i) educational component for physicians (free patient materials for offices,		+			+	**Facilitators:** Inner setting: readiness for implementation: (iii) access to knowledge and information (physicians reported that they felt more comfortable with	Serious

First author, year	Location	Implementation strategy category	Intervention	Practitioner-level outcomes			Patient-level outcomes		Perceived facilitators and barriers	Risk of bias
				Recording smoking status	Providing cessation advice	Prescribing cessation medication	Quit attempts	Cessation		
		Domain 7 54. Prepare patients/consumers to be active participants	continuing medical education programs for physicians and allied health professionals, and information on evidence-based interventions), and (ii) free patient materials which engage patients (patient materials include pre-printed prescription pads with tips on how to quit, brochures, and laminated quitline referral cards. Metal lapel pins and wall posters act as visual cues to encourage patients to ask their family						smoking cessation counselling and billing for this intervention, and that they were more likely to counsel their patients after hearing the presentation)	

First author, year	Location	Implementation strategy category	Intervention	Practitioner-level outcomes			Patient-level outcomes		Perceived facilitators and barriers	Risk of bias
				Recording smoking status	Providing cessation advice	Prescribing cessation medication	Quit attempts	Cessation		
			physician for help, and a guide to tobacco cessation group visits details how practices can organize and bill for counselling sessions)							
Szatkowski, 2011 [33]	England	54. Prepare patients/consumers to be active participants	Introduction of smoke-free legislation			**+ / 0**			**Barriers:** Outer setting: external policies and incentives (contextual factors and social norms continue to influence smoking behaviour: the provision of outdoor facilities for smoking, spending time with smoking friends) Implementation process: executing (cessation support could have been advertised in the months after the smoke-free legislation was enacted)	Moderate

First author, year	Location	Implementation strategy category	Intervention	Practitioner-level outcomes			Patient-level outcomes		Perceived facilitators and barriers	Risk of bias
				Recording smoking status	Providing cessation advice	Prescribing cessation medication	Quit attempts	Cessation		
Langley, 2012 [46]	England (and Wales)	56. Use mass media	Anti-tobacco mass media advertising, and pharmaceutical company-funded smoking cessation medication advertising			**0**			**Barriers:** Implementation process: executing (effect of mass media campaign seems to be restricted to the month of the campaign, suggesting that campaigns need to be sustained over time; the messages of the mass media campaigns could be improved: greater focus on encouraging supported quit attempts, encouraging smokers to seek advice and medication from their GP)	Moderate
Domain 8. Utilize financial strategies										
Alageel, 2019 [31]	England	57. Fund and contract for the clinical innovation	NHS Health Check program (primary prevention of cardiovascular disease and related disorders)		**+**	**+**		**+**	**Barriers:** Characteristics of individuals: knowledge and beliefs about the intervention (lower uptake of health checks	Low

First author, year	Location	Implementation strategy category	Intervention	Practitioner-level outcomes			Patient-level outcomes		Perceived facilitators and barriers	Risk of bias
				Recording smoking status	Providing cessation advice	Prescribing cessation medication	Quit attempts	Cessation		
									among patients at greatest risk of cardiovascular disease) Characteristics of individuals: knowledge and beliefs about the intervention (physicians have doubts about the effectiveness of the EBP, physicians lack guidance on how to implement risk management interventions which follow after risk factor detection) Inner setting: structural characteristics (delivery of EBP is restricted by lack of time and follow-up in primary care)	
Bennett, 2008 [65]	Ireland	57. Fund and contract for the clinical innovation	Heartwatch (secondary prevention of cardiovascular disease)					+	**Barriers:** Outer setting: cosmopolitanism (further improvements may be achieved through improved	Moderate

First author, year	Location	Implementation strategy category	Intervention	Practitioner-level outcomes			Patient-level outcomes		Perceived facilitators and barriers	Risk of bias
				Recording smoking status	Providing cessation advice	Prescribing cessation medication	Quit attempts	Cessation		
									linkages to community-based programmes and support) Outer setting: patient needs and resources (further improvements may be achieved through attention to improving body weight, exercise levels and glucose metabolism)	
Fitzpatrick, 2011 [66]	Ireland	57. Fund and contract for the clinical innovation	Heartwatch (secondary prevention of cardiovascular disease)					+	**Facilitators:** Inner setting: implementation climate: (ii) compatibility (the effect of the intervention is likely to be additive, to the effect from secondary prevention interventions that already exist in primary care) **Barriers:** Inner setting: structural characteristics (delivery of EBP is restricted by	Serious

First author, year	Location	Implementation strategy category	Intervention	Practitioner-level outcomes			Patient-level outcomes		Perceived facilitators and barriers	Risk of bias
				Recording smoking status	Providing cessation advice	Prescribing cessation medication	Quit attempts	Cessation		
									lack of time and follow-up in primary care)	
Forster, 2016 [48]	England	57. Fund and contract for the clinical innovation	NHS Health Check program (primary prevention of cardiovascular disease and related disorders)	+					**Barriers:** Characteristics of individuals: knowledge and beliefs about the intervention (lower uptake of health checks among patients who are smokers)	Low
Frijling, 2003 [69]	Netherlands	57. Fund and contract for the clinical innovation	Cardiovascular disease (secondary) prevention program		+				**Barriers:** Inner setting: readiness for implementation: (ii) available resources (GPs reported time constraints and insufficient financial recompense as a barrier to change, extra resources and personnel will be needed, GPs' current workload needs to be reduced) Outer setting: patient needs and resources	Serious

First author, year	Location	Implementation strategy category	Intervention	Practitioner-level outcomes			Patient-level outcomes		Perceived facilitators and barriers	Risk of bias
				Recording smoking status	Providing cessation advice	Prescribing cessation medication	Quit attempts	Cessation		
									(multi-faceted interventions are more effective)	
Pajak, 2010 [73]	Poland	57. Fund and contract for the clinical innovation	Health Check Program of cardiovascular disease prevention	**+**	**0**	**0**		**0**	**Barriers:** Inner setting: readiness for implementation: (iii) access to knowledge and information (the intervention should be enriched with well-designed structured intervention) Characteristics of individuals: knowledge and beliefs about the intervention (less than 50% of family physicians felt competent to deliver smoking cessation interventions, primary care physicians have been shown to inadequate knowledge and to be not fully aware as to the efficacy	Moderate

First author, year	Location	Implementation strategy category	Intervention	Practitioner-level outcomes			Patient-level outcomes		Perceived facilitators and barriers	Risk of bias
				Recording smoking status	Providing cessation advice	Prescribing cessation medication	Quit attempts	Cessation		
									of intervention on risk factors) Inner setting: structural characteristics (primary care physicians have been shown to have time limitations) **Facilitators:** Inner setting: implementation climate: (iii) relative priority (over 90% of family physicians felt that health promotion should be a part of their daily work) Inner setting: readiness for implementation: (ii) available resources (over 90% of family physicians had educational materials in their waiting rooms)	
Bailey, 2016 [54]	Oregon, USA	59. Place innovation on fee for service lists/formularies	Increasing access to health insurance coverage which			+		+	**Facilitators:** Inner setting: structural characteristics (increased access to	Moderate

First author, year	Location	Implementation strategy category	Intervention	Practitioner-level outcomes			Patient-level outcomes		Perceived facilitators and barriers	Risk of bias
				Recording smoking status	Providing cessation advice	Prescribing cessation medication	Quit attempts	Cessation		
			included smoking cessation treatment						consultations and follow-up consultations in primary care, increased access to cessation medications) Outer setting: cosmopolitanism (increased access to smoking cessation counselling or referral for such services)	
Bailey, 2020 [60]	United States (multi-state)	59. Place innovation on fee for service lists/formularies	Increasing access to health insurance coverage which included smoking cessation treatment			+		+	**Facilitators:** Inner setting: structural characteristics (increased access to consultations in primary care, increased access to cessation medications) Outer setting: cosmopolitanism (increased access to smoking cessation counselling or referral for such services)	Moderate

First author, year	Location	Implementation strategy category	Intervention	Practitioner-level outcomes			Patient-level outcomes		Perceived facilitators and barriers	Risk of bias
				Recording smoking status	Providing cessation advice	Prescribing cessation medication	Quit attempts	Cessation		
Langley, 2011 [37]	England	Domain 8 59. Place innovation on fee for service lists/formularies AND Domain 9 69. Create or change credentialing and/or licensure standards	(i) Introduction of a new cessation medication (varenicline) onto a country's prescription scheme, December 2006 (ii) Introduction of NICE guideline for varenicline, July 2007			**(i) + / 0** **(ii) + / 0**			**Facilitators:** Inner setting: readiness for implementation: (iii) access to knowledge and information (measures to increase physicians' confidence in the effectiveness and safety of the medication) Characteristics of individuals: knowledge and beliefs about the intervention (raising awareness of varenicline amongst smokers)	Moderate
Li, 2018 [61]	United States (multi-state)	59. Place innovation on fee for service lists/formularies	Low-dose computed tomography for lung cancer screening (LDCT-LCS) became a Medicare-covered preventive service	**+**					**Barriers:** Inner setting: readiness for implementation: (ii) available resources (lack of available staff time and financial factors) Intervention characteristics: complexity (information	Serious

First author, year	Location	Implementation strategy category	Intervention	Practitioner-level outcomes			Patient-level outcomes		Perceived facilitators and barriers	Risk of bias
				Recording smoking status	Providing cessation advice	Prescribing cessation medication	Quit attempts	Cessation		
									in new guidelines was complex)	
Marino, 2016 [62]	Oregon, USA	59. Place innovation on fee for service lists/formularies	Increasing access to health insurance coverage which included smoking cessation treatment	+					**Facilitators:** Inner setting: structural characteristics (increased access to primary care office visits)	Low
Miraldo, 2018 [57]	Massachusetts, USA	59. Place innovation on fee for service lists/formularies	Increasing access to health insurance coverage which included smoking cessation treatment				**0**		**Barriers:** Inner setting: structural characteristics (require an extensive amount of physician time) Inner setting: implementation climate: (iii) relative priority (some physicians are not inclined to working with behavioural interventions and perceive risk reduction as something beyond their direct responsibility)	Moderate

First author, year	Location	Implementation strategy category	Intervention	Practitioner-level outcomes			Patient-level outcomes		Perceived facilitators and barriers	Risk of bias
				Recording smoking status	Providing cessation advice	Prescribing cessation medication	Quit attempts	Cessation		
									Characteristics of individuals: knowledge and beliefs about the intervention (differences across race/ethnic groups also suggest the need to tailor health interventions for multiple races, ethnicities and cultures) **Facilitators:** Outer setting: external policies and incentives (methods for encouraging healthy behaviour, coordinating care of chronic diseases) Implementation process: reflecting and evaluating (multifaceted approaches to implementation, with a combination of activities such as audit	

First author, year	Location	Implementation strategy category	Intervention	Practitioner-level outcomes			Patient-level outcomes		Perceived facilitators and barriers	Risk of bias
				Recording smoking status	Providing cessation advice	Prescribing cessation medication	Quit attempts	Cessation		
									and feedback and active education)	
Parnes, 2002 [58]	Colorado, USA	59. Place innovation on fee for service lists/formularies	Health insurance types: uninsured vs Medicaid insured vs private/health maintenance organization (HMO) insured		**+**				**Barriers:** Inner setting: structural characteristics (lack of access to cessation resources/treatment) Inner setting: structural characteristics (competing demands on physicians' time) Characteristics of individuals: other personal attributes (studies have documented a lower quality of care for Medicaid and uninsured patients with chronic diseases)	Moderate
Tilson, 2004 [63]	Ireland	59. Place innovation on fee for service lists/formularies	Introduction of a new cessation medication (NRT) onto a country's prescription scheme			**+ / 0**			**Barriers:** Inner setting: structural characteristics (organisational issues)	Serious

First author, year	Location	Implementation strategy category	Intervention	Practitioner-level outcomes			Patient-level outcomes		Perceived facilitators and barriers	Risk of bias
				Recording smoking status	Providing cessation advice	Prescribing cessation medication	Quit attempts	Cessation		
									Inner setting: structural characteristics (drug reimbursement) Inner setting: readiness for implementation: (iii) access to knowledge and information (education and training)	
Verbiest, 2013 [67]	Netherlands	Domain 8 59. Place innovation on fee for service lists/formularies AND Domain 9 69. Create or change credentialing and/or licensure standards	(i) Increasing access to health insurance coverage which included smoking cessation treatment (ii) Introduction of the first Dutch guideline 'Treatment of Tobacco Dependence'			**(i) +** **(ii) 0**		**(i) +** **(ii) 0**	**Facilitators:** Inner setting: structural characteristics (increased access to cessation medications, health insurance coverage for smoking cessation treatment prompts GPs to prescribe evidence-based pharmaceuticals for smoking cessation)	Moderate
Williams, 2004 [64]	Ireland	59. Place innovation on fee for service lists/formularies	Introduction of a new cessation medication (NRT) onto a country's			**+ / 0**			N/A	Serious

First author, year	Location	Implementation strategy category	Intervention	Practitioner-level outcomes			Patient-level outcomes		Perceived facilitators and barriers	Risk of bias
				Recording smoking status	Providing cessation advice	Prescribing cessation medication	Quit attempts	Cessation		
			prescription scheme							
Bailey, 2017 [50]	Oregon, USA	Domain 8 60. Alter incentive/allowance structures AND Domain 9 67. Change record systems	'Meaningful use' (MU) criteria (i) Change record systems: 2012: addition of 'readiness to quit' and 'counselling given' fields to the vital sign section of the medical record (ii) 2014: Full implementation of policy, including incentive payments	+	+	+		+	**Facilitators:** Inner setting: structural characteristics (inclusion of smoking status as a 'vital sign' increases the rate of identifying smokers)	Moderate
Coleman, 2007 [32]	UK	60. Alter incentive/allowance structures	QOF 2004. Financially incentivised target for general practitioners: to record their patients' smoking status ('ever'); and	+	+	**0**			**Facilitators:** Inner setting: structural characteristics (availability of cessation services to refer patients to, availability of nicotine treatment to prescribe)	Serious

First author, year	Location	Implementation strategy category	Intervention	Practitioner-level outcomes			Patient-level outcomes		Perceived facilitators and barriers	Risk of bias
				Recording smoking status	Providing cessation advice	Prescribing cessation medication	Quit attempts	Cessation		
			to record smoking status every 15 months for patients who have coronary heart disease, diabetes mellitus, COPD, transient ischaemic attack or stroke, asthma, or hypertension, and every 15 months offer cessation advice or referral to a cessation service for these co-morbid patients who smoke						**Barriers:** Implementation process: executing (no targets were set for prescribing nicotine addiction treatments; the rates of NRT prescriptions did not increase)	
Dhalwani, 2013 [38]	UK	60. Alter incentive/allowance structures	QOF 2004	+					**Facilitators:** Inner setting: readiness for implementation: (iii) access to knowledge and information (GPs' awareness of the impending introduction	Serious

First author, year	Location	Implementation strategy category	Intervention	Practitioner-level outcomes			Patient-level outcomes		Perceived facilitators and barriers	Risk of bias
				Recording smoking status	Providing cessation advice	Prescribing cessation medication	Quit attempts	Cessation		
									of the 2004 GP contract)	
Farley, 2017 [40]	UK	60. Alter incentive/allowance structures	QOF 2004	+	+	+		**0**	**Barriers:** Inner setting: culture (cancer patients would benefit if general practitioners became more actively involved in supporting smoking cessation) **Facilitators:** Outer setting: external policy and incentives (QOF incentive not targeting cancer patients resulted in the increase of smoking targets for cancer patients too)	Low
Fichera, 2016 [45]	England	60. Alter incentive/allowance structures	QOF 2004		**0**	**0**			**Facilitators:** Inner setting: structural characteristics (improvements in care induced by the QOF for individuals with the targeted health	Moderate

First author, year	Location	Implementation strategy category	Intervention	Practitioner-level outcomes			Patient-level outcomes		Perceived facilitators and barriers	Risk of bias
				Recording smoking status	Providing cessation advice	Prescribing cessation medication	Quit attempts	Cessation		
									conditions might include better monitoring of the condition, increased contacts with the doctor, healthcare, and lifestyle advice)	
Fortmann, 2020 [56]	United States (multi-state)	Domain 8 60. Alter incentive/allowance structures AND Domain 9 71. Change accreditation or membership requirements	(i) Financial incentives via 'meaningful use' (MU) criteria (ii) Accreditation requirement change: "in 2011, the Health Resources and Services Administration (HRSA)… updated its standards for documenting smoking and cessation counselling; these standards apply to all community health centres	+					**Barriers:** Characteristics of individuals: other personal attributes (smoking status documentation was lower for younger patients, men, non-white subgroups, and patients with opioid use disorders) **Facilitators:** Characteristics of individuals: other personal attributes (most comorbidities were associated with higher odds of documented smoking status)	Moderate

First author, year	Location	Implementation strategy category	Intervention	Practitioner-level outcomes			Patient-level outcomes		Perceived facilitators and barriers	Risk of bias
				Recording smoking status	Providing cessation advice	Prescribing cessation medication	Quit attempts	Cessation		
			(CHCs) certified as Federally Qualified Community Health Centres and meeting all reporting requirements is a condition of funding"							
Hardy, 2014 [39]	UK	60. Alter incentive/allowance structures	QOF 2004		**+ / 0**				**Facilitators:** Outer setting: external policy and incentives (QOF incentive not targeting pregnant patients resulted in the increase of smoking targets for these patients too)	Serious
McGovern, 2008 [43]	Scotland	60. Alter incentive/allowance structures	QOF 2004	**+**	**+**				N/A	Serious
Millett, 2007 [44]	UK	60. Alter incentive/allowance structures	QOF 2004	**+**	**+**				**Facilitators:** Outer setting: external policies and incentives (reduced tobacco use in	Serious

First author, year	Location	Implementation strategy category	Intervention	Practitioner-level outcomes			Patient-level outcomes		Perceived facilitators and barriers	Risk of bias
				Recording smoking status	Providing cessation advice	Prescribing cessation medication	Quit attempts	Cessation		
									society, financial incentives are likely to be most effective in reducing the prevalence of smoking when combined with other quality improvement initiatives [e.g. active dissemination of clinical guidelines on smoking cessation, ongoing training and support for front-line staff] within a comprehensive tobacco control strategy) Inner setting: readiness for implementation: (ii) available resources (ongoing training and support for front-line staff) Inner setting: readiness for implementation: (iii) access to knowledge and information (active dissemination of clinical	

First author, year	Location	Implementation strategy category	Intervention	Practitioner-level outcomes			Patient-level outcomes		Perceived facilitators and barriers	Risk of bias
				Recording smoking status	Providing cessation advice	Prescribing cessation medication	Quit attempts	Cessation		
									guidelines on smoking cessation)	
Simpson, 2006 [49]	Scotland	60. Alter incentive/allowance structures	QOF 2004	+	+				**Barriers:** Characteristics of individuals: knowledge and beliefs about the intervention (patients in deprived areas and males may be less willing to seek advice for their condition) Characteristics of individuals: other personal attributes (average consultation length for deprived patients is ~ 1 to 2 min shorter than for affluent patients; this may have reduced the opportunity for GPs to record risk factors) **Facilitators:** Outer setting: external policies and incentives (other developments	Serious

First author, year	Location	Implementation strategy category	Intervention	Practitioner-level outcomes			Patient-level outcomes		Perceived facilitators and barriers	Risk of bias
				Recording smoking status	Providing cessation advice	Prescribing cessation medication	Quit attempts	Cessation		
									may have also contributed)	
Sutton, 2010 [47]	Scotland	60. Alter incentive/allowance structures	QOF 2004	**+**					N/A	Moderate
Szatkowski, 2010 [29]	UK	60. Alter incentive/allowance structures	QOF 2004	**+**					N/A	Serious
Szatkowski, 2011 [28]	England	60. Alter incentive/allowance structures	QOF 2004		**+ / 0**				**Barriers:** Implementation process (discrepancy between practitioner-reported and patient-reported outcome measures is a problem)	Serious
Szatkowski, 2016 [27]	England	60. Alter incentive/allowance structures	QOF 2012 amendment: encouraging GPs to offer referral to the NHS Stop Smoking Services and prescribe pharmacotherapy to all smokers,		**+**	**0**			**Barriers:** Implementation process: executing (the electronic codes that GPs were able to use to receive payment included the 'record of cessation advice' code that they had used	Moderate

First author, year	Location	Implementation strategy category	Intervention	Practitioner-level outcomes			Patient-level outcomes		Perceived facilitators and barriers	Risk of bias
				Recording smoking status	Providing cessation advice	Prescribing cessation medication	Quit attempts	Cessation		
			regardless of their smoking-related medical history						before the policy change, when the 2012 policy was not intending to incentivise this action)	
Taggar, 2012 [30]	UK	60. Alter incentive/allowance structures	(i) QOF 2004 (ii) QOF 2006, QOF 2008 2006 amendment: recording smoking status in patients without smoking-related morbidity was required periodically (every 27 months) rather than 'ever' 2008 amendment: chronic kidney disease (CKD) and mental illness (schizophrenia, bipolar affective disorder and other psychoses) were added to the list	**(i): +** **(ii): 0**	**(i): +** **(ii): 0**				**Facilitators:** Implementation process: executing (specific wording within QOF targets is influential on clinical behaviour)	Serious

First author, year	Location	Implementation strategy category	Intervention	Practitioner-level outcomes			Patient-level outcomes		Perceived facilitators and barriers	Risk of bias
				Recording smoking status	Providing cessation advice	Prescribing cessation medication	Quit attempts	Cessation		
			of smoking-related conditions which required recording of smoking status and cessation advice every 15 months							
Tahrani, 2007 [42]	England	60. Alter incentive/allowance structures	QOF 2004	+	+				N/A	Serious
Akman, 2017 [72]	Turkey	Domain 8 65. Use capitated payments AND Domain 9 66. Mandate change, 67. Change record systems, 71. Change accreditation or membership requirements	'Health Transformation Program' Capitated payments: "With the introduction of new structure, family doctors are paid on a capitation basis with incentives for selected preventive services"		**0**				**Facilitators:** Outer setting: external policy and incentives (other contributing factors, health agenda has shifted from communicable and vaccine preventable diseases to non-communicable diseases)	Serious

First author, year	Location	Implementation strategy category	Intervention	Practitioner-level outcomes			Patient-level outcomes		Perceived facilitators and barriers	Risk of bias
				Recording smoking status	Providing cessation advice	Prescribing cessation medication	Quit attempts	Cessation		
			Mandate change:" To establish a stronger primary care system, in 2003 the Turkish government introduced the 'Health Transformation Program'." Change record systems: "Facilities for the family health centres were improved compared to former health centres including computerization enabling electronic record keeping." Change accreditation or membership requirements: "Those primary							

First author, year	Location	Implementation strategy category	Intervention	Practitioner-level outcomes			Patient-level outcomes		Perceived facilitators and barriers	Risk of bias
				Recording smoking status	Providing cessation advice	Prescribing cessation medication	Quit attempts	Cessation		
			care doctors who were formerly called 'general practitioners' were re-designated as 'family doctors' after completing a 10-day orientation course."							
Donner-Banzhoff, 1996 [75]	Germany vs UK	65. Use capitated payments	Fee-For-Service (FFS) based systems (Germany) vs Capitation (UK)		**0**	**0**			**Barriers:** Inner setting: culture (physicians show a lack of enthusiasm for encouraging smoking cessation because they are aware of the barriers that prevent their smoking patients from complying with their advice and the work does not conform with the traditional medical curative model)	Serious
Domain 9. Change infrastructure										

First author, year	Location	Implementation strategy category	Intervention	Practitioner-level outcomes			Patient-level outcomes		Perceived facilitators and barriers	Risk of bias
				Recording smoking status	Providing cessation advice	Prescribing cessation medication	Quit attempts	Cessation		
Akman, 2017 [72]	Turkey	Domain 8 65. Use capitated payments AND Domain 9 66. Mandate change, 67. Change record systems, 71. Change accreditation or membership requirements	'Health Transformation Program' Capitated payments: "With the introduction of new structure, family doctors are paid on a capitation basis with incentives for selected preventive services" Mandate change:" To establish a stronger primary care system, in 2003 the Turkish government introduced the 'Health Transformation Program'." Change record systems: "Facilities for the family		**0**				**Facilitators:** Outer setting: external policy and incentives (other contributing factors, health agenda has shifted from communicable and vaccine preventable diseases to non-communicable diseases)	Serious

First author, year	Location	Implementation strategy category	Intervention	Practitioner-level outcomes			Patient-level outcomes		Perceived facilitators and barriers	Risk of bias
				Recording smoking status	Providing cessation advice	Prescribing cessation medication	Quit attempts	Cessation		
			health centres were improved compared to former health centres including computerization enabling electronic record keeping." Change accreditation or membership requirements: "Those primary care doctors who were formerly called 'general practitioners' were re-designated as 'family doctors' after completing a 10-day orientation course."							
Szatkowski, 2021 [36]	England	66. Mandate change	Change to the public health commissioning infrastructure			-			**Barriers:** Outer setting: external policies and incentives (where there is no local	Serious

First author, year	Location	Implementation strategy category	Intervention	Practitioner-level outcomes			Patient-level outcomes		Perceived facilitators and barriers	Risk of bias
				Recording smoking status	Providing cessation advice	Prescribing cessation medication	Quit attempts	Cessation		
									Stop Smoking Service to which general practitioners can refer pregnant women there is a reduced stimulus for discussion of smoking cessation and less direct prescribing of NRT)	
Bailey, 2017 [50]	Oregon, USA	Domain 8 60. Alter incentive/allowance structures AND Domain 9 67. Change record systems	'Meaningful use' (MU) criteria (i) Change record systems: 2012: addition of 'readiness to quit' and 'counselling given' fields to the vital sign section of the medical record (ii) 2014: Full implementation of policy, including incentive payments	+	+	+		+	**Facilitators:** Inner setting: structural characteristics (inclusion of smoking status as a 'vital sign' increases the rate of identifying smokers)	Moderate

First author, year	Location	Implementation strategy category	Intervention	Practitioner-level outcomes			Patient-level outcomes		Perceived facilitators and barriers	Risk of bias
				Recording smoking status	Providing cessation advice	Prescribing cessation medication	Quit attempts	Cessation		
Dhalwani, 2014 [41]	UK	69. Create or change credentialing and/or licensure standards	Clinical guideline change; broadening of indications for NRT for pregnant women			**0**			**Facilitators:** Characteristics of individuals: other personal attributes (females with asthma or mental illnesses and those from more socioeconomically-deprived areas were more likely to receive prescriptions during pregnancy)	Serious
Langley, 2011 [37]	England	Domain 8 59. Place innovation on fee for service lists/formularies AND Domain 9 69. Create or change credentialing and/or licensure standards	(i) Introduction of a new cessation medication (varenicline) onto a country's prescription scheme, December 2006 (ii) Introduction of NICE guideline for varenicline, July 2007			**(i) + / 0** **(ii) + / 0**			**Facilitators:** Inner setting: readiness for implementation: (iii) access to knowledge and information (measures to increase physicians' confidence in the effectiveness and safety of the medication) Characteristics of individuals: knowledge and beliefs about the intervention (raising awareness of	Moderate

First author, year	Location	Implementation strategy category	Intervention	Practitioner-level outcomes			Patient-level outcomes		Perceived facilitators and barriers	Risk of bias
				Recording smoking status	Providing cessation advice	Prescribing cessation medication	Quit attempts	Cessation		
									varenicline amongst smokers)	
Langley, 2011 [34]	England	69. Create or change credentialing and/or licensure standards	Clinical guideline change; broadening of indications for NRT for adolescents			**0**			**Barriers:** Outer setting: patient needs and resources (teenagers make fewer visits to their GP than adults and may be less likely than adults to ask for NRT, therefore general practice may not be an effective setting for the distribution of NRT to people within this age group) Characteristics of individuals: knowledge and beliefs about the intervention (some young people would find using NRT embarrassing, unpleasant or expensive) Characteristics of individuals: knowledge	Moderate

First author, year	Location	Implementation strategy category	Intervention	Practitioner-level outcomes			Patient-level outcomes		Perceived facilitators and barriers	Risk of bias
				Recording smoking status	Providing cessation advice	Prescribing cessation medication	Quit attempts	Cessation		
									and beliefs about the intervention (concerns among healthcare professionals as to the safety of NRT for teenagers) Inner setting: readiness for implementation: (iii) access to knowledge and information (lack of awareness of the licensing change among GPs)	
Langley, 2012 [35]	England	69. Create or change credentialing and/or licensure standards	Clinical guideline change; broadening of indications for NRT for patients with cardiovascular disease			**0**			**Barriers:** Outer setting: external policies and incentives (factors other than the licensing change have led to a widespread decrease in prescribing for NRT)	Moderate
Li, 2020 [55]	United States (multi-state)	69. Create or change credentialing and/or licensure standards	US Preventive Services Task Force (USPSTF) 2013 guideline recommendation	**+**	**+**	**+**			**Facilitators:** Outer setting: external policies and incentives (rereleased USPSTF recommendation in	Serious

First author, year	Location	Implementation strategy category	Intervention	Practitioner-level outcomes			Patient-level outcomes		Perceived facilitators and barriers	Risk of bias
				Recording smoking status	Providing cessation advice	Prescribing cessation medication	Quit attempts	Cessation		
			to provide low-dose computed tomography for lung cancer screening (LDCT-LCS)						2015 for clinicians to offer cessation support to smokers)	
Thorndike, 2007 [53]	United States (multi-state)	69. Create or change credentialing and/or licensure standards	Release and update of the US Public Health Service evidence-based national guidelines for the treatment of tobacco use	**0**	**0**				**Barriers:** Inner setting: structural characteristics (lack of time to provide adequate preventive counselling, lack of insurance coverage for smoking cessation pharmacotherapies) Characteristics of individuals: other personal attributes (competing demands of other medical problems during a visit) **Facilitators:** Outer setting: cosmopolitanism (embedding physicians in a broader system that integrates smoking	Moderate

First author, year	Location	Implementation strategy category	Intervention	Practitioner-level outcomes			Patient-level outcomes		Perceived facilitators and barriers	Risk of bias
				Recording smoking status	Providing cessation advice	Prescribing cessation medication	Quit attempts	Cessation		
									cessation treatment more easily into practice [facilitating referral] and cessation support outside the office) Inner setting: implementation climate: (iii) relative priority (most physicians regard addressing smoking as important) Characteristics of individuals: knowledge and beliefs about the intervention (most physicians report feeling prepared to counsel about smoking)	
Verbiest, 2013 [67]	Netherlands	Domain 8 59. Place innovation on fee for service lists/formularies AND Domain 9	(i) Increasing access to health insurance coverage which included smoking cessation treatment			**(i) +** **(ii) 0**		**(i) +** **(ii) 0**	**Facilitators:** Inner setting: structural characteristics (increased access to cessation medications, health insurance coverage for smoking	Moderate

First author, year	Location	Implementation strategy category	Intervention	Practitioner-level outcomes			Patient-level outcomes		Perceived facilitators and barriers	Risk of bias
				Recording smoking status	Providing cessation advice	Prescribing cessation medication	Quit attempts	Cessation		
		69. Create or change credentialing and/or licensure standards	(ii) Introduction of the first Dutch guideline 'Treatment of Tobacco Dependence'						cessation treatment prompts GPs to prescribe evidence-based pharmaceuticals for smoking cessation)	
Fortmann, 2020 [56]	United States (multi-state)	Domain 8 60. Alter incentive/allowance structures AND Domain 9 71. Change accreditation or membership requirements	(i) Financial incentives via 'meaningful use' (MU) criteria (ii) Accreditation requirement change: "in 2011, the Health Resources and Services Administration (HRSA)… updated its standards for documenting smoking and cessation counselling; these standards apply to all community health centres (CHCs) certified as	+					**Barriers:** Characteristics of individuals: other personal attributes (smoking status documentation was lower for younger patients, men, non-white subgroups, and patients with opioid use disorders) **Facilitators:** Characteristics of individuals: other personal attributes (most comorbidities were associated with higher odds of documented smoking status)	Moderate

First author, year	Location	Implementation strategy category	Intervention	Practitioner-level outcomes			Patient-level outcomes		Perceived facilitators and barriers	Risk of bias
				Recording smoking status	Providing cessation advice	Prescribing cessation medication	Quit attempts	Cessation		
			Federally Qualified Community Health Centres and meeting all reporting requirements is a condition of funding"							
Peterson, 2016 [52]	United States (multi-state)	71. Change accreditation or membership requirements	Accreditation program for primary care physicians		+				**Barriers:** Inner setting: implementation climate: (ii) compatibility (QI is difficult to sustain if it is not integrated into the existing culture and systems of care)	Serious
Shi, 2017 [59]	United States (multi-state)	71. Change accreditation or membership requirements	Changing standards for primary care practices—'Patient-centered medical home' (PCMH) recognition status	+	+	+			N/A	Moderate

First author, year	Location	Implementation strategy category	Intervention	Practitioner-level outcomes			Patient-level outcomes		Perceived facilitators and barriers	Risk of bias
				Recording smoking status	Providing cessation advice	Prescribing cessation medication	Quit attempts	Cessation		
Van Doorn-Klomberg, 2014 [68]	Netherlands	71. Change accreditation or membership requirements	Changing standards for primary care practices	**+ / 0**	**+ / 0**			**0**	**Facilitators:** Implementation process: reflecting and evaluating (audit and feedback as a central mechanism) Outer setting: external policies and incentives (other developments in the primary care field) Intervention characteristics: complexity (adaptations to the program were made to reduce the burden of work) Intervention characteristics: adaptability (health professionals can take ownership of the improvement plans that are tailored to the individual practices)	Moderate
Multiple domains [a]										

First author, year	Location	Implementation strategy category	Intervention	Practitioner-level outcomes			Patient-level outcomes		Perceived facilitators and barriers	Risk of bias
				Recording smoking status	Providing cessation advice	Prescribing cessation medication	Quit attempts	Cessation		
Akman, 2017 [72]	Turkey	Domain 8 65. Use capitated payments AND Domain 9 66. Mandate change, 67. Change record systems, 71. Change accreditation or membership requirements	'Health Transformation Program' Capitated payments: "With the introduction of new structure, family doctors are paid on a capitation basis with incentives for selected preventive services" Mandate change:" To establish a stronger primary care system, in 2003 the Turkish government introduced the 'Health Transformation Program'." Change record systems: "Facilities for the family		**0**				**Facilitators:** Outer setting: external policy and incentives (other contributing factors, health agenda has shifted from communicable and vaccine preventable diseases to non-communicable diseases)	Serious

First author, year	Location	Implementation strategy category	Intervention	Practitioner-level outcomes			Patient-level outcomes		Perceived facilitators and barriers	Risk of bias
				Recording smoking status	Providing cessation advice	Prescribing cessation medication	Quit attempts	Cessation		
			health centres were improved compared to former health centres including computerization enabling electronic record keeping." Change accreditation or membership requirements: "Those primary care doctors who were formerly called 'general practitioners' were re-designated as 'family doctors' after completing a 10-day orientation course."							
Bailey, 2017 [50]	Oregon, USA	Domain 8 60. Alter incentive/allowance structures	'Meaningful use' (MU) criteria (i) Change record systems: 2012:	+	+	+		+	**Facilitators:** Inner setting: structural characteristics (inclusion of smoking	Moderate

First author, year	Location	Implementation strategy category	Intervention	Practitioner-level outcomes			Patient-level outcomes		Perceived facilitators and barriers	Risk of bias
				Recording smoking status	Providing cessation advice	Prescribing cessation medication	Quit attempts	Cessation		
		AND Domain 9 67. Change record systems	addition of 'readiness to quit' and 'counselling given' fields to the vital sign section of the medical record (ii) 2014: Full implementation of policy, including incentive payments						status as a 'vital sign' increases the rate of identifying smokers)	
Fortmann, 2020 [56]	United States (multi-state)	Domain 8 60. Alter incentive/allowance structures AND Domain 9 71. Change accreditation or membership requirements	(i) Financial incentives via 'meaningful use' (MU) criteria (ii) Accreditation requirement change: "in 2011, the Health Resources and Services Administration (HRSA)… updated its standards for documenting smoking and	+					**Barriers:** Characteristics of individuals: other personal attributes (smoking status documentation was lower for younger patients, men, non-white subgroups, and patients with opioid use disorders) **Facilitators:** Characteristics of individuals: other personal attributes	Moderate

First author, year	Location	Implementation strategy category	Intervention	Practitioner-level outcomes			Patient-level outcomes		Perceived facilitators and barriers	Risk of bias
				Recording smoking status	Providing cessation advice	Prescribing cessation medication	Quit attempts	Cessation		
			cessation counselling; these standards apply to all community health centres (CHCs) certified as Federally Qualified Community Health Centres and meeting all reporting requirements is a condition of funding"						(most comorbidities were associated with higher odds of documented smoking status)	
Langley, 2011 [37]	England	Domain 8 59. Place innovation on fee for service lists/formularies AND Domain 9 69. Create or change credentialing and/or licensure standards	(i) Introduction of a new cessation medication (varenicline) onto a country's prescription scheme, December 2006 (ii) Introduction of NICE guideline for varenicline, July 2007			**(i) + / 0** **(ii) + / 0**			**Facilitators:** Inner setting: readiness for implementation: (iii) access to knowledge and information (measures to increase physicians' confidence in the effectiveness and safety of the medication) Characteristics of individuals: knowledge and beliefs about the	Moderate

First author, year	Location	Implementation strategy category	Intervention	Practitioner-level outcomes			Patient-level outcomes		Perceived facilitators and barriers	Risk of bias
				Recording smoking status	Providing cessation advice	Prescribing cessation medication	Quit attempts	Cessation		
									intervention (raising awareness of varenicline amongst smokers)	
Mullins, 2009 [51]	Delaware, USA	Domain 5 40. Distribute educational materials 42. Conduct educational meetings AND Domain 7 54. Prepare patients/consumers to be active participants	'Ask and Act program' Program contains: (i) educational component for physicians (free patient materials for offices, continuing medical education programs for physicians and allied health professionals, and information on evidence-based interventions), and (ii) free patient materials which engage patients (patient materials include pre-printed		+			+	**Facilitators:** Inner setting: readiness for implementation: (iii) access to knowledge and information (physicians reported that they felt more comfortable with smoking cessation counselling and billing for this intervention, and that they were more likely to counsel their patients after hearing the presentation)	Serious

First author, year	Location	Implementation strategy category	Intervention	Practitioner-level outcomes			Patient-level outcomes		Perceived facilitators and barriers	Risk of bias
				Recording smoking status	Providing cessation advice	Prescribing cessation medication	Quit attempts	Cessation		
			prescription pads with tips on how to quit, brochures, and laminated quitline referral cards. Metal lapel pins and wall posters act as visual cues to encourage patients to ask their family physician for help, and a guide to tobacco cessation group visits details how practices can organize and bill for counselling sessions)							
Verbiest, 2013 [67]	Netherlands	Domain 8 59. Place innovation on fee for service lists/formularies AND Domain 9	(i) Increasing access to health insurance coverage which included smoking cessation treatment			**(i) +** **(ii) 0**		**(i) +** **(ii) 0**	**Facilitators:** Inner setting: structural characteristics (increased access to cessation medications, health insurance coverage for smoking	Moderate

First author, year	Location	Implementation strategy category	Intervention	Practitioner-level outcomes			Patient-level outcomes		Perceived facilitators and barriers	Risk of bias
				Recording smoking status	Providing cessation advice	Prescribing cessation medication	Quit attempts	Cessation		
		69. Create or change credentialing and/or licensure standards	(ii) Introduction of the first Dutch guideline 'Treatment of Tobacco Dependence'						cessation treatment prompts GPs to prescribe evidence-based pharmaceuticals for smoking cessation)	

A summary of the key results. The included studies are ordered by implementation strategy domain (5, 7, 8 and 9 and 'Multiple domains'). Within the domains, the studies are ordered by implementation strategy category then alphabetically by first author surname.

(Wright, 2018) [71] was excluded from narrative synthesis as it was at critical risk, so it is excluded from this table.

[a] Note: the studies under 'Multiple domains' are also listed above in the relevant separate domains.

Effectiveness outcomes key:
- + : positive effect on outcome
- -: negative effect on outcome
- 0: no significant effect on outcome
- •: outcome was not assessed

Table 3.3. Summary of perceived facilitators and barriers

Construct	Perceived facilitators and barriers
Intervention characteristics	Facilitators: Intervention should be simple, accessible, and adaptable.
Outer setting	Facilitators: policies and incentives (tobacco control measures, anti-smoking social norms, funding for public health and cessation clinics), systems-level interventions allowing easy referral to cessation programs or community-based support.
Inner setting	Barriers: time and resource constraints, lack of access to free cessation medications and follow-up appointments, incompatibility with and lower priority of smoking cessation compared to existing clinical demands, lack of knowledge and training around guideline changes.
Patient/physician characteristics	Barriers: smokers with greatest risk of cardiovascular disease are less likely to take up health check invitations, some patient characteristics are associated with worse smoking outcome measures, smokers' lack of awareness of, and negative perceptions about, the effectiveness of cessation medications; physicians having doubts about the effectiveness and safety of cessation interventions and not feeling competent to deliver cessation counselling.
Implementation process	Facilitators: multifaceted approaches to intervention implementation (which include audit and feedback) Barriers during the execution of intervention implementation delivery: wording/coding of targets not optimally targeting the desired clinical behaviours/outcome measures, focussing on the 'risk factor identification' and not the 'intervention' aspects of cessation treatment, lack of sustained advertising of cessation support, insufficient messaging to patients trying to quit smoking about the cessation support options that are available

This table shows a condensed summary of the key facilitators and barriers from the included studies. Perceived facilitators and barriers, extracted from the studies, were mapped to the constructs defined by the Consolidated Framework for Implementation Research (CFIR) [26] (Appendix 7).

Chapter 4 – Vaping recording in electronic health records

Preface

The objective of this chapter was to describe and characterise the extent to which nicotine vaping has been recorded in UK primary care electronic health records, in order to assess the current utility of population-level EHR vaping status data.

This chapter presents the study I conducted using 2006–2022 UK primary care electronic health record data from Clinical Practice Research Datalink (CPRD), published as a peer-reviewed publication [2]:

> Tildy, B. E., McNeill, A., Robins, J., Dregan, A., Richardson, S., & Brose, L. S. (2023). How is nicotine vaping product (e-cigarette) use monitored in primary care electronic health records in the United Kingdom? An exploratory analysis of Clinical Practice Research Datalink (CPRD). *BMC Public Health*, *23*(1), 1–13. https://doi.org/10.1186/S12889-023-17200-7

The supplementary materials referred to in my publication are available in **Appendix C** of this thesis.

In this chapter, the Author's Accepted Manuscript version of the publication [2] is included, rather than the publisher's typeset PDF of the manuscript, which allowed me to edit the format (font type and size, line spacing) to ease reading. For the references cited in the manuscript, I have retained their original in-text citation number (but have made these superscript numbers to distinguish them from the in-text citations in the thesis), and a reference list for this manuscript is provided at the end of this chapter.

Declaration of roles

I developed this manuscript in collaboration with Dr Leonie Brose, Professor Ann McNeill, Dr Alexandru Dregan and Dr John Robins (King's College London), and Dr Sol Richardson (Tsinghua University).

I formulated the research questions and wrote the protocol to access the CPRD data, with input from LB, AM, SR, and AD. SR provided epidemiological statistical input into the design of the study. After the protocol was approved by the body that holds CPRD data, AD granted me access to the data – AD is one of the multi-study license holders at King's College London who provides data access to approved researchers. I conducted the data analysis, and JR provided programming advice. All authors gave feedback on the analysis and interpretation of the data. I wrote the initial manuscript. All co-authors reviewed and provided input on drafts. During peer review of the manuscript, one of the peer reviewers recommended that the effect of the EVALI outbreak on the outcome measure is tested using a statistical test. I provided SR access to the cleaned and prepared data, and he conducted interrupted time series analyses. I handled the manuscript submission and responded to peer reviews. All authors read and approved the final manuscript.

Publication

How is nicotine vaping product (e-cigarette) use monitored in primary care electronic health records in the United Kingdom? An exploratory analysis of Clinical Practice Research Datalink (CPRD)

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Abstract

Background: Electronic health records (EHRs) could identify long-term health effects of nicotine vaping. We characterised the extent to which vaping is recorded in primary care EHRs in the UK, on a population level.

Methods: We performed descriptive analysis of Clinical Practice Research Datalink (CPRD), primary care electronic health records of 25% of the UK population (~16 million patients). Patients aged ≥18 years whose vaping status was recorded using medical codes between 2006–2022 were identified. We reported the frequency of vaping codes; their distribution by patient age, gender, and ethnicity; trends in vaping recording over time (including interrupted time series analyses); and transitions in patient smoking status.

Results: Seven medical codes indicated current or former vaping, from 150,114 patients. When their vaping status was first recorded, mean patient age was 50.2 years (standard deviation: 15.0), 52.4% were female, and 82.1% were White. Of those recorded as currently

vaping, almost all (98.9%) had records of their prior smoking status: 55.0% had been smoking, 38.3% had stopped smoking, 5.6% had never smoked. Of those who were smoking prior to being recorded as vaping, more than a year after the vaping record, over a third (34.2%) were still smoking, under a quarter (23.7%) quit smoking, 1.7% received a 'never smoked' status, and there was no smoking status for 40.4%. The 'e-cigarette or vaping product use-associated lung injury' (EVALI) outbreak was significantly associated with a declining trend in new records of current vaping between September 2019 and March 2020; and an immediate significant increase in new records of former vaping, followed by a declining trend.

Conclusions: Few patients are being asked about vaping. Most who vape had smoked, and many quit smoking after starting vaping. To enable electronic health records to provide stronger evidence on health effects, we recommend improved completeness, accuracy and consistency.

Background

Smoking is a leading preventable cause of illness and premature death in the United Kingdom (UK) and worldwide [1]. Evidence suggests that using nicotine vaping products (NVPs, or e-cigarettes) is less harmful than smoking tobacco [2], and NVPs improve smoking cessation likelihood compared to nicotine replacement therapy [3]. However, due to uncertainty about the long-term health effects of NVPs and concerns around youth uptake, policy and guidelines around NVPs vary internationally [4]. Some clinical guidelines recommend that health professionals encourage the use of NVPs as another option for smoking cessation on a par with medicinally licensed pharmacotherapies and behavioural support [4,5]. For example, the UK National Institute for Health and Care Excellence clinical guidelines recommend that adults who smoke have access to NVPs alongside other smoking cessation interventions [6]. In the UK, NVPs are regulated as consumer products and NVPs are available on the open market to those aged ≥18 years [2]. NVPs are the most popular smoking cessation aid in the UK [2] and 9.1% of adults in Great Britain regularly used NVPs in 2023 [7].

Monitoring NVP use prevalence and uptake can establish the long-term benefits and harms of NVP use [5]. Although population surveys can generate NVP use prevalence estimates [7–9], these are often cross-sectional, under-sample vulnerable populations, have short-term follow-up, or do not enquire extensively about health outcomes. Electronic health records (EHRs) could help identify long-term health effects of NVP use, pending NVP use data completeness.

Currently, studies about how health professionals are documenting NVP use in EHRs are limited (Supplementary Box 1). Studies from the United States (US), found low vaping screening rates in EHRs, ranging from: 14.3% in 2019 [10] to 34.8% in 2021–2022 [11]; 0% in 11–17-year-olds in 2016–2017 [12] and 16% in 18–35-year-olds who had never smoked in 2020 [13]. US studies found that patients with documented (current) vaping were more likely to be male, aged 18–44 years, and White [14,15]. Although the prevalence of US patients who have vaping documentation is still low (<1%), it is increasing. First-time incidence of vaping documentation increased from 0.1 to 95 per 100,000 patients from 2006 to 2015 [14,16] and the prevalence of vaping documentation (including 'never vaping') increased from 0.0032% to 0.46% in progress notes between 2009–2014 [17]. Similar to population surveys, the rate of current/former vaping in non-smoking populations is relatively low in EHRs [13]; patients are more likely to be screened for vaping if they have indicated that they smoke [11], hence there are high proportions of current and former smoking among those who have vaping documentation [14,16,17]. Two US studies used EHRs (2012–2015 [16], 2018–2020 [15]) to examine transitions between current vaping and smoking status, finding that smoking cessation was more likely among those who received current vaping documentation compared to those not vaping.

To our knowledge, there have been no studies specifically investigating health professionals' documentation of vaping in the UK. In the UK, general practitioners (GPs) are required to record standardised information on clinical conditions, such as smoking status. Although a 2018 Royal College of Physicians (UK) consultation recommended NVP use recording in EHRs [18], GPs are not currently incentivised to record this via the pay-for-performance scheme (Quality and Outcomes Framework, QOF). UK QOF guidelines (2018/19–2022/23 [19]) recommend that NVP users "who have never smoked or given up smoking should be classified as non-smokers or ex-smokers respectively", which may lead to under-recording

of NVP use in EHRs. Other UK guidance (2020 [20], 2021 [6]) recommended that health professionals ask about NVP use routinely. This guidance was in response to an outbreak of severe lung injuries largely confined to the US: 'e-cigarette or vaping product use-associated lung injury' (EVALI) [21]. EVALI was purported to be associated with conventional nicotine vaping, but the US CDC concluded that vaping products which contained tetrahydrocannabinol and Vitamin E acetate were linked to most cases [2,21]. EVALI was identified in July 2019, followed by a peak in cases and US news coverage [22] in September 2019, then a steady decline through early 2020 [21].

It is not known to what extent vaping is recorded in UK EHRs. The use of existing medical codes to record vaping is hypothesised to be suboptimal [23]. We aimed to describe and characterise the extent to which NVP use is being recorded in primary care in the UK, using Clinical Practice Research Datalink (CPRD) data.

Research questions (RQs)

RQ1. Which medical codes indicative of current vaping and former vaping are most frequently used in primary care EHRs in the UK between 2006 and March 2022?

RQ2. What are temporal trends in the first-time incidence of current and former vaping codes, and was there a change in the incidence pre- and post-EVALI outbreak in the US?

RQ3. How does the distribution of vaping codes vary with patient demographics (age, gender, ethnicity)?

RQ4. What are the transitions in smoking status among patients who received their first current or former vaping code, comparing previous and subsequent (>12 months) smoking status records?

Methods

Data source

CPRD includes anonymised medical records from UK general practices from 1990 to the present [24]. CPRD includes detailed medical data for approximately 16 million active patients (25% of the UK population) and 60 million historical patients from around 2,000 UK practices (26% of UK practices). The dataset is representative of the UK population in terms of geography, relative social deprivation, age and gender [25]. In a recent CPRD dataset (linked with Hospital Episode Statistics), over 80% of currently registered patients had their ethnicity recorded and the distribution was broadly representative of the UK population [26]. Prevalence estimates from 2007–2011 CPRD data for current smoking, and non-smoking, were found to be similar to those from nationally representative surveys [27]. CPRD collects diagnostic, therapeutic, laboratory, referral, and demographic data from GP practices on a monthly basis [24]. For this study, we pooled data from the CPRD GOLD April 2023 build and the CPRD Aurum March 2023 build; both had a cut-off event date of 31 March 2022, because CPRD was experiencing temporary issues with data quality after this date [28].

Recording vaping product use

GPs can record a vaping event in EHRs via specific SNOMED or Read medical codes during consultations with patients [24], these codes are not carried forward automatically to future consultation records. GPs can also save free-text comments, but these are not available for research purposes.

Patient population

All patients (aged ≥18 years at the date of the consultation) who received a code related to vaping at any point ('incidence') from 1 September 2006 to 31 March 2022 were extracted. Records from patients classified as 'acceptable' by CPRD were included (those with a valid gender and birth date; and logically consistent and valid registration and transferred-out

dates). Records from 'up-to-standard practices' (CPRD GOLD quality marker) were included. Duplicate records were excluded, following data specification documents [28].

After exclusions (Supplementary Figure 1), the analytical sample included 225,111 observations from 150,114 unique patients. In total, there were 152,277 first-time incident events of current or former vaping codes: 147,130 patients ever received a current vaping code, 5,147 patients ever received a former vaping code, and 2,163 received both codes (Supplementary Figure 2).

Outcome

Our main outcome variable was the incidence of codes indicating current or former vaping. Using the CPRD medical code browser, we identified ten codes used between 1 September 2006 and 31 March 2022 which relate to electronic cigarettes/e-cigarettes, vaping/vaper, electronic nicotine delivery systems (ENDS), and e-liquid (Supplementary Table 1). We derived a new variable which aggregated seven of the codes which indicated 'current vaping' or 'former vaping' specifically (Table 4.1).

Covariates

Covariates included: patient gender (male, female, non-binary/unknown), patient age when they received the vaping code (year of birth minus event date of consultation where the patient received the vaping code), geographical region of the patient's practice (North East, North West, Yorkshire and The Humber, East Midlands, West Midlands, East of England, London, South East, South West, Wales, Scotland, Northern Ireland), patient ethnicity (Asian, Black, Mixed, White, Other, unknown) and patient smoking status (never smoked, currently smoke, formerly smoked, unknown).

Ethnicity was coded using higher-level UK Census 2011 Ethnicity Categories [26]. We mapped ethnicity and smoking status-related codes to classifications used in previous studies (Supplementary Tables 2a, 2b, 3a, 3b). Ethnicity and smoking status data recorded prior to when a patient was 18 years old were retained.

For each first-time incidence of a vaping code, we sought to derive a current smoking status at three time points:

1. **Previous smoking status**: smoking status that was recorded in the patient consultation that chronologically immediately preceded receiving a vaping code.

2. **Concurrent smoking status**: smoking status that was recorded in the patient consultation that occurred on the same date as receiving a vaping code.

3. **Subsequent smoking status**: smoking status that was recorded in the chronologically latest patient consultation that took place >12 months (>365 days) after receiving a vaping code, to capture a long-term smoking cessation outcome.

Where a patient had multiple records of smoking status in their preceding, concurrent or subsequent consultation, if any of the smoking status records were 'currently smoking', this was designated as the smoking status for the respective time period.

Data analysis

Analyses were conducted in R (version 4.2.1), except the interrupted time-series analysis which was conducted in Stata 17.

RQ1: We used descriptive statistics to report the frequency of vaping codes classified as current vaping or former vaping. We calculated the number of unique patients receiving one or more vaping codes over time.

RQ2: To characterise trends in patient-level first-time incidence of vaping codes, if a unique patient had multiple consultations over time where they received a current vaping or former vaping code, only the first instance (earliest) of a particular vaping code (i.e., current vaping or former vaping) was included in the frequency count for that particular code (similar to previous work [14,16]). Following this, using CPRD denominator files (Supplementary Box 2), patient-level proportions of vaping code first-time incidence over time were calculated by dividing the number of current/former vaping patients, by the denominator

(all eligible patients contributing data to CPRD), per month. We also calculated patient-level proportions of vaping code first-time incidence over time, by geographical region.

To investigate any pre- and post-EVALI outbreak effects, we performed single-group ordinary least-squares interrupted time-series analysis using the Stata package *itsa* [29]. We fitted two models with monthly numbers of current and former vaping status records from August 2015 (when a government-commissioned report [30] on vaping increased discussion around vaping) to January 2022 as their dependent variables. Time was fitted as a linear variable representing months since September 2011. Two interruptions were modelled as occurring in September 2019 (month 97), corresponding to the peak of US media coverage about EVALI [22]; and April 2020 (month 104), corresponding to the start of the first national Coronavirus disease (COVID-19) pandemic lockdown in the UK. Models were fitted with a maximum lag term of 12 months to account for autocorrelation in the dependent variable. Both models were also adjusted for monthly numbers of all eligible patients contributing data to CPRD as a linear variable. Results were expressed as regression coefficients for the change in monthly numbers of new current or former vaping records, with Newey–West standard errors accounting for autocorrelation and potential heteroskedasticity.

RQ3: Using our patient-level first-time incidence of vaping codes, we used descriptive statistics to report the proportions of patients who received a vaping code by age, gender, and ethnicity.

RQ4: Using our patient-level first-time incidence of vaping codes, we reported the concurrent smoking status for patients who received a current vaping or former vaping code. We plotted previous smoking status and subsequent (>12 month) smoking status, separately for first-time current and former vaping, to describe transitions in smoking status over time. As a sensitivity analysis, we plotted a supplementary graph where the subsequent smoking status was the smoking status recorded in the chronologically latest patient consultation that took place >12 months (>365 days) but ≤24 months (≤730 days) after receiving the first-time current vaping code.

Ethical approval

The study protocol was granted scientific and ethical approval by the Medicine and Healthcare Regulatory Agency Independent Scientific Advisory Committee (ISAC: Protocol No. 21_000706).

Results

RQ1: Medical codes indicating current vaping and former vaping

Of the seven codes indicating current vaping or former vaping, the "Electronic cigarette user" code in the CPRD Aurum dataset was the first (13 October 2011) and most frequently used; the "Vaper with nicotine" code was not used at all (Table 4.1). There were 219,478 consultations where a patient received a current vaping code and 5,633 consultations where a patient received a former vaping code.

Of 150,114 unique patients, 107,901 (71.9%) received only one code; 42,213 (28.1%) received multiple vaping codes, including 1,857 (1.2%) receiving more than five (Supplementary Table 4). There were 2,163 (1.4%) unique patients who had ever received both a current vaping and former vaping code – of these, 1,677 patients received a current vaping code before they received a former vaping code, and 486 vice versa. For those who received both a current and former vaping code, the mean time difference between receiving their first vaping code and their second was 729.0 days (standard deviation [SD]: 558.4), median: 616.0, range: 0.0–2,710.0.

RQ2: Temporal trends and EVALI outbreak

Temporal trends

Across the 150,114 unique patients, there were 152,277 first-time incident events of current or former vaping codes: 147,130 patients ever received a current vaping code, 5,147 patients ever received a former vaping code, and 2,163 received both codes (Supplementary Figure 2).

Figure 4.1 shows the proportion of patients who received a vaping code indicating first-time current vaping or former vaping out of all patients (≥18 years old) in CPRD that month, per month. (Supplementary Graph 1 shows the trend by geographical region.) First-time incidence of vaping codes increased from September 2013. There was apparent seasonality, with a decrease in incidence during April and December. There was a notable decrease in incidence of current and former vaping codes in April 2020, the first month fully affected by the first Coronavirus disease (COVID-19) pandemic lockdown in the UK when of GP consultation frequency reduced significantly. Peak first-time incidence of current vaping codes was in November 2021: 17.8 per 100,000 patients contributing data to CPRD. Peak first-time incidence of former vaping codes was in October 2019: 0.9 per 100,0000 patients.

Interrupted time series analysis

The Breusch-Godfrey test for autocorrelation indicated that autocorrelation was present at up to eight months of lag for current vaping record outcomes and 12 months for former vaping record outcomes; these results suggested that the models appropriately accounted for autocorrelation.

Figure 4.2a shows the interrupted time-series postestimation plot for current vaping record outcomes, including actual and predicted numbers of new monthly records. Model outputs showed that numbers of new current vaping records increased at a rate of 23.2 (95% CI: 14.1–32.2, p<0.001) per month over the period analysed. After the peak of media coverage on EVALI, there was no significant step change in monthly numbers of new current vaping records (regression coefficient: 10.5, 95% CI: -221.1–242.1, p=0.928). However, we found a significant change in the linear time trend in monthly numbers of new current vaping records, with a post-interruption linear time trend of -95.1 per month (95% CI: -122.6–-67.6, p<0.001), between September 2019 and March 2020. After implementation of the first COVID-19 lockdown in the UK, there was a post-interruption decrease in monthly new current vaping records of -434.4 (95% CI: -738.9–-130.0, p=0.006) followed by a rising post-interruption time trend in monthly numbers of records of 50.4 (95% CI: 38.9–62.0, p<0.001) per month.

Figure 4.2b shows the interrupted time-series postestimation plot for new former vaping record outcomes, including actual and predicted numbers of monthly records. Model outputs showed that numbers of new former vaping records increased at a rate of 0.76 (95% CI: 0.10–1.43, p=0.025) per month over the period analysed. After the peak of media coverage on EVALI, there was a statistically-significant step change in numbers of monthly numbers of new former vaping records (regression coefficient: 36.2, 95% CI: 17.9–54.4, p<0.001). We found a significant change in the linear time trend in monthly numbers of new former vaping records, with a post-interruption linear time trend of -4.6 per month (95% CI: -5.8–-3.3, p<0.001), between September 2019 and March 2020. After implementation of the first COVID-19 lockdown in the UK, there was a post-interruption decrease in monthly new former vaping records of -12.2 (95% CI: -20.3–-4.1, p<0.001) followed by a gradually declining post-interruption time trend in monthly numbers of records of -0.4 (95% CI: -0.7–-0.2, p<0.001) per month.

RQ3: Distribution of vaping codes by patient demographics: age, gender, ethnicity

The mean age of patients when they received their first current vaping code was 50.2 years (SD: 15.0, median: 51.0, range: 18.0–99.0), and 52.2 years (SD: 15.0, median: 53.0, range: 18.0–96.0) when they received their first former vaping code (Figure 4.3).

The gender distribution in our sample was approximately balanced: 52.4% female, 47.7% male (Table 4.2).

Of 150,114 unique patients, ethnicity was recorded as ‘unknown’ for 18,553 (12.6%). The high-level ethnicity categories of patients who received a vaping code were: 2.3% Asian, 0.9% Black, 0.5% Mixed, 1.6% Other, 82.1% White and 12.6% unknown (Table 4.2).

RQ4: Smoking status transitions among patients who received a vaping code

Of 150,114 unique patients, 149,624 had at least one smoking status record, while 490 (0.3%) had no smoking status record (unknown).

Concurrent smoking status

Over three quarters (115,932/152,277, 76.1%) of patients had their concurrent smoking status recorded within the same consultation when they first received any (current/former) vaping code (Figure 4.4). Of these, the majority (n=113,822, 98.2%) were either currently smoking (n=54,491, 47.0%) or had quit smoking in the past (n=59,331, 51.2%), and those recorded as having never smoked comprised a small proportion (n=2,110, 1.8%). These proportions were similar for those who received a current vaping code. Among those who received a former vaping code, a larger proportion were currently smoking compared to among those who received a current vaping code (53.5% vs 35.2%).

Smoking status transitions

Current vaping

Of all patients who received a first-time *current* vaping code, 98.9% (145,497/147,130) had a previous current smoking status recording. The majority were smoking (n=80,986, 55.0%) or formerly smoked (n=56,300, 38.3%) before receiving the vaping code, while 5.6% (n=8,211) of patients had never smoked (Figure 4.5).

Over half (80,937/147,130, 55.0%) of patients had a subsequent current smoking status recording.

Over a year after receiving the initial *current* vaping code, over a third (34.2%) of people who were smoking before they received the vaping code were still smoking, just under a quarter (23.7%) were indicated to have quit smoking, 1.7% received a 'never smoked' status, and there was no smoking status record for 40.4%.

Over a year after receiving the initial *current* vaping code, 11.9% of people who had quit smoking before they received the vaping code had returned to smoking, over a third (37.3%) were indicated to still be quit smoking, 2.7% received a 'never smoked' status, and there was no smoking status record for 48.0%.

Over a year after receiving the initial *current* vaping code, 7.7% of people who had never smoked before they received the vaping code had initiated smoking, 18.8% were indicated to have quit smoking, 8.4% still had a 'never smoked' status, and there was no smoking status record for 65.1%.

Former vaping

Out of all patients who received for the first-time a *former* vaping code, 99.3% (5,110/5,147) had a previous current smoking status recording and 60.6% (3,121/5,147) had a subsequent current smoking status recording (Supplementary Graph 2).

See Supplementary Tables 5a and 5b for additional detail. Results from the sensitivity analysis (Supplementary Graph 3) where the subsequent smoking status was recorded between >12 months to ≤24 months after receiving the first-time current vaping code were similar to the main analysis (Figure 4.5).

Discussion

Using 2006–2022 CPRD UK primary care data, we identified seven medical codes indicating current or former vaping. Vaping code incidence increased from September 2013. The EVALI outbreak in the US (and peak media coverage in September 2019) was significantly associated with a reduction in new records of current vaping, manifested as a declining trend over a period of seven months (September 2019 to March 2020); additionally, there was an immediate increase in new records of former vaping, followed by a declining trend over the subsequent seven-month period. When patients received their first vaping code, mean age was 50.2 years, 52.4% were female, and 82.1% were White. When receiving the first vaping code, the majority of patients were either smoking or had quit smoking in the past, and <2% were recorded as having never smoked. Of those recorded as currently vaping, 98.9% had records of their previous smoking status, and 55.0% had records of their >12 months smoking status. Over a year after being recorded as vaping, 34.2% of people who were smoking prior to being recorded as vaping were still smoking, 23.7% quit smoking, 1.7% received a 'never smoked' status, and there was no smoking status for 40.4%.

Similar to US studies [10–14,16,17], we found that vaping documentation incidence in UK EHRs is low, but has increased over time. We found no medical codes indicating never vaping. There was a rising trend in new current and former vaping records over time, this may be attributed to an increase in: awareness of vaping or the relevant vaping codes among GPs; GPs screening the vaping status of their patients; or patients volunteering their vaping status or having questions about their vaping status to GPs.

The changes associated with the EVALI outbreak could be attributable to increasing numbers of patients quitting vaping due to negative media coverage of potential health harms or GPs paying greater attention to asking and recording about (former) vaping. To our knowledge, no other study has examined the effect of EVALI on vaping documentation in EHRs.

The reduction in monthly number of new current and vaping records following implementation of the first national COVID-19 lockdown could be attributable to reduced access to GP appointments.

Unlike US studies [14,15], where patients with vaping documentation were more likely to be younger, the mean age of patients in our sample when they first received a vaping code was 50 years. A 2022 Great Britain vaping survey [31] found that 11% of 18–44-year-olds, and 10% of 45–55-year-olds used NVPs, indicating that a relatively high proportion of middle-aged people use NVPs. Our finding may reflect the NVP prevalence in Great Britain, that we excluded patients <18 years, and that older people may be more likely to visit a health professional, and hence have more opportunities to receive a vaping code.

The gender distribution in our sample of patients who have ever received a vaping medical code was similar to the 2021 England and Wales Census [32] (51.0% female). However, Great Britain vaping surveys [31] found that a higher proportion of males use NVPs compared to females, similar to two US studies [14,15].

Similar to US studies [14,15], we found that most patients who have ever received a vaping code were White (82.1%), reflecting UK population ethnicity proportions [33]. However, our other ethnicity categories were confounded by 12.6% being ‘unknown’ (similar to a previous CPRD study [26]).

Our findings are similar to previous studies where a high proportion of those with vaping documentation were currently smoking (57% [14,16], 52.4% [17]) or formerly smoked (35% [14,16]).

Two US studies found that among those who smoked and vaped, 20.8% [15] and 23.0% [16] reported quitting smoking during the following year. Our finding was similar: >12 months after receiving a current vaping code, 23.7% of people who were smoking before they received the vaping code were indicated to have quit smoking. Additionally, Young-Wolff et al. [16] found that among those who quit smoking before vaping, 14.0% of those currently vaping reported returning to smoking in the following year; we found that 11.9% of people who had quit smoking before they received the vaping code had returned to smoking after 12 months. Lastly, we found that among those who have never smoked before they received the vaping code, 7.7% had initiated smoking after >12 months after receiving the current vaping code, compared with 8.0% in the prior study [16]. However, we cannot make inferences about the effectiveness of NVP use on smoking cessation from our analyses because ~45% of patients did not have a >12-month follow-up smoking status record, vaping documentation is likely to be missing not at random, and we did not control for any confounding factors.

Strengths & limitations

Our study has several strengths. This is the first study to comprehensively describe and characterise NVP use recording in UK EHRs. We used data from CPRD which covers 25% of the UK population. Our study covers 16 years from when NVPs appeared in England in 2006 to March 2022. We found that CPRD vaping record data were sufficiently sensitive to be able to detect statistically significant effects of events (EVALI, COVID-19 lockdown) on vaping record incidence.

Our study also has limitations. We could not analyse free-text comments that GPs can log, as these are not available for research purposes. While CPRD data have been shown to be largely representative of the UK population [25–27], CPRD may be less representative for specific subgroups, such as people who vape. Vaping status and smoking status may not be accurately captured in EHRs, e.g., some patients were recorded to be smoking or have quit

smoking before receiving a vaping code, but they received a 'never smoked' record >12 months after. In our smoking status transition analyses, the time between the vaping code consultation date and the subsequent smoking status consultation date varied between patients because we wanted to capture the longest possible smoking cessation outcome for each patient. Given that smoking is a relapsing and remitting condition, the variable duration of the follow-up record may limit the interpretation of our results, however, we conducted a sensitivity analysis to mitigate this. The interpretation of the smoking status transitions is limited regarding the smoking cessation rate following receiving a vaping code because a high proportion of patients (44.8%, 68,219/152,277) did not have a subsequent smoking status recording.

Implications

Vaping documentation rates in primary care UK EHRs are very low. Increased completeness, accuracy and consistency of vaping status recording would further increase the value of these data. Refining existing medical codes would enable health professionals to unambiguously record current vaping, former vaping or never vaping. Financially incentivising health professionals has increased smoking status recording [34]; in the UK, a QOF indicator could be introduced for recording vaping status. In clinical practice, vaping screening could be assigned to specific clinical team members [13] or integrated into existing processes, such as alongside routine smoking screening during annual health checks [13].

Improving the completeness of EHR vaping status data would result in longitudinal population-level data for vaping surveillance which is linkable to other electronic health information. This could be employed to investigate long-term health outcomes of vaping [14,23], evidence on which is currently lacking. We found that nearly all first-time incidence of vaping records had a previous smoking status recording, and more than half had a subsequent smoking status recording. Future studies could employ matched control samples to investigate if there are any differences between longer-term smoking cessation outcomes [15,16] or health outcomes between patients who vape and do not vape. Also, studies using EHRs could investigate how long patients use NVPs, and transitions between current and former vaping and vice versa.

Conclusion

Using 2006–2022 CPRD UK primary care data, we found that vaping code incidence increased from September 2013 but vaping documentation rates were overall very low. When receiving the first vaping code, the majority of patients were either smoking or had quit smoking in the past. Of those who were smoking prior to being recorded as currently vaping, more than a year after the vaping record, over a third were still smoking, under a quarter quit smoking, and there was no follow-up smoking status record for 40%. Increased completeness, accuracy and consistency of vaping status recording would further increase the value of longitudinal population-level EHR data, enabling the investigation of the long-term health effects of vaping.

List of abbreviations

CPRD: Clinical Practice Research Datalink

EHR: electronic health records

EVALI: e-cigarette or vaping product use-associated lung injury

GP: general practitioner

NVPs: nicotine vaping products (or e-cigarettes typically used with nicotine)

UK: United Kingdom

US: United States

QOF: Quality and Outcomes Framework

Declarations

Ethical approval and consent to participate

CPRD research data services are delivered by the Medicines and Healthcare products Regulatory Agency (MHRA) with support from the National Institute for Health and Care Research (NIHR), as part of the Department of Health and Social Care. CPRD collects anonymised patient data from a network of GP practices across the UK. Primary care data are linked to a range of other health related data to provide a comprehensive longitudinal, representative UK population health dataset. CPRD has ethical approval from the Health Research Authority (HRA) to support research using anonymised patient data, reference: East Midlands - Derby Research Ethics Committee (REC): 21/EM/0265. For more information see: https://cprd.com/data-access and https://cprd.com/safeguarding-patient-data and https://www.hra.nhs.uk/planning-and-improving-research/application-summaries/research-summaries/clinical-practice-research-datalink-cprd-research-database/.

In order for researchers to access CPRD data, researchers complete a study protocol which is reviewed via CPRD's Research Data Governance (RDG) Process. (The RDG process was formerly called the ISAC.) Independent scientific and patient advice is provided by Expert Review Committees (ERCs) and the Central Advisory Committee (CAC). The RDG process ensures that investigators using CPRD data for research have viable plans that maintain public and professional trust, ensure the research is of public benefit, and are methodologically robust. Informed consent from individual patients included in research studies is not gained by individual investigators because the data that CPRD manages is anonymised.

This study protocol was granted scientific and ethical approval by this process; the Medicine and Healthcare Regulatory Agency (MHRA) Independent Scientific Advisory Committee (ISAC: Protocol No. 21_000706).

Availability of data and materials

Source data for this study were obtained from the Clinical Practice Research Datalink (CPRD). These data sources are made available for scientific and medical research after submission of a study protocol to be reviewed and approved by the CPRD Independent Scientific Advisory Committee (ISAC). Owing to ethical restrictions, the data used in this analysis are not publicly available, in line with the data privacy rules set up by CPRD/ISAC. Data access queries can be directed to enquiries@cprd.com.

Competing interests

None of the authors have conflicts of interest to declare.

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Figures and Tables

Table 4.1. Frequency of current vaping and former vaping codes

Derived vaping code variable	Medical code term in CPRD	Dataset	Freq (n)	Month, year first used	Freq (n)
Current vaping	Electronic cigarette user	Aurum	212,522	Oct 2011	219,478
	User of electronic cigarette	GOLD	6,940	Oct 2013	
	User of electronic cigarette	Aurum	13	Oct 2013	
	e-cigarette user	Aurum	3	Dec 2019	
	Vaper with nicotine	Aurum	0	NA	
Former vaping	Ex user of electronic cigarette	Aurum	5,587	Feb 2014	5,633
	Ex user of electronic cigarette	GOLD	46	Sept 2015	
TOTAL observations					225,111

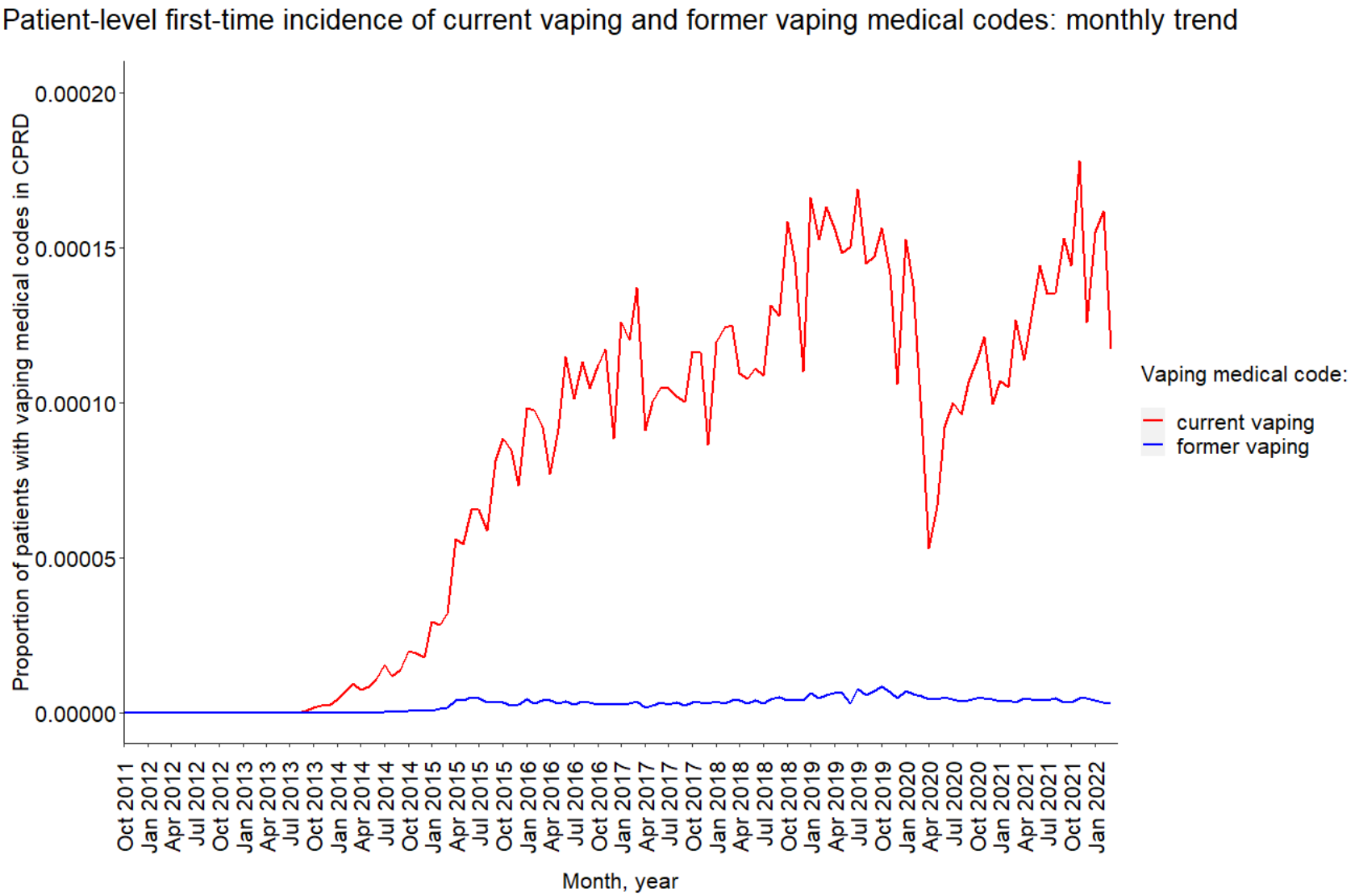
We identified 10 medical codes used between 1 September 2006 and 31 March 2022 (Supplementary Table 1). We derived a new variable which aggregated seven of the codes which indicated 'current vaping' or 'former vaping'. Three ambiguous medical codes ("e-cigarette", "Electronic cigarette", "Electronic cigarette liquid", n=57 observations) were excluded.

Table 4.2. Gender and ethnicity of patients who received a vaping medical code

Patient characteristic	**Current vaping code, n (%)** **147,130 (100.0)**	**Former vaping code, n (%)** **5,147 (100.0)**	**Current or Former vaping code, n (%)** **150,114 (100.0)**
Gender			
Male	69,993 (47.6)	2,615 (50.8)	71,538 (47.7)
Female	77,133 (52.4)	2,532 (49.2)	78,572 (52.3)
Indeterminate	4 (0.0)	0 (0.0)	4 (0.0)
Ethnicity			
Asian	3,367 (2.3)	121 (2.4)	3,449 (2.3)
Black	1,320 (0.9)	47 (0.9)	1,358 (0.9)
Mixed	781 (0.5)	28 (0.5)	803 (0.5)
Other	2,319 (1.6)	44 (0.9)	2,344 (1.6)
White	120,790 (82.1)	4,426 (86.0)	123,310 (82.1)
Unknown	18,553 (12.6)	481 (9.4)	18,850 (12.6)

Table showing the frequency and proportion of patients who received a vaping code between 1 September 2006 and 31 March 2022 by gender and ethnicity.

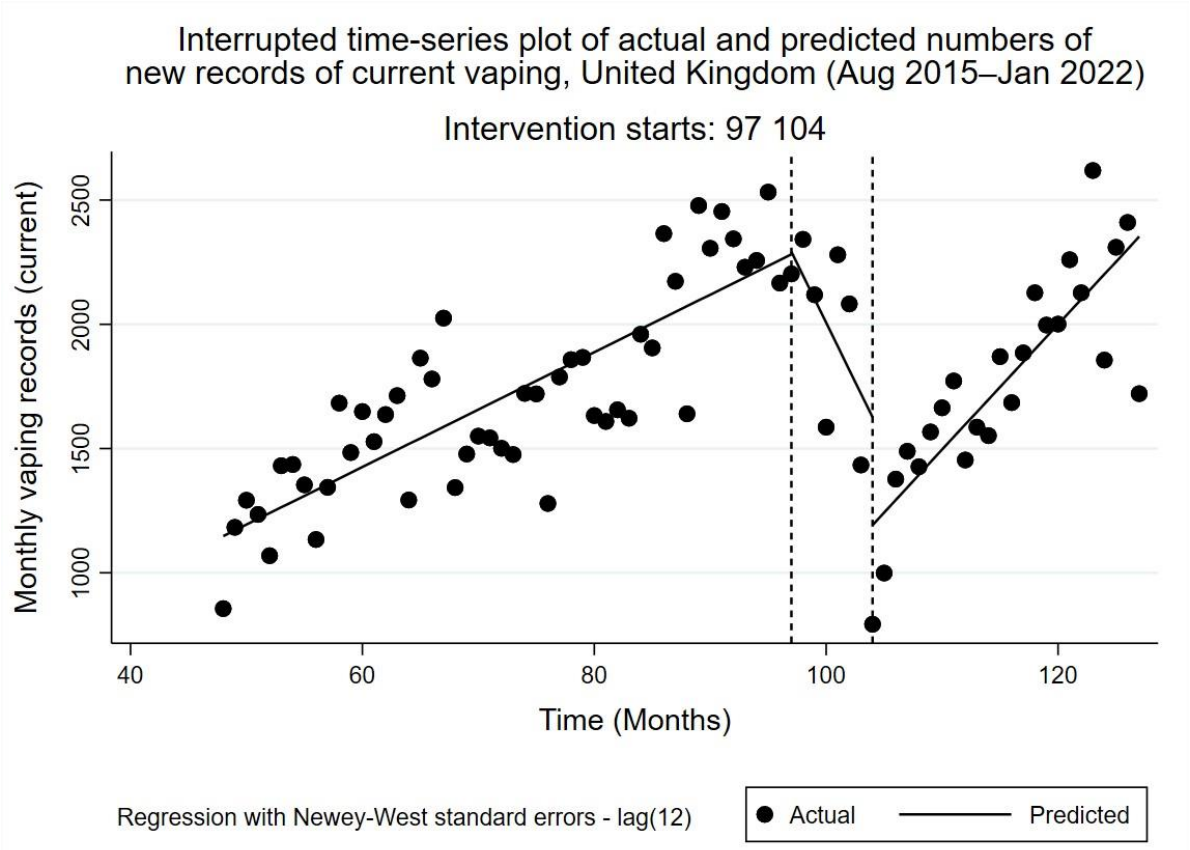
Figure 4.1. Patient-level first-time incidence of current vaping and former vaping medical codes



Graph showing the proportion of patients who received a vaping code indicating first-time current vaping or former vaping out of all patients (≥18 years old) in CPRD that month, per month.

Figure 4.2. Interrupted time-series plot of current and former vaping records (August 2015 to January 2022)

a: Current vaping records



b: Former vaping records

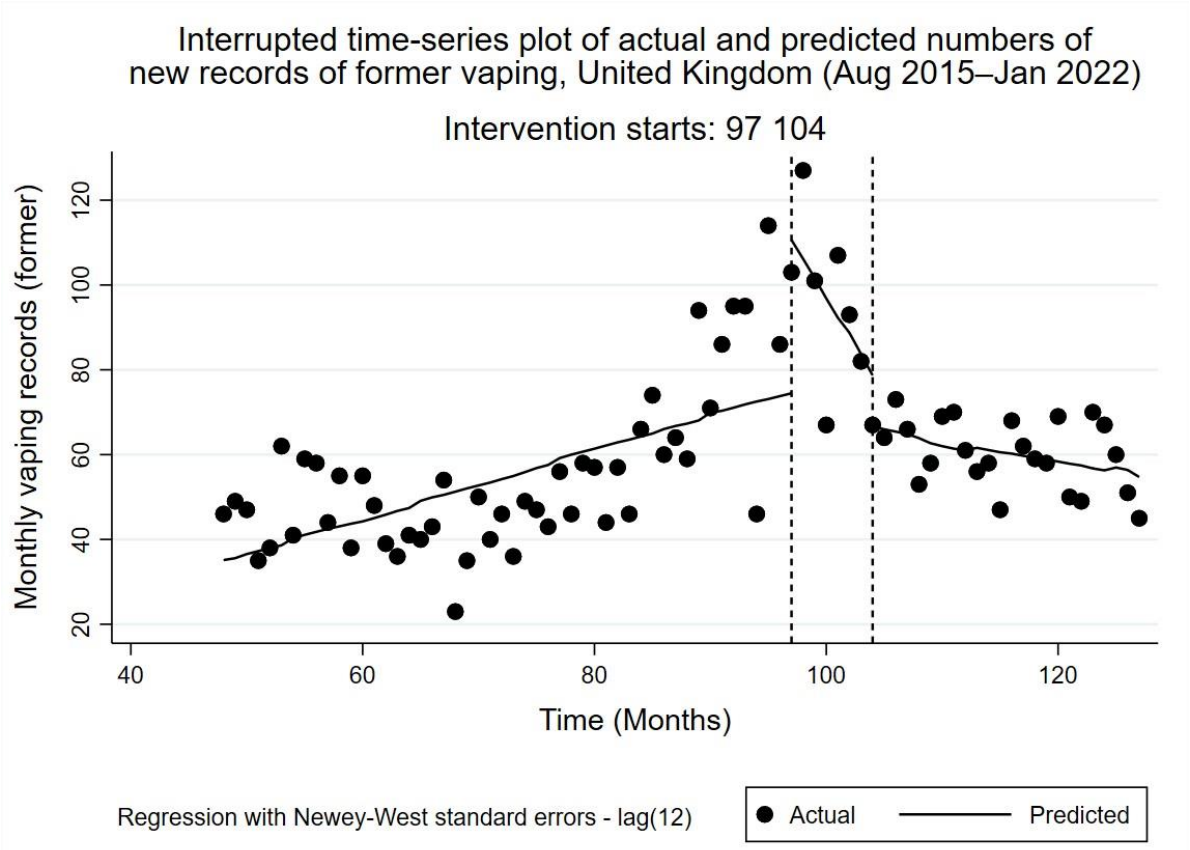
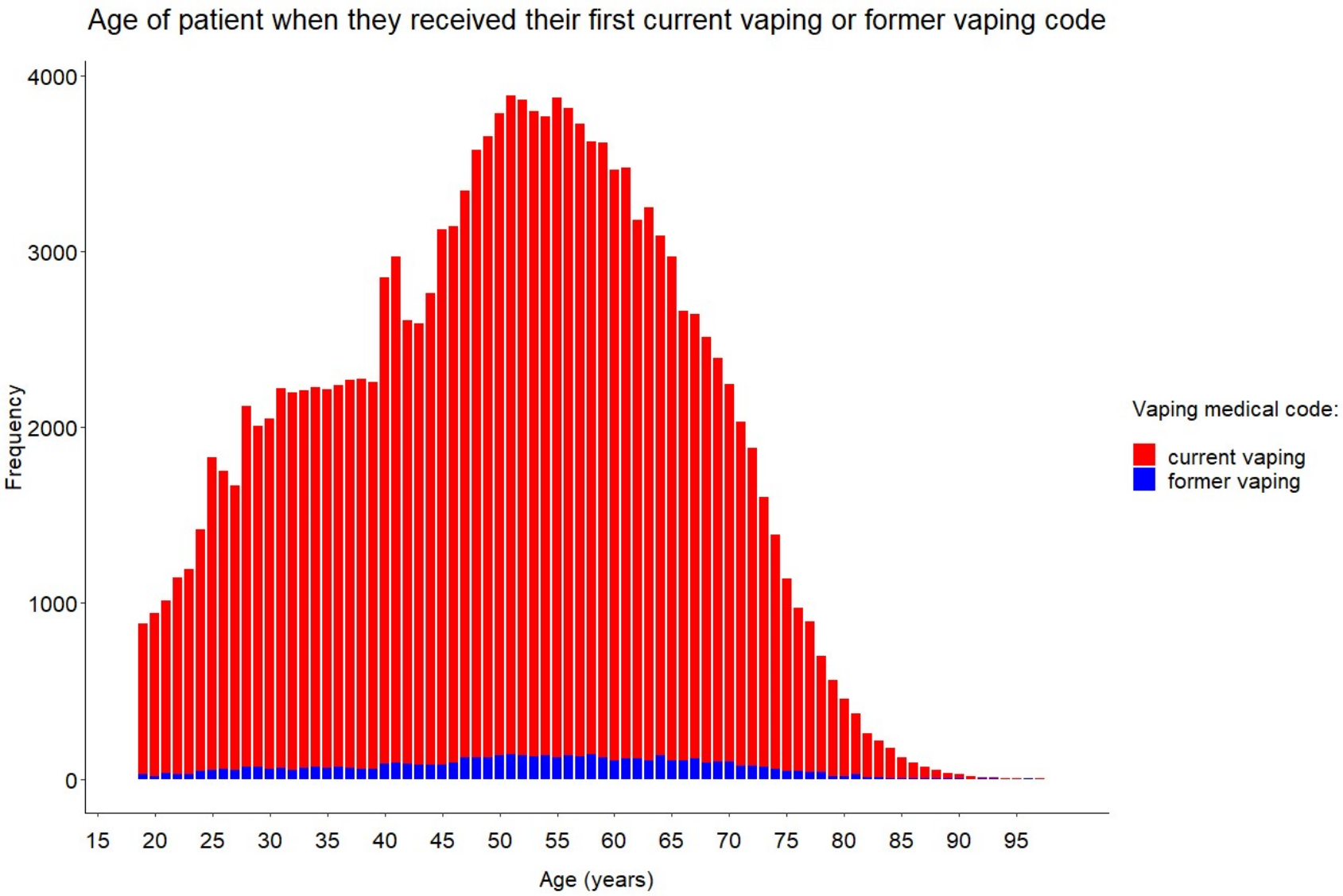


Figure 4.2a shows the interrupted time-series postestimation plot for **current** vaping record outcomes, including actual and predicted numbers of new monthly records.

Figure 4.2b shows the interrupted time-series postestimation plot for **former** vaping record outcomes, including actual and predicted numbers of new monthly records.

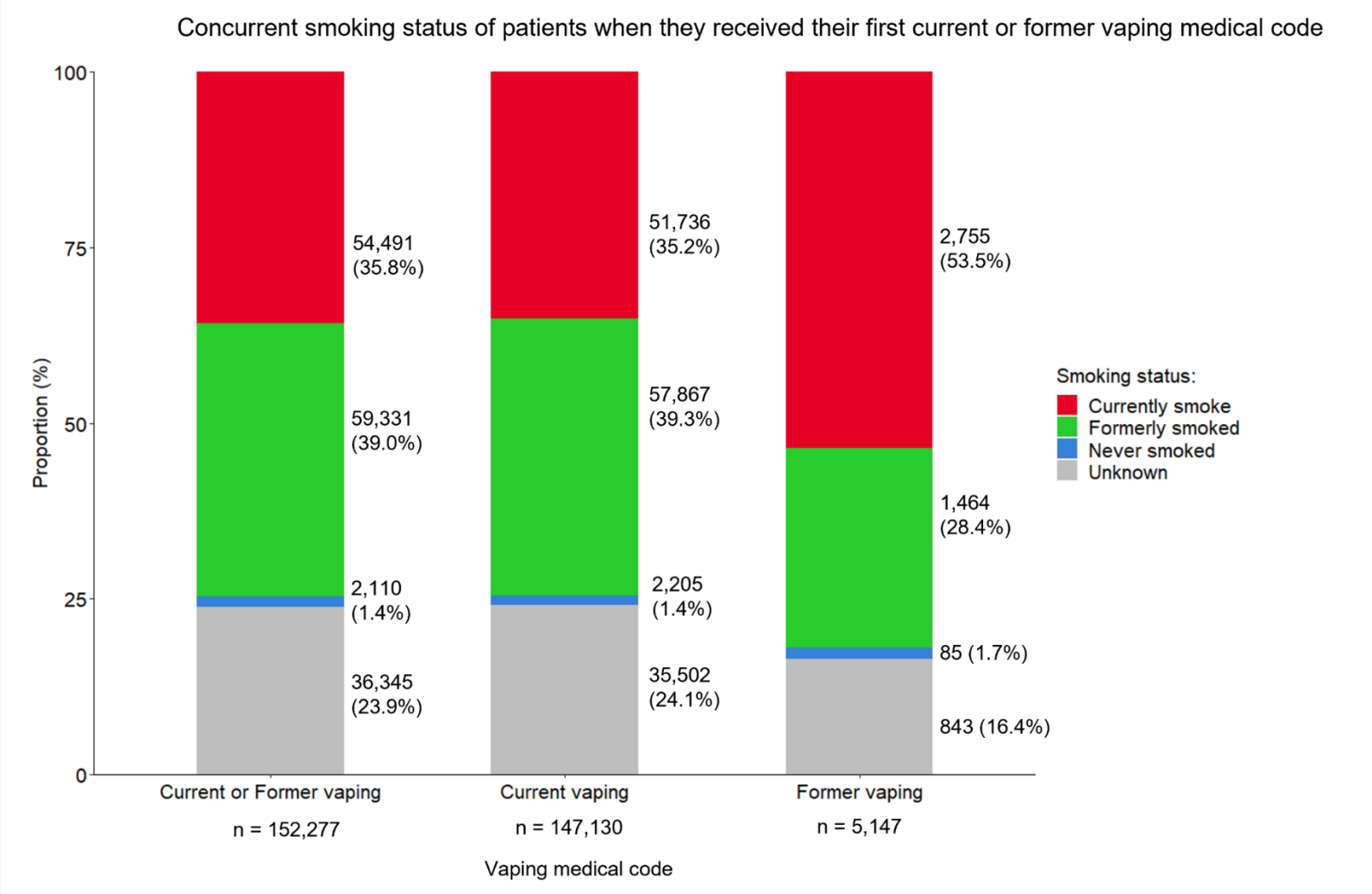
Time was fitted as a linear variable representing months since September 2011. Two interruptions were modelled as occurring in September 2019 (month 97), corresponding to the peak of media coverage in the UK on the US outbreak of severe lung injuries attributed to EVALI; and April 2020 (month 104), corresponding to the start of the first national COVID-19 lockdown policy in the UK. Both models were also adjusted for monthly numbers of patients included in the CRPD database as a linear variable.

Figure 4.3. Age of patient when they received their first current vaping or former vaping code



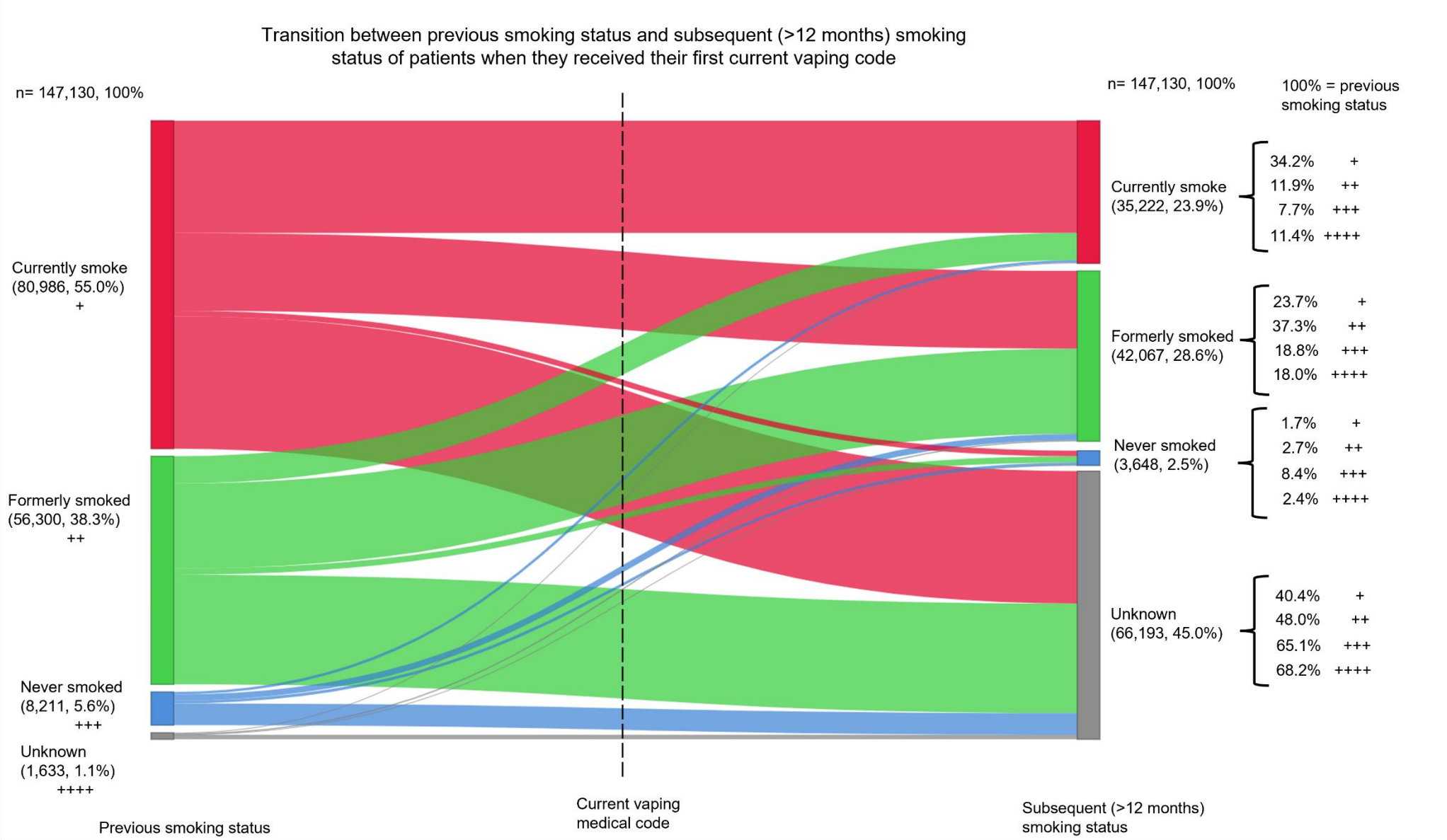
Graph showing the frequency of patients who received a vaping code indicating first-time current vaping or former vaping in CPRD, by the patient age at the time of receipt of the vaping code.

Figure 4.4. Concurrent smoking status of patients when they received their first current or former vaping code



Graph showing the concurrent smoking status of patients when they received a vaping code indicating first-time current vaping or former vaping. Concurrent smoking status: the smoking status that was recorded for the patient on the same date as when the patient received the first-time current or former vaping code.

Figure 4.5. Transition between previous smoking status and subsequent (>12 months) smoking status of patients when they received their first current vaping code



The ‘nodes’ (vertical bars) are coloured to represent the smoking status record obtained in the consultation (red: currently smoke, green: formerly smoked, blue: never smoked, unknown: grey). The ‘connections’ (transitions from left to right) are coloured to represent the previous smoking status (red: currently smoke, green: formerly smoked, blue: never smoked, unknown: grey).

The + signs on the right side (subsequent smoking status) indicate the proportion breakdown of previous smoking status categories. For example: Those who ‘currently smoke’ before receiving the current vaping code, >12 months after they received the current vaping code: 34.2% of them were currently smoking, 23.7% of them had quit smoking, 1.7% received a ‘never smoked’ code, and 40.4% had no smoking status recorded. (34.2% + 23.7% + 1.7% + 40.4% = 100%)

The mean time difference between the previous smoking status record and the current vaping medical code record was 542.6 days (SD: 668.1 days, range: 1.0 to 14,729.0, median: 344.0). The mean time difference between the subsequent smoking status record and the current vaping medical code record was 1,180.0 days (SD: 561.8, range: 366.0 to 3,372.0, median: 1,085.0).

Chapter 5 – Mental health and health professional interactions regarding smoking cessation and nicotine vaping

Preface

The objective of this chapter was to examine interactions between health professionals and people who smoke with and without common mental health conditions (depression and/or anxiety), about smoking cessation and nicotine vaping products.

This chapter presents the study I conducted using 2018 International Tobacco Control (ITC) Four Country Smoking and Vaping (4CV) Survey data from Australia, Canada, England and the US, published as a peer-reviewed publication [3]:

> Tildy, B., McNeill, A., East, K., Gravely, S., Fong, G. T., Cummings, K. M., Borland, R., Chan, G., Lim, C., Gartner, C. E., Yong, H., & Brose, L. S. (2023). Self-reported depression and anxiety and healthcare professional interactions regarding smoking cessation and nicotine vaping: Findings from 2018 International Tobacco Control Four Country Smoking and Vaping (ITC 4CV) Survey. *Tobacco Prevention & Cessation*, *9*(8), 1–12. https://doi.org/10.18332/TPC/168288

The supplementary materials referred to in my publication are available in **Appendix D** of this thesis.

In this chapter, the Author's Accepted Manuscript version of the publication [3] is included, rather than the publisher's typeset PDF of the manuscript, which allowed me to edit the format (font type and size, line spacing) to ease reading. For the references cited in the manuscript, I have retained their original in-text citation number (but have made these superscript numbers to distinguish them from the in-text citations in the thesis), and a reference list for this manuscript is provided at the end of this chapter.

Declaration of roles

I developed this publication in collaboration with Dr Leonie Brose, Professor Ann McNeill, Dr Katherine East (King's College London), Dr Shannon Gravely, Professor Geoffrey T. Fong (University of Waterloo), Professor K. Michael Cummings (Medical University of South Carolina), Professor Ron Borland (University of Melbourne), Dr Gary C. K. Chan, Dr Carmen C. W. Lim, Professor Coral Gartner (University of Queensland), Dr Hua H. Yong (Deakin University).

KMC and GTF were the Principal Investigators of the International Tobacco Control Policy Evaluation (ITC) Project Four Country Survey and designed the survey together with Co-Investigators RB and AM. The survey and measures were developed in collaboration with the ITC Project Research Team and survey firms. The ITC Project Research Team and survey firms were responsible for sample recruitment and maintenance.

I led the write-up of this publication, formulated the research questions, and analysed the data. I wrote the pre-registered analysis plan with input from LB, AM, KE, HHY, and SG – researchers who are involved with the ITC Project and had published in similar topic areas. Following approval to use the data, ITC Project Analysts (Dr Anne Quah and Dr Pete Driezen) granted me data access and facilitated the usage of the most appropriate survey weights for my analyses. RB, GTF, KMC, GCKC, CCWL and CG gave feedback on the analysis and interpretation. I wrote the initial manuscript. All co-authors reviewed and provided input on drafts. I handled the manuscript submission and responded to peer reviews. All authors read and approved the final manuscript.

Publication

Self-reported depression and anxiety and healthcare professional interactions regarding smoking cessation and nicotine vaping: Findings from 2018 International Tobacco Control (ITC) Four Country Smoking and Vaping Survey

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Abstract

Introduction: People with mental health conditions are disproportionately affected by smoking-related diseases and death. The aim of this study was to assess whether health professional (HP) interactions regarding smoking cessation and nicotine vaping products (NVPs) differ by mental health condition.

Methods: Cross-sectional 2018 ITC Four Country (Australia, Canada, England, United States) Smoking and Vaping Survey data included n=11,040 adults currently smoking or recently quit. Adjusted weighted logistic regressions examined associations between mental health (self-reported current depression and/or anxiety) and visiting a HP in last 18 months; receiving advice to quit smoking; discussing NVPs with a HP; and receiving a recommendation to use NVPs.

Results: Overall, 16.1% self-reported depression and anxiety, 7.6% depression only, 6.6% anxiety only. Compared with respondents with no depression/anxiety, those with depression (84.7%, aOR=2.65, 95% CI: 2.17–3.27), anxiety (82.2%, aOR=2.08, 95% CI: 1.70–2.57), and depression and anxiety (87.6%, aOR=3.74, 95% CI: 3.19–4.40) were more likely to have visited a HP. Among those who had visited a HP, 47.9% received advice to quit smoking; which was more likely among respondents with depression (aOR=1.58, 95% CI: 1.34–1.86); NVP discussions were more likely among those with depression and anxiety (aOR=1.63, 95% CI: 1.29–2.06). Of the 6.1% who discussed NVPs, 33.5% received a recommendation to use them, with no difference by mental health.

Conclusions: People with anxiety and/or depression who smoke were more likely to visit a HP than those without, but only those with depression were more likely to receive cessation advice, and only those with depression and anxiety were more likely to discuss NVPs. There are missed opportunities for HPs to deliver cessation advice. NVP discussions and receiving a positive recommendation to use them were rare overall.

Introduction

Smoking is a leading preventable cause of illness and premature death in the United Kingdom (UK) and worldwide [1]. Smoking prevalence is considerably higher in disadvantaged groups, including people with mental health conditions [2–5]. For example, in England in 2014, among those with a current common mental health condition, smoking prevalence was 34.1%, compared to 19.6% in people without [4]. In the United States (US), among those who reported any past-year mental illness in 2019, past-month cigarette smoking was 28.2%, compared to 15.8% in people without past-year mental illness [6]. People with mental health conditions are more likely to smoke heavily, and be highly dependent on cigarettes [4]. Smoking is a significant contributor to the discrepancy in life expectancy between people with and without mental health conditions [2,7,8]; smoking cessation should improve physical and mental health [9].

Most adults who smoke say they want to quit smoking [10,11], including people with mental health conditions [5]. Approximately 40-50% of adults who smoke report making a quit attempt annually, but most quit attempts are made without evidence-based treatments and end in relapse back to smoking [10,11]. Health professionals (HPs) can trigger patients' interest in quitting [12] and provide treatments to support quit attempts, which can markedly increase cessation rates [13]. However, research has shown that the rate at which HPs provide advice to quit smoking and offer cessation support/treatment is suboptimal, internationally [14,15]. Nicotine vaping products (NVPs) are substantially less harmful than smoking combustible tobacco [16] and improve cessation rates compared to nicotine replacement therapy (NRT) and non-nicotine vaping products [17]. However, there are concerns due to uncertainty about the long-term health effects of NVPs and youth uptake of NVPs. Some experts recommend that HPs encourage the use of NVPs as another option for smoking cessation on a par with medicinally licensed pharmacotherapies and behavioural support [18,19].

Policy and guidelines around NVPs vary internationally [18]. Currently, in the UK, NVPs are widely available as consumer products and clinical guidelines recommend that NVPs are "accessible to adults who smoke" [20]. In Australia, the sale of NVPs is prohibited unless on prescription from a licensed HP – clinical guidelines recommend NVPs for those "who have tried to achieve smoking cessation with first-line therapy but failed" [21]. In Canada, NVPs are

widely available in various retail locations, but clinical guidelines do not include NVPs in the list of recommended smoking cessation treatment options [22]. In the US, historically NVPs were widely available on the open market, but only some tobacco-flavoured brands have received market approval since 2021 [23]. NVPs are not recommended in US clinical guidelines – "recommend that clinicians direct patients who use tobacco to other tobacco cessation interventions with proven effectiveness and established safety" [24].

HPs rarely discuss NVPs with patients who smoke: in 2016 among people who smoked who visited a HP, only 6.8% of survey respondents from Australia, Canada, England, and the US reported their HP discussing NVPs with them [15]. A cohort study found that the prevalence of NVP discussions were low and remained relatively unchanged between 2016, 2018 and 2020 [25]. Further, among respondents who discussed NVPs with HPs, only one third (37.8%) reported that their HP recommended that they use them [15]. The likelihood of receiving NVP recommendations from HPs in England was higher and increased significantly between 2016 and 2020; but did not change significantly in Australia, Canada or the US [25].

To reduce smoking and narrow the inequalities in smoking prevalence that exist between people with and without mental health conditions, HPs needs to do more to assist those who do smoke to quit – such as, increased guidance/encouragement for cessation and advising on harm reduction approaches (switching from smoking to using NVPs) [26,27]. One study [28] using UK electronic health record data collected between 2009 and 2010 found that the annual mean number of consultations for patients who smoke and have a mental health condition was higher than for those without a mental health condition; however, the proportion of consultations in which cessation advice was recorded was lower for people with a mental health condition, compared to those without. Research into discussions and recommendations to use NVPs is sparse; one study [15] – using 2016 survey data from Australia, Canada, England, and the US – found no difference in the proportion of people who smoke with and without self-reported current diagnosis/treatment of depression or anxiety who had discussions with a HP about NVPs, but fewer people who smoke with anxiety were recommended to use an NVP from their HPs, compared to people who smoke without anxiety.

In our study, we build on these findings, focussing on comparing respondents with and without depression and/or anxiety, as these are two of the most common mental health conditions globally [29] but receive less attention compared to serious mental health illness [30]. Using cross-sectional 2018 International Tobacco Control (ITC) Four Country Smoking and Vaping (4CV) Survey data from Australia, Canada, England and the US, this study investigated whether there were differences between those with and without a current diagnosis/treatment for depression and/or anxiety in (1) visiting a HP, (2) receiving advice to quit smoking from a HP, (3) their HP discussing NVPs, and (4) receiving a positive recommendation to use NVPs from a HP. We also aimed to investigate if the association between depression and/or anxiety and each outcome varied by country.

Methods

Data source and sample

This study used data from Wave 2 (March–June 2018) of the longitudinal ITC 4CV survey, a cohort study of people who smoke, vape or those who recently quit smoking from Australia, Canada, England, and the US. Respondents (adults ≥18 years) were recruited using either probability-based sampling frames or non-probability opt-in sampling frames, or a combination of these methods, aiming to be representative of people who smoke, or vape at least weekly, in each country. Participants included those who were re-contacted from the previous wave and new participants who were recruited to address attrition and maintain sample size over time. Full methodological details are available elsewhere (https://itcproject.org/methods) [31]. This manuscript adhered to the STROBE guidelines.

The study sample consisted of n=11,040 adult respondents who were either currently smoking cigarettes (daily/weekly/monthly) or had recently quit (quit smoking in the last 18 months AND had smoked >100 cigarettes in their lifetime), at the time of the 2018 survey (see Figure 5.1).

Ethical approval

The survey protocols and all materials of Wave 2 ITC 4CV Survey, including the survey questionnaires, were cleared for ethics by Office of Research Ethics, University of Waterloo, Canada (REB#20803/30570, REB#21609/30878); Research Ethics Office, King's College London, UK (RESCM-17/18-2240); Human Research Ethics, Cancer Council Victoria, Australia (HREC1603) and, Human Ethics, Research Management Office, University of Queensland, Australia (2016000330/HREC1603); and Institutional Review Board Medical University of South Carolina (waived due to minimal risk). All participants provided consent to participate.

Measures

A more detailed description of the variables is provided in the pre-registered analysis plan https://osf.io/y72cj [31].

Independent variable

Mental health condition:

The 2018 wave was the most recent ITC 4CV survey wave which contained survey questions about depression and anxiety (assessed with a single item measure, similar to past research [15,32]). All respondents were asked: *"Are you currently being treated for, or have you been diagnosed (current diagnosis) with, any of the following… [select all that apply]? Depression. Anxiety*. …" Response options: Selected/Not selected/Refused (excluded)/Don't know (excluded). The answers were recoded into the mutually exclusive categories:

- No depression/anxiety: 'Not selected' to both depression and anxiety.
- Depression only: 'Selected' to depression but 'Not selected' to anxiety.
- Anxiety only: 'Selected' to anxiety but 'Not selected' to depression.
- Depression and anxiety: 'Selected' to both depression and anxiety.

Outcome measures

(1) Visiting a HP:

All respondents were asked: *"In the last 18 months, have you visited a doctor or other health professional?"*. Responses options were: yes, no, or refused to answer (excluded)/don't know (excluded).

(2) Advice to quit smoking from HP:

Respondents who indicated visiting a HP were asked: *"On any visit to a doctor or health professional in the last 18 months, did you receive any advice to quit smoking?"*. Responses options were: yes, no, or refused to answer (excluded)/don't know (excluded).

(3) Discussion about NVPs:

Respondents who indicated visiting a HP were asked: *"On any visit to a doctor or health professional in the last 18 months, did the doctor or health professional talk to you about e-cigarettes?"*. Responses options were: yes, no, or refused to answer (excluded)/don't know (excluded).

(4) Positive recommendation to use NVPs:

Respondents who indicated visiting a HP and indicated that their HP had discussed NVPs were asked: *"What advice did the doctor or health professional give you about e-cigarettes?"*. The response options were recoded into the categories in brackets: 'They specifically recommended that I use e-cigarettes' (Yes)/ 'They advised me against using e-cigarettes' (No)/ 'They didn't express a view for or against e-cigarettes' (No)/ Refused (excluded)/ Don't know (excluded). Responses options were: yes, no, or refused to answer (excluded)/don't know (excluded).

Covariates

Covariates included: sex (male, female), age group (18–24, 25–39, 40–54, ≥55 years), country of residence (Australia, Canada, England, US), highest level of education (Low, Moderate, High), ethnicity (Minority group, Majority group), annual household income (Low, Moderate, High, No answer [valid response option]), cigarette smoking status (Daily, Non-daily [including weekly and monthly], Former [quit smoking in the last 18 months AND had smoked >100 cigarettes in their lifetime]), and problematic alcohol use (total score out of 12 based on Alcohol Use Disorders Identification Test Consumption (AUDIT C) [33] where: ≥5 points [Yes]/ ≤4 points [No]/No answer [valid response option]).

Respondents who refused to answer or answered 'Don't know' to education or ethnicity questions were excluded from the sample (Figure 5.1).

Data analysis

Unweighted frequencies and weighted proportions were calculated. The sample was weighted using derived cross-sectional survey weights [31] to account for the stratified sampling design (defined by geographic regions within each country). Respondents who refused to answer or responded 'don't know' to a question related to the outcome measures were excluded from logistic regression analyses (Supplementary Table 1). Three separate weighted logistic regression models were generated to investigate the relationship between mental health condition and the four outcomes: (1) visiting a HP, (2) receiving advice to quit smoking from a HP, among those who visited a HP, (3) their HP discussing NVPs, among those who visited a HP, (4) receiving a positive recommendation to use NVPs from a HP, among those who visited a HP and whose HP discussed NVPs. The weighted regression models were: (Model 1) unadjusted model with mental health condition as the only independent variable; (Model 2) model adjusted for country, sex, age, education, ethnicity, and income; (Model 3), fully adjusted model additionally adjusted for cigarette smoking status and problematic alcohol use. To assess whether the association between mental health condition and each outcome varies by country, for each outcome, a likelihood-ratio test assessed whether there was a significant difference between Model 3

and a new model (Model 4) which contained interaction terms between mental health condition and country.

Assumptions of logistic regression were met [34]. The analysis plan was pre-registered: https://osf.io/y72cj. Analyses were conducted using RStudio (version 4.0.3), regression models were generated using the *'glm'* command of the *'mlogit'* package. As the regressions were weighted, the 'family=quasibinomial' argument was used. Exact p-values and 95% (likelihood ratio-based [34]) confidence intervals (CIs) are reported. Results were adjusted for multiple comparisons, where the significance level, alpha, was evaluated at 0.0125 level, as per the Bonferroni correction (α=0.05/4 outcomes= 0.0125).

Results

Sample characteristics

The unweighted analytical sample included n=11,040 respondents (Table 5.1). The weighted sample was 54.2% male, and respondents were more likely to be in the majority ethnic group (white) and aged ≥40 years. Most of the respondents were residing in England (38.6%), followed by Canada (27.8%), then the US (21.1%), then Australia (12.5%). The most common cigarette smoking status was current 'daily' (77.7%). The 'non-daily' smoking category (11.8%) was made up of 8.4% who currently smoked weekly, and 3.4% who currently smoked monthly. People who recently quit smoking comprised 10.5% of respondents. The majority of respondents had moderate-level highest level of education (47.7%), moderate-level annual household income (33.9%), and did not have problematic alcohol use (62.9%). Slightly less than one third of the respondents had self-reported depression and/or anxiety (30.3%), 7.6% had depression only, 6.6% had anxiety only, and 16.1% had both depression and anxiety.

Visiting a HP

Most (74.6%) respondents reported visiting a HP in the last 18 months (Table 5.1).

In all three regression models, compared to respondents with no depression/anxiety, the odds of visiting a HP in the last 18 months were significantly higher for respondents with these mental health conditions (Table 5.2). In the fully adjusted model (Model 3), the odds of visiting a HP were significantly higher for respondents with depression alone (aOR=2.65, 95% CI: 2.17–3.27, p<0.001), anxiety alone (aOR=2.08, 95% CI: 1.70–2.57, p<0.001), and both depression and anxiety (aOR=3.74, 95% CI: 3.19–4.40, p<0.001), compared to respondents with no depression/anxiety (Table 5.2).

Advice to quit smoking from HP

Among respondents who reported visiting a HP in the last 18 months, less than half (47.9%) reported receiving advice to quit smoking (Table 5.1).

In all three models, the odds of reporting receiving advice to quit smoking from a HP were significantly higher for respondents with depression alone, compared to respondents with no depression/anxiety (Table 5.2). In the fully adjusted model (Model 3), the odds of reporting receiving advice to quit smoking from a HP were 1.58 times higher (95% CI: 1.34–1.86, p<0.001) for respondents with depression alone, compared to respondents with no depression/anxiety (Table 5.2). There was no significant difference in the odds of receiving advice to quit smoking between respondents with anxiety alone, and those with both depression and anxiety, compared to respondents with no depression/anxiety in any of the three models (Table 5.2).

Discussion about NVPs

Among respondents who reported visiting a HP in the last 18 months, 6.1% (n=859) reported that their HP discussed NVPs with them (Table 5.1).

In all three models, there was a statistically significant difference in the odds of reporting a discussion about NVPs between respondents with both depression and anxiety compared to respondents with no depression/anxiety (Table 5.2). In the fully adjusted model (Model 3), the odds of reporting that their HP discussed NVPs were 1.63 times higher (95% CI: 1.29–

2.06, p<0.001) for respondents with both depression and anxiety, compared to respondents with no depression/anxiety (Table 5.2). There was no significant difference in the odds of reporting HP NVP discussions between respondents with anxiety alone, and those with depression alone, compared to respondents with no depression/anxiety in any of the three models (Table 5.2).

Positive recommendation to use NVPs

Among respondents who reported visiting a HP in the last 18 months and reported that the HP discussed NVPs with them, one third (33.5%, n=288) reported receiving a positive recommendation from their HP to use NVPs (Table 5.1).

We did not find a significant association between mental health condition and the odds of receiving a positive recommendation to use NVPs in any of the three regression models (Table 5.2), however, sample sizes were small, so findings should be treated with caution.

Country differences

Likelihood-ratio tests indicated a significant difference between the model with and without the mental health condition*country interaction terms for the 'visiting a HP' (p=0.002) and 'receiving advice to quit smoking' (p=0.009) outcomes. When we examined the individual interaction terms for mental health condition*country for these outcomes, only the depression and anxiety*Canada individual interaction term for 'visiting a HP' (p=0.001) was significant at p<0.01 (Supplementary Table 2d, 2h). We did not investigate country differences further.

Discussion

Most (74.6%) respondents reported visiting a HP in the last 18 months; the odds were higher for those respondents who reported anxiety and/or depression, compared to those with no depression/anxiety. Less than half of respondents (47.9%) who visited a HP

reported receiving advice to quit smoking, with higher odds for those with depression alone. Among respondents who visited a HP, only 6.1% of respondents reported that their HP discussed NVPs with them; those with both depression and anxiety had higher odds. Lastly, among respondents who visited a HP and discussion with HPs included NVPs, one third of respondents (33.5%) reported receiving a positive recommendation to use them and the odds did not differ by mental health condition (but our sample size was small). We also found that there may be a significant interaction between mental health condition and country regarding visiting a HP and receiving advice to quit smoking.

Our finding concerning HP visits was consistent with past research (which used 2009–2010 UK electronic health record data) which found that people with mental health conditions were more likely to visit HPs than those without [28]. Regarding cessation advice provision, past research found that the proportion of consultations in which cessation advice was recorded was lower for people with a mental health condition, compared to those without [28]. In our study, we found that people who had depression alone had higher odds of reporting being given advice to quit smoking from a HP compared to people with no depression/anxiety, with no significant differences for anxiety alone or having both conditions. However, as the number of consultations was not collected in the ITC survey, we could not explore whether this was due to a higher consultation rate among those with depression.

Regarding NVP discussions with HPs, consistent with existing studies which used survey data from Australia, Canada, England, and US from 2016 [15] and 2016–2020 [25], we found that a very low proportion of respondents who visited their HP reported their HP discussing NVPs with them. However, we found some evidence that those with both depression and anxiety had higher odds of their HPs discussing NVPs, compared to respondents with no depression/anxiety. The study investigating this in 2016 [15] found no difference by mental health status; however, they analysed no anxiety versus anxiety and no depression versus depression. It may be that people who smoke who have both depression and anxiety were more likely to ask their doctor about NVPs or they may experience greater difficulty in quitting which may prompt their HP to mention NVPs as an alternative method to obtain

nicotine. Further research is needed to substantiate this finding.

Lastly, unlike previous research – which found, using a previous wave (2016) of this survey, that people who smoke with anxiety were less likely to be recommended by their HP to use an NVP, compared to people who smoke without anxiety [15] – we did not find an association between mental health condition and receiving a positive recommendation from a HP to use NVPs. Perhaps between 2016 and 2018, HPs increased the rate of recommendation of NVPs to their patients who have anxiety, so it was in line with their recommendation rate to patients who smoke without mental health conditions.

The consistency between older studies [14,15] and our finding (using 2018 data) that less than half of all respondents received advice to quit smoking is notable because it indicates a lack of improvement in cessation advice provision in healthcare settings. It is promising that respondents with depression had a higher rate of receiving cessation advice (albeit only 57.2%), than respondents with no depression or anxiety, but this may be due to having a higher number of consultations in the last 18 months, as opposed to having a higher cessation intervention per visit rate [28]. Additionally, although those with anxiety either alone or with depression were also more likely to visit a HP, they were not more likely to receive cessation advice from their doctor (compared to those with no depression/anxiety), suggesting lower overall rates of intervention per visit among these groups. We advise that HPs increase the rate that they provide cessation advice and support to all their patients who smoke; this is particularly important for those who have mental health conditions to close the inequality gap of differential smoking rates [2–5]. Our finding that people who smoke with mental health conditions had higher odds of visiting a HP suggests that there are more opportunities for HPs to deliver cessation advice.

Our findings that only 6.1% of respondents who visited their HP reported their HP discussing NVPs with them, and only 2% received a positive recommendation to use them, are concerning given that NVPs have been found by Cochrane systematic reviews to be an effective quit method [17]. Furthermore, there was no association between receiving a positive recommendation by a HP to use NVPs and having anxiety or depression. It is

especially important for people with anxiety/depression to be given accurate information about and access to NVPs, as various studies using surveys (e.g. 1993–2014 data from Great Britain [4]) have found that people with mental health conditions are more likely to smoke heavily and be highly dependent on cigarettes, and are motivated to quit smoking (e.g. 2016–2017 data from England [5]), but are less likely to succeed (e.g. 2016–2017 data from England [5,35], 2016 data from Australia, Canada, England and the US [36].

To summarise, the main implications of this study are that there are missed opportunities for HPs to deliver cessation advice and to discuss NVPs in an evidence-based way with people who smoke with anxiety and/or depression. Given the higher smoking rates among people with mental health conditions [2–5], to reduce the resultant health inequalities, HPs should increase the rate that they provide cessation advice and support per visit among people with mental health conditions. Also, although HPs should always consider the potential risks and benefits of recommending certain treatments, given that evidence suggests that using NVPs is substantially less harmful than smoking combustible tobacco [16] and that NVPs have been shown to be a more efficacious smoking cessation aid than NRT [17], HPs should at least discuss NVPs with their patients who smoke (with and without mental health conditions) when advising them about cessation options. This is particularly important given that currently effective licensed medications for smoking cessation (varenicline and bupropion) have been limited since 2021 and 2022.

Future research

Future research could explore reasons behind why HPs provide differing care regarding smoking cessation to people with mental health conditions, and investigate if other forms of cessation support that HPs recommend to people who smoke (such as licensed cessation aids) differ by mental health status. Also, the effect of other mental health conditions should be investigated. To further investigate country effects, we recommend stratification by country, but a larger sample size will be required.

Strengths and limitations

The strength of our cross-sectional study is that it used data from large population-based samples of people who smoke from four countries. However, there are some limitations. The study relies on self-reported measures which were not verified with health records, or other external measures, and may be subject to recall and other biases. It is not possible to know when a respondent was first diagnosed with depression and/or anxiety and the question used was not intended as a diagnostic tool. The sample size for some of our analyses was small.

Conclusion

Using cross-sectional 2018 ITC Four Country (Australia, Canada, England, US) Survey data, this study found that people with anxiety and/or depression who smoke were more likely to visit a HP, but only people with depression alone were more likely to receive cessation advice, and only people with both depression and anxiety were more likely to discuss NVPs with their HP. Receiving a positive recommendation to use NVPs did not differ by mental health condition and few respondents received positive recommendations overall. More people who smoke should be given smoking cessation advice and information about effective smoking cessation support (including NVPs) to increase the likelihood of smoking cessation.

Data availability statement

In each country participating in the international Tobacco Control Policy Evaluation (ITC) Project, the data are jointly owned by the lead researcher(s) in that country and the ITC Project at the University of Waterloo. Data from the ITC Project are available to approved researchers 2 years after the date of issuance of cleaned data sets by the ITC Data Management Centre. Researchers interested in using ITC data are required to apply for approval by submitting an International Tobacco Control Data Repository (ITCDR) request application and subsequently to sign an ITCDR Data Usage Agreement. The criteria for data

usage approval and the contents of the Data Usage Agreement are described online (http://www.itcproject.org).

Abbreviations

NVP – nicotine vaping product

HP – health professional

NRT – nicotine replacement therapy

ITC 4CV Survey – International Tobacco Control Four Country Smoking and Vaping Survey

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Declaration of interests

KMC has served as a paid expert witness in litigation filed against cigarette manufacturers. GTF has served as an expert witness/consultant for governments defending their country's policies/regulations in litigation. All other authors have no conflict of interest to declare.

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Figures and Tables

Figure 5.1. Inclusion flow diagram for study sample

Flow diagram showing the inclusion/exclusion criteria to generate the study sample, from Wave 2 (2018) of the International Tobacco Control Four Country Smoking and Vaping (ITC 4CV) Survey; unweighted frequencies.

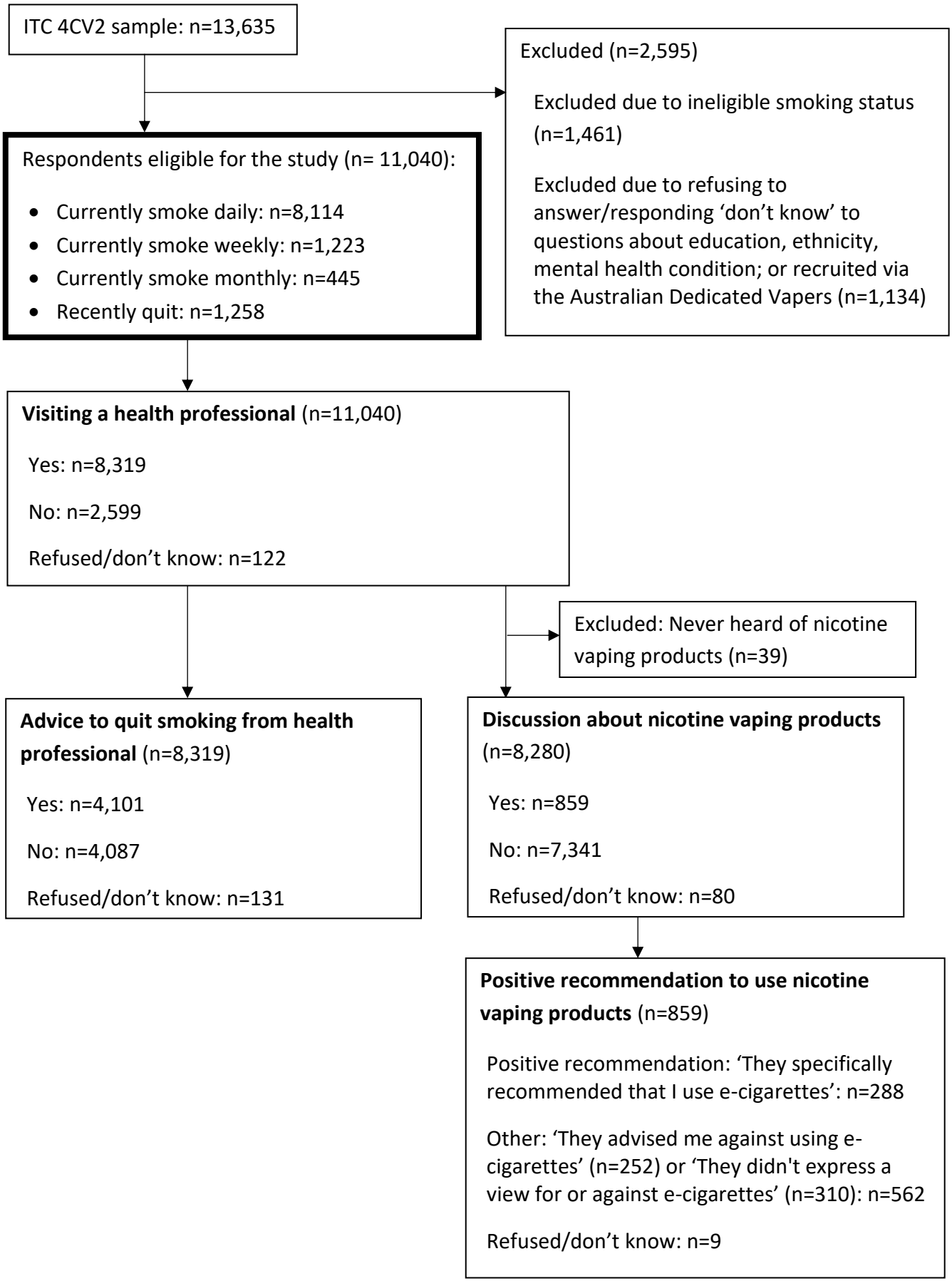

Table 5.1. Mental health condition and covariates by study sample and healthcare professional interactions regarding smoking cessation and nicotine vaping

Cross-sectional International Tobacco Control Four Country Smoking and Vaping (ITC 4CV) Survey, 2018.

Variable categories	**Study sample** (n=11,040)	**1. Visiting a health professional** (n*= 11,040)	**2. Advice to quit smoking from health professional** (n*= 8,319)	**3. Discussion about nicotine vaping products** (n*= 8,280)	**4. Positive recommendation to use nicotine vaping products** (n*= 859)
	11,040 (100.0)	**Yes,** 8,319[+] (74.6[++])	**Yes,** 4,101[+] (47.9[++])	**Yes,** 859[+] (6.1[++])	**Yes,** 288[+] (33.5[++])
Mental health status					
No depression/anxiety	7,393 (69.7)	5,279 (69.8)	2,550 (47.2)	459 (5.4)	150 (31.3)
Depression only	918 (7.6)	763 (84.7)	437 (57.0)	110 (7.4)	42 (38.8)
Anxiety only	844 (6.6)	662 (82.2)	317 (44.1)	89 (6.9)	28 (37.1)
Depression and anxiety	1,885 (16.1)	1,615 (87.6)	797 (47.3)	201 (8.0)	68 (35.0)
Country					
Australia	1,372 (12.5)	1,222 (85.7)	650 (53.5)	52 (3.0)	12 (16.6)
Canada	3,157 (27.8)	2,473 (79.3)	1,159 (45.5)	228 (5.2)	64 (35.2)
England	4,217 (38.6)	2,822 (67.1)	1,242 (42.1)	389 (8.4)	166 (39.0)
US	2,294 (21.1)	1,802 (75.3)	1,050 (56.8)	190 (6.0)	46 (24.8)
Gender					

Variable categories	**Study sample** (n=11,040)	**1. Visiting a health professional** (n*= 11,040)	**2. Advice to quit smoking from health professional** (n*= 8,319)	**3. Discussion about nicotine vaping products** (n*= 8,280)	**4. Positive recommendation to use nicotine vaping products** (n*= 859)
Male	5,372 (54.2)	3,777 (69.1)	1,940 (49.5)	488 (6.8)	170 (38.0)
Female	5,668 (45.8)	4,542 (81.0)	2,161 (46.2)	371 (5.5)	118 (27.9)
Age group (years)					
18-24	2,167 (9.8)	1,427 (66.2)	610 (36.4)	262 (8.6)	93 (34.6)
25-39	2,406 (33.6)	1,617 (67.0)	708 (42.5)	215 (6.7)	83 (44.5)
40-54	2,872 (28.6)	2,198 (76.5)	1,088 (48.1)	187 (5.8)	58 (27.1)
55 and up	3,595 (28.0)	3,077 (84.5)	1,695 (55.7)	195 (5.3)	54 (26.4)
Ethnicity					
Minority group	1,636 (13.2)	1,168 (72.7)	603 (50.9)	190 (8.3)	66 (33.5)
Majority group	9,404 (86.8)	7,151 (74.9)	3,498 (47.4)	669 (5.8)	222 (33.4)
Education					
Low	3,519 (31.1)	2,616 (74.5)	1,283 (51.9)	224 (5.2)	72 (26.0)
Moderate	4,627 (47.7)	3,543 (74.5)	1,771 (47.6)	346 (6.5)	97 (33.4)
High	2,894 (21.2)	2,160 (75.0)	1,047 (42.7)	289 (6.8)	119 (42)

Variable categories	**Study sample** (n=11,040)	**1. Visiting a health professional** (n*= 11,040)	**2. Advice to quit smoking from health professional** (n*= 8,319)	**3. Discussion about nicotine vaping products** (n*= 8,280)	**4. Positive recommendation to use nicotine vaping products** (n*= 859)
Income					
Low	3,533 (31.0)	2,725 (76.5)	1,347 (49.2)	242 (5.4)	67 (29.5)
Moderate	3,706 (33.9)	2,673 (72.7)	1,331 (47.9)	278 (6.1)	94 (32.8)
High	3,249 (30.0)	2,499 (75.3)	1,239 (46.7)	308 (6.9)	118 (38.8)
No answer	552 (5.1)	422 (71.0)	184 (45.8)	31 (6.0)	9 (22.6)
Cigarette smoking status					
Daily	8,114 (77.7)	6,142 (74.7)	3,252 (51.8)	611 (6.0)	227 (34.6)
Non-daily	1,668 (11.8)	1,143 (69.8)	455 (32.1)	181 (8.2)	48 (31.5)
Former	1,258 (10.5)	1,034 (78.7)	394 (35.5)	67 (5.5)	13 (27.0)
Problematic alcohol use					
No	6,951 (62.9)	5,451 (76.9)	2,735 (48.9)	501 (5.7)	160 (28.8)
Yes	3,669 (33.4)	2,599 (71.3)	1,263 (46.2)	340 (7.2)	120 (41.0)
No answer	420 (3.7)	269 (65.1)	103 (43.3)	18 (4.3)	8 (33.3)

* n is unweighted frequency, total number of respondents who were asked this survey question

+ Unweighted frequency of respondents who responded ‘Yes’ to the outcome

++ Weighted proportion of respondents who responded ‘Yes’ to the outcome. Numerator: frequency of respondents who responded ‘Yes’ to the outcome. Denominator is frequency of respondents who responded ‘Yes’ and ‘No’ to the outcome (excludes refused and don’t know responses).

Table 5.2. Logistic regression models to assess the association between mental health condition and healthcare professional interactions regarding smoking cessation and nicotine vaping

Cross-sectional International Tobacco Control Four Country Smoking and Vaping (ITC 4CV) Survey, 2018.

	Model 1 (unadjusted)			**Model 2**			**Model 3 (fully adjusted)**		
	OR	**95% CI**	**p-value**	**aOR**	**95% CI**	**p-value**	**aOR**	**95% CI**	**p-value**
1. Visiting a health professional (n* = 11,040)									
No depression/anxiety (ref)	1.00			1.00			1.00		
Depression only	2.40	1.98–2.93	**<0.001**	2.62	2.15–3.23	**<0.001**	2.65	2.17–3.27	**<0.001**
Anxiety only	2.00	1.64–2.44	**<0.001**	2.08	1.70–2.57	**<0.001**	2.08	1.70–2.57	**<0.001**
Depression and anxiety	3.08	2.65–3.58	**<0.001**	3.71	3.17–4.36	**<0.001**	3.74	3.19–4.40	**<0.001**
2. Advice to quit smoking from health professional (n* = 8,319)									
No depression/anxiety (ref)	1.00			1.00			1.00		
Depression only	1.48	1.27–1.74	**<0.001**	1.58	1.34–1.86	**<0.001**	1.58	1.34–1.86	**<0.001**
Anxiety only	0.88	0.74–1.05	0.152	0.95	0.80–1.14	0.601	0.94	0.79–1.12	0.493
Depression and anxiety	1.00	0.90–1.12	0.951	1.15	1.02–1.30	0.022	1.14	1.01–1.29	0.031
3. Discussion about nicotine vaping products (n* = 8,280)									
No depression/anxiety (ref)	1.00			1.00			1.00		
Depression only	1.40	1.02–1.88	0.032	1.44	1.04–1.95	0.023	1.44	1.04–1.95	0.023

	Model 1 (unadjusted)			Model 2			Model 3 (fully adjusted)		
	OR	**95% CI**	**p-value**	**aOR**	**95% CI**	**p-value**	**aOR**	**95% CI**	**p-value**
Anxiety only	1.30	0.92–1.81	0.126	1.45	1.01–2.03	0.036	1.45	1.01–2.03	0.037
Depression and anxiety	1.52	1.22–1.89	**<0.001**	1.65	1.30–2.09	**<0.001**	1.63	1.29–2.06	**<0.001**
4. Positive recommendation to use nicotine vaping products (n* = 859)									
No depression/anxiety (ref)	1.00			1.00			1.00		
Depression only	1.39	0.87–2.21	0.166	1.39	0.83–2.3	0.204	1.36	0.81–2.26	0.240
Anxiety only	1.30	0.76–2.17	0.331	1.06	0.60–1.86	0.831	1.02	0.57–1.81	0.954
Depression and anxiety	1.18	0.83–1.67	0.343	1.28	0.86–1.9	0.218	1.27	0.85–1.89	0.240

- Model 1: unadjusted model with mental health condition as the only independent variable
- Model 2: model adjusted for country, sex, age, education, ethnicity, and income
- Model 3: fully adjusted model adjusted for country, sex, age, education, ethnicity, income, cigarette smoking status, and problematic alcohol use

* n is unweighted frequency, total number of respondents who were asked this survey question

p-values smaller than our Bonferroni correction adjusted p-value (0.0125) are indicated in bold

OR: odds ratio

aOR: adjusted odds ratio

CI: confidence interval

Chapter 6 – Mental health and smoking cessation support use

Preface

The objective of this chapter was to assess cessation aid utilisation by people who smoke with and without common mental health conditions (depression and/or anxiety) used in their last attempt to quit smoking.

This chapter presents the study I conducted using 2018 International Tobacco Control (ITC) Four Country Smoking and Vaping (4CV) Survey data from Australia, Canada, England and the US. This chapter presents the manuscript that I have prepared for submission to a peer-reviewed journal, but it has not been accepted for publication at the time of thesis submission.

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The supplementary materials referred to in this manuscript are available in **Appendix E** of this thesis.

For the references cited in the manuscript, I have retained their original in-text citation number (but have made these superscript numbers to distinguish them from the in-text citations in the thesis), and a reference list for this manuscript is provided at the end of this chapter.

Declaration of roles

I developed this publication in collaboration with Dr Leonie Brose, Professor Ann McNeill, Dr Katherine East (King's College London), Dr Shannon Gravely, Professor Geoffrey T. Fong (University of Waterloo), Professor K. Michael Cummings (Medical University of South Carolina), Professor Ron Borland (University of Melbourne), Dr Gary C. K. Chan, Dr Carmen C. W. Lim, Professor Coral Gartner (University of Queensland), Dr Hua H. Yong (Deakin University).

KMC and GTF were the Principal Investigators of the International Tobacco Control Policy Evaluation (ITC) Project Four Country Survey and designed the survey together with Co-Investigators RB and AM. The survey and measures were developed in collaboration with the ITC Project Research Team and survey firms. The ITC Project Research Team and survey firms were responsible for sample recruitment and maintenance.

I led the write-up of this manuscript, formulated the research questions, and analysed the data. I wrote the pre-registered analysis plan with input from LB, AM, KE, HHY, and SG – researchers who are involved with the ITC Project and had published in similar topic areas. Following approval to use the data, ITC Project Analysts (Dr Anne Quah and Dr Pete Driezen) granted me data access and facilitated the usage of the most appropriate survey weights for my analyses. RB, GTF, KMC, GCKC, CCWL and CG gave feedback on the analysis and interpretation. I wrote the initial manuscript. All co-authors reviewed and provided input on drafts. I handled the manuscript submission and responded to peer reviews. All authors read and approved the final manuscript.

Manuscript

Self-reported depression and anxiety and smoking cessation support used at last quit attempt: Findings from 2018 International Tobacco Control Four Country Smoking and Vaping Survey

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Abstract

Background: People with mental health conditions are disproportionately affected by tobacco-related diseases and premature death. We investigated whether using smoking cessation support during quit attempts differed by self-reported depression and/or anxiety.

Methods: Cross-sectional 2018 ITC Four Country Smoking and Vaping Survey (Australia, Canada, England, US) data were used. Adults self-reporting making a quit attempt in the 18 months prior to the survey and were currently smoking (daily/weekly/monthly, n=3919) or not smoking (n=1258) were included. Weighted logistic regressions examined associations between self-reported current depression and/or anxiety and use of cessation support (nicotine vaping products [NVP], nicotine replacement therapy [NRT], varenicline/bupropion, behavioural support [cessation program/face-to-face advice], or any support) at last quit attempt.

Results: 18.9% of respondents reported having both depression and anxiety, 8.8% depression only, 8.5% anxiety only. Odds for using any cessation aid (59.8%) were higher for those with anxiety (aOR=1.43, 95%CI: 1.14–1.81) and depression and anxiety (aOR=1.31, 95%CI: 1.12–1.54), compared to no depression/anxiety. Using NVPs (31.0%), and varenicline/bupropion (12.1%) did not differ by depression/anxiety. Odds for using NRT (29.0%) were higher for those with depression and anxiety (aOR=1.41, 95%CI: 1.19–1.67). Odds for using behavioural support (11.0%) were higher for those with depression (aOR=1.56, 95%CI: 1.14–2.11), anxiety (aOR=1.53, 95%CI: 1.09–2.10), and depression and anxiety (aOR=1.65, 95%CI: 1.30–2.08).

Conclusions: As 40% of respondents were quitting smoking unaided, opportunities are missed for maximising success. People who smoke and self-reported having depression and anxiety were more likely to use support (and NRT and behavioural support, individually),

and as likely to use NVPs and varenicline/bupropion, in smoking quit attempts than those without depression/anxiety.

Introduction

Smoking is a leading preventable cause of illness and premature death in the United Kingdom (UK) [1] and worldwide [2] and there are significant disparities in smoking prevalence among individuals with and without mental health conditions [3–8]. For example, in the United States (US), among those who reported any past-year mental illness in 2019, past-month cigarette smoking was 28.2%, compared to 15.8% in people without past-year mental illness [9]. This study sought to address a critical gap in our understanding by investigating the utilisation of various smoking cessation aids in smoking quit attempts, particularly among those with depression and/or anxiety, which are among the most common mental health conditions globally [10] but receive less attention in relation to smoking compared to serious mental health illness [11,12].

Smoking contributes to substantial health disparities and plays a significant role in the discrepancy in life expectancy between individuals with and without mental health conditions [3,13–15]. Successful smoking cessation is associated with improved physical and mental health [16], and cessation may allow for a reduction in the dose of some psychotropic medications, minimising side effects [3]. Addressing the needs of priority populations, such as those with mental health conditions, are essential steps toward reaching tobacco endgame/smoke-free goals (reducing adult smoking prevalence to ≤5%). Previous research has shown that people with mental health conditions smoke more heavily and are more highly dependent on cigarettes [6,9]. Although, most adults who smoke express intention to quit smoking [17–19] – including those with mental health conditions [6,20,21] – most quit attempts end in relapse [17,18,22,23]. Some studies have found that the quit success rate is lower in those with mental health conditions, compared to those without [24–30], while other studies have found that the quit rate in people with mental health conditions is generally equal to the quit success rate in people without mental health conditions [6,24,29–38] (especially when heaviness of smoking is taken into account [6]).

Using evidence-based treatments during attempts to quit smoking can increase cessation likelihood up to three times [39]. The cessation support available varies across countries but usually includes nicotine replacement therapy (NRT), varenicline, bupropion, and behavioural support [40–43] (and cytisine is also available in some countries [41]). More recently, nicotine-containing vaping products (NVPs) have been found to improve cessation rates compared to NRT and non-nicotine containing vaping products [44]. However, international policies regarding NVPs differ considerably [45,46]. In the UK, NVPs are available as consumer products and clinical guidelines recommend that NVPs are "accessible to adults who smoke" [40]. In Australia, the sale of NVPs is prohibited unless on prescription from a licensed health professional – clinical guidelines recommend NVPs for those "who have tried to achieve smoking cessation with first-line therapy but failed" [47]. In Canada, NVPs are available in various retail locations, but clinical guidelines do not include NVPs in the list of recommended smoking cessation treatment options [41]. In the US, historically NVPs were available on the open market, but in 2020, the FDA announced a nationwide ban on any non-tobacco and non-menthol flavoured vaping products that used pod or cartridge systems [48], however, the ones not approved have not yet been taken off the market (in 2023). NVPs are not recommended in US clinical guidelines: "clinicians [should] direct patients who use tobacco to other tobacco cessation interventions with proven effectiveness and established safety" [49]. It is important to examine how these diverse approaches impact people who smoke.

Despite the availability of effective cessation aids and recommendations for health professionals to assist patients in their quit attempts, the provision of Very Brief Advice has been suboptimal [50]. Recent studies indicate that a significant proportion of people who smoke do not receive advice to quit from their healthcare providers, for example, in an earlier study [51], we used 2018 International Tobacco Control Four Country Smoking and Vaping (ITC 4CV) Survey data from Australia, Canada, England and the US to investigate health professional interactions, finding that among those who had visited a health professional in the last 18 months, only 48% received advice to quit smoking. Also, a large proportion of quit attempts are made without cessation aids [18,52,53], recently Gravely et al. [53] used the 2020 Four Country survey data, finding that 39% of those who had made a quit attempt in the last 24 months used no cessation aid in their last quit attempt.

Previous studies have explored cessation support utilisation and trends, however, only a few studies have considered differences between people who smoke with and without mental health conditions. These studies found that people who smoke and have mental health conditions are either equally likely [26,38,54–56] or more likely [54,57–59] to use some cessation support in quit attempts, compared to people who smoke and do not have mental health conditions. One study [60] using 2009–2010 electronic health record data from the UK found higher prescribing of cessation medications (NRT, bupropion or varenicline) among people who smoke and have a mental health condition diagnosis, but a lower proportion of consultations with a recording of a cessation medication prescription than for those without a mental health diagnosis. Brose et al. [31] found mixed findings using 2016–17 survey data from England, that people with mental health conditions were less likely to use over-the-counter NRT but more likely to use prescription medication and/or behavioural support, and they found no difference in the use of NVPs during their last quit attempt between people who smoke with and without mental health conditions. However, using a different outcome measure, most recently, Yimsaard et al. (2023) reported differential findings for the use of NVPs between people who self-reported treatment/diagnosis for anxiety or depression compared with those without that condition among a sample of people who had successfully quit smoking (were at least one-month smoking abstinent) at follow-up – those who had depression in 2018 were equally likely to be using NVPs in 2020, while those who had anxiety in 2018 were more likely to be using NVPs in 2020 [29].

To our knowledge, there have been no studies published using post-2017 data which have looked specifically at cessation aid utilisation in quit attempts in people with mental health conditions who smoke. Hence this current study builds on previous research by focusing on respondents with depression and/or anxiety, using cross-sectional data from the 2018 ITC 4CV Survey (Australia, Canada, England and the US). Our study aimed to investigate if there were differences between those with and without a current self-reported diagnosis or treatment for depression and/or anxiety in using various cessation support (NRT, varenicline, bupropion, behavioural support, or NVPs) during their last attempt to quit smoking, and whether any differences vary across countries.

Methods

This manuscript adhered to the STROBE guidelines.

Data source and sample

This study used cross-sectional data from the Wave 2 (March–June 2018) ITC 4CV Survey, a cohort study of people who smoke, vape or those who recently quit smoking from Australia, Canada, England, and the US. Respondents (adults ≥18 years) were recruited using either probability-based sampling frames or non-probability opt-in sampling frames, or a combination of these methods, aiming to be representative of people who smoke (smoked >100 cigarettes in their lifetime), or vape at least weekly, in each country. Participants included those who were re-contacted from the previous wave and new participants who were recruited to address attrition and maintain sample size over time. Full methodological details are available elsewhere (https://itcproject.org/methods) [61,62].

The study sample consisted of 5,177 respondents classified as adults who had made at least one attempt to quit smoking in the past 18 months and who were currently smoking cigarettes (at least monthly) or not smoking cigarettes at the time of the survey (Figure 6.1).

Ethical approval

The survey protocols and all materials of Wave 2 ITC 4CV Survey, including the survey questionnaires, were cleared by Office of Research Ethics, University of Waterloo, Canada (REB#20803/30570, REB#21609/30878); Research Ethics Office, King's College London, UK (RESCM-17/18-2240); Human Research Ethics, Cancer Council Victoria, Australia (HREC1603) and, Human Ethics, Research Management Office, University of Queensland, Australia (2016000330/HREC1603); and Institutional Review Board Medical University of South Carolina (waived due to minimal risk). All participants provided consent to participate.

Measures

A more detailed description of the variables is provided in the pre-registered analysis plan https://osf.io/y72cj [63,64].

Study eligibility

Respondents who answered: *"less than 1 week ago", "1-2 weeks ago", "3-4 weeks ago", "1-3 months ago", "4-6 months ago", "7-12 months ago"* or *"13-18 months ago"* to *"How long ago did you quit smoking?",* or answered: "*1 attempt", "2 attempts"* or *"3 or more attempts"* to *"How many times have you tried to quit in the past 18 months?"* were asked about the use of cessation support options in their quit attempt(s).

Independent variable

Mental health condition:

The 2018 wave was the most recent ITC 4CV survey wave which contained survey questions about depression and anxiety (assessed with a single item measure, similar to past research [24,56,59,65]). All respondents were asked: *"Are you currently being treated for, or have you been diagnosed (current diagnosis) with, any of the following…? [Select all that apply.]: Depression. Anxiety*. …" Response options: Selected/Not selected/Refused (excluded)/Don't know (excluded). The answers were recoded into four mutually exclusive categories: (1) No depression/anxiety: 'Not selected' to both depression and anxiety; (2) Depression only: 'Selected' to depression but 'Not selected' to anxiety; (3) Anxiety only: 'Selected' to anxiety but 'Not selected' to depression; (4) Depression and anxiety: 'Selected' to both depression and anxiety.

Outcome measures: Use of support in last quit attempt

Response options to the individual cessation aid options were: Yes/ No/ Refused (excluded)/ Don't know (excluded). Respondents could select 'Yes' to multiple responses. Five outcome measures were derived.

Used NVPs

Eligible respondents were classified as either currently using NVPs, or had ever used NVPs were asked: "*Did you use an e-cigarette/vaping device on your [LAST/CURRENT] quit attempt?"*.

Respondents who were not asked this survey question (n=1042) because they indicated that they had *"never tried vaping products"* or *"never heard of vaping products"* were recoded as 'No' for NVP use.

For the next three outcomes, all eligible respondents were asked *"Which of the following forms of help did you receive or use as part of your [LAST/CURRENT] quit attempt [apart from the use of e-cigarettes, which you have already told us about]?"*

Used NRT

"Any type of nicotine replacement product, such as patches, gum, mouth spray, etc.".

Used varenicline or bupropion

"Varenicline or Chantix or Champix". Or *"Bupropion or Zyban or Wellbutrin".* Answers were recoded into two categories: (1) Yes: 'Yes' to varenicline and/or to bupropion; (2) No: 'No' to varenicline and to bupropion.

Used behavioural support

Cessation program *"Canada, US: Clinic, individual or group counselling, stop-smoking course, or behaviour therapy/England: Local stop smoking service (e.g., clinics or specialists)/Australia: Face-to-face specialised stop smoking program").* Or *"Face-to-face advice from a doctor or other health care professional (dentist, pharmacist, etc.)".* Answers were recoded into two categories: (1) Yes: 'Yes' to cessation program and/or to face-to-face advice; (2) No: 'No' to cessation program and to face-to-face advice.

Used any cessation aids

This aggregate outcome measure was derived from the above four measures, into two categories: (1) Yes: 'Yes' to any of the above four; (2) No: 'No' to all of the above four.

Covariates

Covariates included: sex (male, female), age group (18–24, 25–39, 40–54, ≥55 years), country of residence (Australia, Canada, England, US), highest level of education (low, moderate, high), ethnicity (minority group, majority group), annual household income (low, moderate, high, no answer [valid response option]), cigarette smoking status (daily, non-daily [including weekly and monthly], quit [quit smoking in the last 18 months AND had smoked >100 cigarettes in their lifetime]), and problematic alcohol use (total score out of 12 based on Alcohol Use Disorders Identification Test Consumption (AUDIT C) [66] where: ≥5 points [Yes]/ ≤4 points [No]/No answer [valid response option]).

Respondents who refused to answer or answered 'Don't know' to education or ethnicity questions were excluded from the sample (Figure 6.1).

Data analysis

Unweighted frequencies and weighted proportions were calculated. The sample was weighted using derived cross-sectional survey weights [63] to account for the stratified sampling design (defined by geographic regions within each country). Three separate

weighted logistic regression models were generated to investigate the relationship between mental health condition and the five outcomes: (1) used any cessation aids, (2) used NVPs, (3) used NRT, (4) used varenicline or bupropion, (5) used behavioural support. The weighted regression models were: (A) unadjusted model with mental health condition as the only independent variable; (B) model adjusted for country, sex, age, education, ethnicity, and income; (C), fully adjusted model additionally adjusted for cigarette smoking status and problematic alcohol use. To assess whether the association between mental health condition and each outcome varies by country, for each outcome, a likelihood-ratio test assessed whether there was a significant difference between model C and a new model (D) which contained interaction terms between mental health condition and country.

Assumptions of logistic regression were met [67]. Analyses were conducted using RStudio (version 4.0.3), regression models were generated using the *'glm'* command of the *'mlogit'* package. As the regressions were weighted, the 'family=quasibinomial' argument was used. Exact p-values and 95% (likelihood ratio-based [67]) confidence intervals (CIs) are reported. Results were adjusted for multiple comparison, where the significance level was evaluated at 0.01 level, as per the Bonferroni correction (α=0.05/5 outcomes= 0.01).

Results

Sample characteristics

The unweighted analytical sample included 5,177 respondents who indicated that they had made a quit attempt in the last 18 months (Table 6.1). Supplementary Table 1 shows the 'Yes', 'No', 'Don't know' and refused to answer responses to the outcome measure questions. The weighted sample was 53.0% female, and respondents were more likely to be in the majority ethnic group (white) and aged ≥40 years. Most of the respondents were residing in England (34.4%), followed by Canada (32.8%), the US (20.2%), and Australia (12.6%). The most common cigarette smoking status was current 'daily' (59.7%). The 'non-daily' smoking category (16.0%) was made up of 12.0% who currently smoked weekly, and 4.0% who currently smoked monthly. At the

time of the survey, 75.7% of respondents were currently smoking and 24.3% of respondents were not smoking. Large proportions of respondents had moderate-level education (43.2%), moderate-level annual household income (32.9%), and did not have problematic alcohol use (64.8%). Over a third of respondents had self-reported depression and/or anxiety (36.1%), 8.8% had depression only, 8.5% had anxiety only, and 18.9% had both depression and anxiety.

Used any cessation aids

A small majority (59.8%) of the sample reported using any cessation aid (Table 6.1). Approximately 40.5% of respondents used no aids, 40.4% used one aid, and 19.1% used between two and six aids (Supplementary Table 2a).

In our unadjusted regression model (Model A), we did not find an association between using any cessation aid and having depression and/or anxiety (Table 6.2). However, in the adjusted models, there was an association between using any cessation aid and having anxiety alone and both depression and anxiety. In the fully adjusted model (Model C), the odds of using any aid were significantly higher for respondents with anxiety alone (aOR=1.43, 95% CI: 1.14–1.81, p=0.002), and both depression and anxiety (aOR=1.31, 95% CI: 1.12–1.54, p=0.001), compared to respondents with no depression/anxiety (Table 6.2).

Used NVPs

Just under one third (31.0%) of respondents reported using NVPs in their last quit attempt (Table 6.1). Approximately 17.0% of respondents exclusively used NVPs in their last quit attempt, 14.0% used NVPs and any other cessation aid, and 69.0% did not use NVPs (Supplementary Table 2b).

We did not find a significant association between depression and/or anxiety and the odds of using NVPs in a quit attempt in any regression model (Table 6.2).

Used NRT

Less than a third (29.0%) of respondents used NRT in their last quit attempt (Table 6.1).

In all three regression models, the odds of using NRT were significantly higher for respondents with both depression and anxiety, compared to those with no depression/anxiety (Table 6.2). In the fully adjusted model (Model C), the odds of using NRT were 1.41 times higher (95% CI: 1.19–1.67, p<0.001) for respondents with both depression and anxiety, compared to respondents with no depression/anxiety (Table 6.2). In Model B, the odds of using NRT were also significantly higher for respondents with anxiety only (aOR=1.40, 95% CI: 1.11–1.77, p=0.005) (Table 6.2); however, this was not statistically significant in our fully adjusted model (p=0.011). Lastly, the association between having depression only and using NRT was not significant in any of the three models.

Used varenicline or bupropion

The overall proportion of respondents who used varenicline or bupropion in their last quit attempt was 12.1% (Table 6.1).

We did not find an association between depression and/or anxiety and the odds of using these cessation medications in any regression model (Table 6.2).

Used behavioural support

The overall proportion of respondents who used behavioural support in their last quit attempt was 11.0% (Table 6.1).

In all three models, the odds of using behavioural support were significantly higher for respondents with depression alone, and those with both depression and anxiety, compared to respondents with no depression/anxiety (Table 6.2). Although not significant in the unadjusted model (Model A) (p=0.021), the odds of using behavioural support were significantly higher for respondents with anxiety alone in our two adjusted regression models. In the fully adjusted model (Model C), the odds of using behavioural support were 1.56 times higher (95% CI: 1.14–2.11, p=0.005) for

respondents with depression alone, 1.53 times higher (95% CI: 1.09–2.10, p=0.010) for respondents with anxiety alone, and 1.65 times higher (95% CI: 1.30–2.08, p<0.001) for respondents with both depression and anxiety, compared to respondents with no depression/anxiety (Table 6.2).

Country differences

Likelihood-ratio tests indicated a significant difference between the model with and without the mental health condition*country interaction terms for the 'used behavioural support' outcome, but not for the other outcomes. For the outcome on using behavioural support, although the overall joint effect was statistically significant (p=0.007), none of the individual interaction terms for mental health condition*country were significant at p<0.01 (Supplementary Table 3t).

Discussion

This study investigated if there were differences between those with and without a current diagnosis/treatment for depression and/or anxiety in using cessation support, including NVPs, during their last attempt to quit smoking cigarettes. Around 60% of adults who currently smoke or recently quit smoking reported using any cessation aid; fewer than a third reported using NVPs (31%) or NRT (29%); and the proportion using varenicline or bupropion (12%) or behavioural support (11%) was low. People with anxiety alone and with both depression and anxiety who smoke were more likely to use some form of support in their quit attempt, compared to those with no depression/anxiety. Those with both depression and anxiety were more likely to use NRT; and those with depression alone, anxiety alone, or both depression and anxiety were more likely to use behavioural support. We found that those with depression and/or anxiety and those without were equally likely to use varenicline/bupropion or NVPs in their last quit attempt. We also found that there may be a significant interaction between mental health condition and country regarding using behavioural support.

The overall proportion of quit attempts which involved any cessation aid (60%), not specifically considering mental health conditions, is similar to the findings of other studies [53,68]. Consistent with past research [31,54,56], our study found that using NVPs to quit smoking was similar among adults with and without depression and/or anxiety. Yimsaard et al. (2023) found that those who self-reported treatment/diagnosis for anxiety in 2018 and had successfully quit smoking in 2020 were more likely to be using NVPs in 2020, compared to those with no anxiety [29]. However, studies (including ours) which investigated the use of NVPs in quit attempts found no significant difference between individuals with mental health conditions and those without. This might suggest that using NVPs post-cessation might help prevent relapse among people with anxiety. However, as far as we are aware, only a few studies [26,31,58] have examined whether the effectiveness of smoking cessation aids differ between people with and without mental health conditions in the 'real world', and they have not appeared to find evidence of a significant difference between the two groups. Although previous research has suggested that a higher proportion of people who smoke with mental health conditions use prescription cessation medications than those without [31,54,58–60], our study found that the use of varenicline or bupropion to quit smoking was similar among adults with depression and/or anxiety and those without – similar to studies which used older survey data (2006–2011 [26] and 2012 [55]). We found that those with both depression and anxiety were more likely to use NRT, compared to those with no depression/anxiety, but the likelihood of using NRT was not higher for those with depression alone or anxiety alone. The findings regarding NRT in previous studies have been mixed – some studies found that people with mental health conditions were equally likely [38,55] to use NRT, and some found that they were more likely [54,57,58] to use NRT, compared to people without mental health conditions. The reason for mixed findings may be the differentiation between over-the-counter NRT and NRT that is prescribed by a health professional (in our study, the survey question did not differentiate) – for example, Brose et al. [31] found that people with mental health conditions were less likely to use over-the-counter NRT, while Falcaro et al. [57] and Taylor et al. [58] found that those with mental health conditions were more likely to be prescribed NRT. Lastly, regarding behavioural support, there were fewer existing studies to compare our findings to. Two previous studies found that those with mental health conditions were more likely to use behavioural support [31,54], while one found that they were equally likely to use it, compared to those with no mental

health conditions [26]. Our study showed that those with depression and/or anxiety were more likely to use behavioural support, compared to those with no depression/anxiety. One possible explanation for this may be that individuals with these mental health conditions may be reluctant to use cessation medications if they already take psychotropic drugs. However, it is worth noting that the overall proportion of people who use behavioural support has tended to be low historically, and its availability varies between countries. For example, under 10% of those who had made a quit attempt used NHS Stop Smoking Services between 2007 and 2023 in England [68], and under 8% used a stop smoking service, counselling, advice from a doctor or a quitline in Australia (9%), Canada (6%), England (11%), and the US (5%) in 2020 [53].

Nonetheless, a large proportion (40%) of respondents did not use any cessation aid in their last quit attempt and there was a high rate of unsuccessful quit attempts. The majority (76%) of those who indicated that they had made a quit attempt were not successful, because they indicated that they were still smoking at the time of the survey. These findings highlight the challenges of quitting smoking. It is important to acknowledge, that for many people who smoke, it can take multiple quit attempts before successfully quitting [22]. Ongoing support is therefore crucial, for both people with and without mental health conditions. We recommend enhancing treatment access for people who smoke, to support smoking quit attempts.

Smoking cessation may be more challenging for people with mental health conditions because they are more likely to smoke heavily and be highly dependent on cigarettes [6,9]. Using cessation support in quit attempts can increase the likelihood of successful smoking cessation [39]. Therefore, our finding that people with anxiety, and both anxiety and depression were more likely to use support than those without either condition is promising, because this may help to narrow the disparity in smoking prevalence that exists between those with and without mental health conditions. However, we also found that people with depression alone were only equally likely to use any cessation support, compared to those with no depression/anxiety. Given that the respondents in our study would have had to be in contact with a health professional to receive a current diagnosis/treatment for depression or anxiety, the findings of a previous study by Szatkowski et al. (2023) are important to consider. They found that although people with

mental health conditions were more likely use health services, the proportion of consultations where a cessation medication was prescribed was lower than for patients without a mental health condition [60]. Importantly, our findings, coupled with Szatkowski et al.'s (2013) findings, suggest that there are missed opportunities for health professionals to provide cessation advice and support for those with mental health conditions.

We would like to highlight this missed opportunity regarding the use of NVPs in smoking quit attempts. We found that the use of NVPs in quit attempts was similar among adults with and without depression/anxiety. Given that varenicline and bupropion have been unavailable internationally since 2021 [69] and 2022 [70], respectively; NVPs are potentially the most effective smoking cessation support option currently available (because NVPs have been found to be more effective in achieving smoking cessation than using NRT [44]). In order to achieve further reductions in population smoking prevalence, we recommend that healthcare professionals provide accurate information about and access to NVPs to people who smoke, especially for individuals with mental health conditions.

Future research

Future research could explore whether health professionals provide differential care regarding smoking cessation to people who smoke with mental health conditions. It is important to explore the factors influencing the choice of cessation aid (if any) a person who smokes decides on using to support their quit attempt. Also, the effect of various mental health conditions beyond depression and anxiety should also be investigated. Furthermore, a more nuanced approach to defining mental health variables in studies may lead to a better understanding of the impact of mental health on the outcome measures. To further investigate country effects, we recommend stratification by country, but a larger sample size will be required.

Strengths and limitations

A strength is that our study used data from large population-based samples of people who recently made an attempt to quit smoking from four countries. However, there are some limitations. The 2018 wave of the ITC 4CV Survey was used because this was the most recent wave for which data are available and which contained survey questions about depression and anxiety. The study relies on self-reported measures which were not verified with health records and may be subject to recall bias. The survey questions used to identify depression and/or anxiety were not intended as a diagnostic tool; it is not possible to know the severity or length of time since diagnosis of the condition(s), or whether respondents use medications to control the mental health condition(s). We used categorical variables to represent all our control variables used in our analysis (reflecting the response categories in the survey questionnaire), including one which could be coded as continuous (age) to be consistent with prior studies using ITC data (e.g., [29,53,54,65,71]. This may result in a loss of granularity in the data or the simplification of complex relationships, which may increase the risk of Type I and Type II errors. The sample size for some of our outcome measures was small, but our aggregate outcome measure helped mitigate this issue.

Conclusion

We found that people who smoke and self-reported receiving a current diagnosis/treatment for depression/anxiety were more likely to use some types of cessation support. At last quit attempt, those with both depression and anxiety were more likely to use NRT, and those with depression and/or anxiety were more likely to use behavioural support, compared to those with no depression/anxiety. Use of NVPs and varenicline/bupropion to quit smoking was similar among adults with and without depression/anxiety.

It is important to acknowledge that, overall, a substantial proportion (40%) of people made a smoking quit attempt without using any type of cessation support, and there was a high rate (76%) of unsuccessful quit attempts. Hence, it is important for health professionals to systematically offer ongoing cessation support to all patients, regardless of mental health status.

Smoking cessation may be more challenging for people with mental health conditions because they are more likely to smoke heavily and be highly dependent on cigarettes. We found that those with mental health conditions were more likely to use some cessation support than those without depression/anxiety. This is promising, as this may help to narrow the disparity in smoking prevalence that exists between those with and without mental health conditions. However, we also found evidence of missed opportunities for health professionals to provide cessation support for those with mental health conditions: people with depression alone were only equally likely to use any cessation support, compared to those with no depression/anxiety; and the use of NVPs in quit attempts was similar among adults with and without depression/anxiety. As NVPs are potentially the most effective smoking cessation support option currently available, it is important that healthcare professionals provide accurate information about and access to NVPs to people who smoke, especially for individuals with mental health conditions.

Our study highlighted the need for accessible treatment options, increased awareness, and better dissemination of information about effective cessation support options. Further research is needed to refine our understanding of the nuances in providing care for this population and the role of different mental health conditions.

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Declaration of interests

KMC has served as a paid expert witness in litigation filed against cigarette manufacturers. GTF has served as an expert witness/consultant for governments defending their country's policies/regulations in litigation. All other authors have no conflict of interest to declare.

Data availability statement

In each country participating in the international Tobacco Control Policy Evaluation (ITC) Project, the data are jointly owned by the lead researcher(s) in that country and the ITC Project at the University of Waterloo. Data from the ITC Project are available to approved researchers 2 years after the date of issuance of cleaned data sets by the ITC Data Management Centre. Researchers interested in using ITC data are required to apply for approval by submitting an International Tobacco Control Data Repository (ITCDR) request application and subsequently to sign an ITCDR Data Usage Agreement. The criteria for data usage approval and the contents of the Data Usage Agreement are described online (http://www.itcproject.org).

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Figures and Tables

Figure 6.1. Inclusion flow diagram for study sample

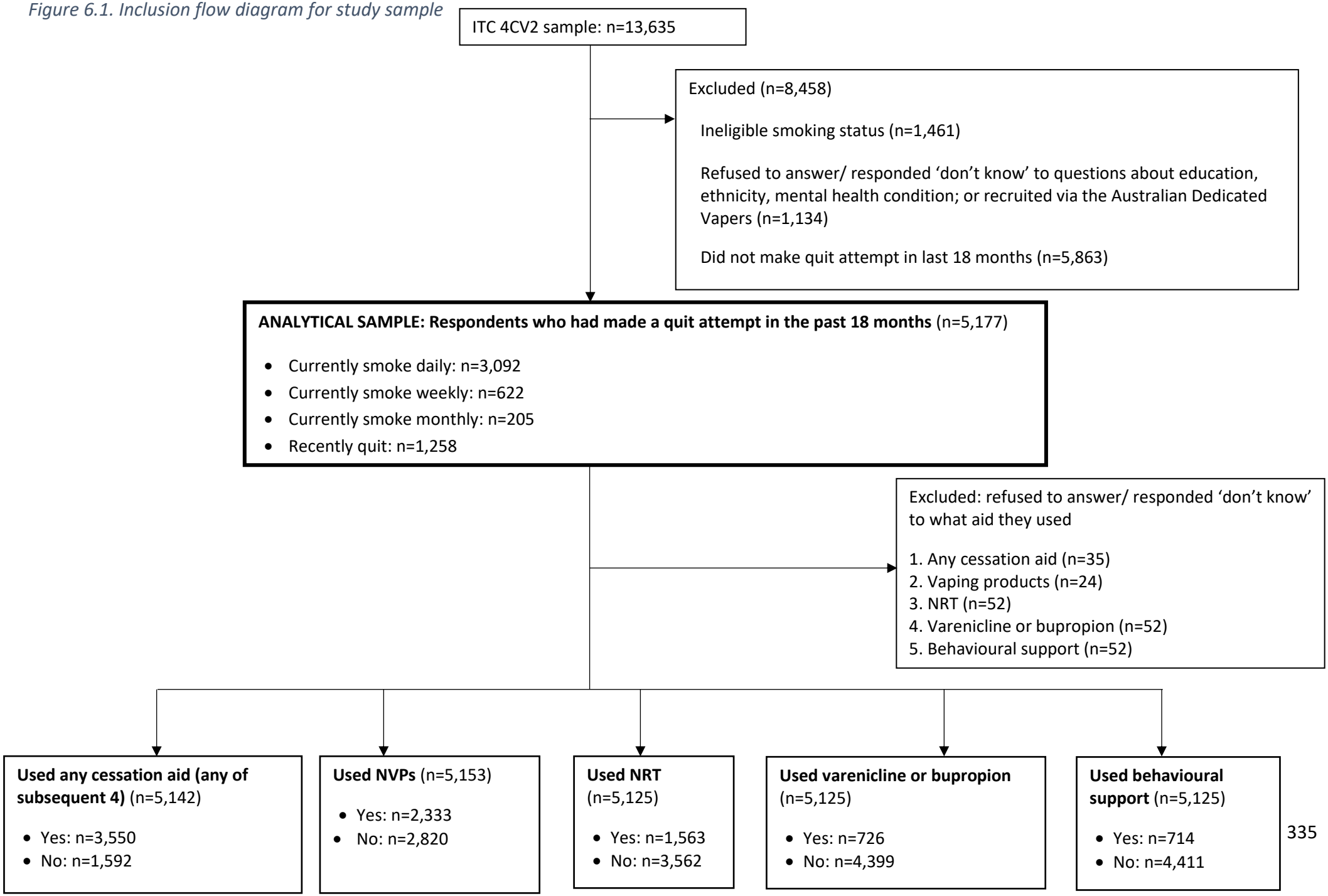

Table 6.1. Mental health condition and covariates by study sample and smoking cessation support used in last quit attempt

Cross-sectional International Tobacco Control Four Country Smoking and Vaping (ITC 4CV) Survey, 2018.

Variable categories	**Study sample** (n=5,177)	**Used any cessation aid** (n*= 5,142)	**Used NVPs** (n*= 5,153)	**Used NRT** (n*= 5,125)	**Used varenicline or bupropion** (n*= 5,125)	**Used behavioural support** (n*= 5,125)
TOTAL	5,177 (100.0)	**Yes**, 3,550[+] (59.8[++])	**Yes**, 2,333[+] (31.0[++])	**Yes**, 1,563[+] (29.0[++])	**Yes**, 726[+] (12.1[++])	**Yes**, 714[+] (11.0[++])
Mental health						
No depression/anxiety	3,306 (63.9)	2,206 (58.2)	1,430 (30.6)	954 (27.4)	408 (11.3)	405 (9.7)
Depression only	453 (8.8)	335 (61.5)	207 (30.2)	152 (30.4)	103 (15.1)	78 (14.4)
Anxiety only	441 (8.5)	319 (64.9)	221 (34.5)	141 (33.3)	82 (14.9)	73 (13.5)
Depression and anxiety	977 (18.9)	690 (62.7)	475 (31.7)	316 (32.7)	133 (12.7)	158 (13.7)
Country						
Australia	650 (12.6)	429 (60.3)	165 (20.1)	222 (30.9)	128 (17.2)	70 (10.6)
Canada	1,700 (32.8)	1,121 (61.0)	686 (26.4)	589 (35.3)	208 (12.8)	231 (11.7)
England	1,782 (34.4)	1,322 (61.7)	1,045 (43.6)	487 (25.2)	224 (7.6)	294 (11.5)
US	1,045 (20.2)	678 (54.1)	437 (24.7)	265 (24.0)	166 (15.1)	119 (9.4)
Gender						

Variable categories	**Study sample** (n=5,177)	**Used any cessation aid** (n*= 5,142)	**Used NVPs** (n*= 5,153)	**Used NRT** (n*= 5,125)	**Used varenicline or bupropion** (n*= 5,125)	**Used behavioural support** (n*= 5,125)
Male	2,434 (47.0)	1,721 (60.9)	1,159 (32.1)	730 (29.1)	368 (12.5)	370 (11.2)
Female	2,743 (53.0)	1,829 (58.5)	1,174 (29.8)	833 (28.9)	358 (11.7)	344 (10.8)
Age group (years)						
18-24	1,173 (22.7)	770 (53.8)	599 (36.5)	336 (25.4)	107 (4.3)	169 (9.6)
25-39	1,309 (25.3)	890 (56.9)	671 (35.0)	342 (24.4)	176 (9.0)	182 (10.6)
40-54	1,263 (24.4)	911 (65.1)	563 (30.4)	409 (32.6)	205 (16.3)	174 (11.2)
55 and up	1,432 (27.7)	979 (62)	500 (22.4)	476 (34.5)	238 (16.8)	189 (12.3)
Ethnicity						
Minority group	827 (16.0)	563 (57.9)	374 (29.3)	268 (27.6)	122 (9.6)	154 (15.7)
Majority group	4,350 (84.0)	2,987 (60.1)	1,959 (31.3)	1,295 (29.2)	604 (12.6)	560 (10.2)
Education						
Low	1,544 (29.8)	1,053 (60.6)	640 (26.4)	472 (32.5)	214 (13.7)	179 (9.4)
Moderate	2,236 (43.2)	1,536 (60.6)	1040 (34.6)	672 (28.6)	287 (10.5)	299 (11.0)
High	1,397 (27.0)	961 (57.0)	653 (29.5)	419 (25.4)	225 (13.5)	236 (13.1)

Variable categories	**Study sample** (n=5,177)	**Used any cessation aid** (n*= 5,142)	**Used NVPs** (n*= 5,153)	**Used NRT** (n*= 5,125)	**Used varenicline or bupropion** (n*= 5,125)	**Used behavioural support** (n*= 5,125)
Income						
Low	1,596 (30.8)	1,063 (60.9)	644 (27.1)	500 (30.9)	219 (13.4)	221 (12.0)
Moderate	1,703 (32.9)	1,223 (61.3)	857 (35.8)	490 (28.4)	222 (9.7)	245 (9.9)
High	1,631 (31.5)	1,109 (57.7)	744 (30.2)	493 (27.9)	263 (13.7)	223 (11.6)
No answer	247 (4.8.0)	155 (56.1)	88 (28.3)	80 (28.2)	22 (9.6)	25 (8.9)
Cigarette smoking status						
Daily	3,092 (59.7)	2,205 (64.0)	1,382 (31.0)	1,086 (34.6)	502 (13.7)	462 (12.3)
Non-daily	827 (16.0)	561 (49.6)	434 (31.1)	235 (23.8)	86 (7.2)	122 (10.1)
Quit	1,258 (24.3)	784 (53.9)	517 (31.2)	242 (17.1)	138 (10.6)	130 (8.1)
Problematic alcohol use						
No	3,357 (64.8)	2,302 (60.4)	1,478 (30.7)	1,041 (29.1)	457 (12.7)	460 (11.8)
Yes	1,659 (32.0)	1,144 (58.2)	791 (31.4)	478 (28.1)	252 (11.3)	236 (9.2)
No answer	161 (3.1)	104 (64.6)	64 (33.9)	44 (36.5)	17 (8.1)	18 (13.1)

'Study sample' column shows the characteristics of the analytical study sample who had made a quit attempt in the last 18 months (n=5,177), from Wave 2 (2018) of the ITC 4CV Survey; unweighted frequencies and weighted proportions

*n is unweighted frequency, total number of respondents who were asked this survey question

+ Unweighted frequency of respondents who responded 'Yes' to the outcome

++ Weighted proportion of respondents who responded 'Yes' to the outcome. Denominator is frequency of respondents who responded 'Yes' and 'No' to the outcome (excludes refused and don't know responses for each outcome measure)

Any aid: nicotine vaping products/nicotine replacement therapy/varenicline/bupropion/behavioural support

Table 6.2. Logistic regression models to assess the association between mental health condition and smoking cessation support used in last quit attempt

Cross-sectional International Tobacco Control Four Country Smoking and Vaping (ITC 4CV) Survey, 2018.

	Model A (unadjusted)			Model B			Model C (fully adjusted)		
	OR	**95% CI**	**p-value**	**OR**	**95% CI**	**p-value**	**OR**	**95% CI**	**p-value**
Used any cessation aid (n*= 5,142)									
No depression/anxiety (ref)	1.00			1.00			1.00		
Depression only	1.15	0.93–1.42	0.210	1.14	0.92–1.41	0.241	1.13	0.91–1.40	0.277
Anxiety only	1.32	1.06–1.66	0.014	1.46	1.16–1.84	**0.001**	1.43	1.14–1.81	**0.002**
Depression and anxiety	1.20	1.04–1.40	0.016	1.31	1.12–1.54	**0.001**	1.31	1.12–1.54	**0.001**
Used NVPs (n*= 5,153)									
No depression/anxiety (ref)	1.00			1.00			1.00		
Depression only	0.98	0.78–1.23	0.875	1.02	0.80–1.28	0.899	1.02	0.80–1.29	0.861
Anxiety only	1.20	0.95–1.50	0.121	1.35	1.06–1.70	0.013	1.34	1.06–1.70	0.013
Depression and anxiety	1.05	0.90–1.23	0.515	1.05	0.89–1.25	0.538	1.06	0.89–1.25	0.501
Used NRT (n*= 5,125)									
No depression/anxiety (ref)	1.00			1.00			1.00		

	Model A (unadjusted)			Model B			Model C (fully adjusted)		
	OR	**95% CI**	**p-value**	**OR**	**95% CI**	**p-value**	**OR**	**95% CI**	**p-value**
Depression only	1.16	0.92–1.45	0.201	1.17	0.93–1.47	0.181	1.13	0.89–1.42	0.318
Anxiety only	1.32	1.05–1.66	0.017	1.40	1.11–1.77	**0.005**	1.36	1.07–1.73	0.011
Depression and anxiety	1.29	1.10–1.51	**0.002**	1.43	1.21–1.69	**<0.001**	1.41	1.19–1.67	**<0.001**
Used varenicline or bupropion (n*= 5,125)									
No depression/anxiety (ref)	1.00			1.00			1.00		
Depression only	1.40	1.03–1.86	0.026	1.34	0.98–1.80	0.056	1.34	0.98–1.80	0.060
Anxiety only	1.37	1.00–1.85	0.042	1.45	1.05–1.98	0.021	1.43	1.03–1.95	0.028
Depression and anxiety	1.14	0.91–1.42	0.253	1.33	1.04–1.68	0.020	1.30	1.02–1.65	0.031
Used behavioural support (n*= 5,125)									
No depression/anxiety (ref)	1.00			1.00			1.00		
Depression only	1.57	1.15–2.10	**0.003**	1.59	1.17–2.15	**0.003**	1.56	1.14–2.11	**0.005**
Anxiety only	1.46	1.05–1.99	0.021	1.55	1.11–2.13	**0.008**	1.53	1.09–2.10	**0.010**
Depression and anxiety	1.47	1.18–1.83	**0.001**	1.66	1.31–2.09	**<0.001**	1.65	1.30–2.08	**<0.001**

Model A: unadjusted model with mental health condition as the only independent variable
Model B: model adjusted for country, sex, age, education, ethnicity, and income
Model C: fully adjusted model adjusted for country, sex, age, education, ethnicity, income, cigarette smoking status, and problematic alcohol use

* Unweighted frequency, total number of respondents who were asked this survey question (excludes refused and don't know responses for each outcome measure)

p-values below our Bonferroni correction adjusted p-value (0.01) are indicated in bold

Any aid: nicotine vaping products/nicotine replacement therapy/varenicline/bupropion/behavioural support

Chapter 7 – Discussion

Thesis aim and objectives

The overarching aim of this thesis was to contribute to the evidence base regarding how the provision and uptake of smoking cessation support options (including NVPs) in the UK could be improved, to further reduce the prevalence of smoking and meet national smoke-free targets (≤5% adult smoking prevalence), including reducing the prevalence of smoking in people with mental health conditions.

My four objectives were:

Objective 1:
Review the evidence for the effectiveness of interventions (implementation strategies), which were implemented on a national or state-wide scale, aiming to increase the provision of smoking cessation treatment in primary care.

Objective 2:
Describe and characterise the extent to which NVP use has been recorded in primary care electronic health records in the UK.

Objective 3:
Examine interactions between health professionals and people who smoke with and without common mental health conditions (depression and/or anxiety), about smoking cessation and nicotine vaping products.

Objective 4:
Assess cessation aid utilisation by people who smoke with and without common mental health conditions (depression and/or anxiety) used in their last attempt to quit smoking.

In this final Chapter, I first summarise my key findings and their interpretation in the context of the existing literature. Then, I discuss the overall strengths and limitations of this thesis. Lastly, I consider the implications of my findings for clinical practice, policy and research.

Objective 1 – Strategies to increase smoking cessation support provision

Chapter 3 presented the systematic review I conducted [1], which aimed to find evidence (observational studies) for the adoption and effectiveness of implementation strategies on a national/state-wide scale regarding smoking cessation treatment provision and patient smoking outcomes in 'real world' primary care settings. Secondary aims included synthesising any available cost-effectiveness metrics, and summarising the facilitators and barriers the authors proposed to explain why certain implementation strategies were effective or not effective.

Key findings

My systematic review [1] found 49 studies which measured either practitioner-level or patient-level outcomes – only 12 measured patient-level outcomes (quit attempts and smoking cessation). No studies assessed cost-effectiveness.

My review used the framework developed by the Expert Recommendations for Change (ERIC) programme to characterise the intervention (implementation strategies). The interventions I found were from the implementation strategy domains: 'Train and educate stakeholders', 'Engage consumers', 'Utilize financial strategies', 'Change infrastructure'.

Interventions utilizing financial strategies appeared to increase the recording of smoking status and cessation advice, but the effect on cessation medication prescribing was mixed. Only one study assessed quit attempts and it found no effect, but seven out of nine studies which assessed smoking cessation found an increase.

Interventions changing infrastructure had mixed results for smoking status recording, cessation advice provision and cessation medication prescribing. No studies measured quit attempts, and one out of three studies which assessed smoking cessation found an increase.

Interventions which involved training and educating stakeholders indicated a beneficial impact on smoking status and cessation advice recording, and smoking cessation, but should be interpreted with caution because the evidence was low-quality.

Interventions which involved engaging consumers showed no effect on cessation medication prescribing. One study assessed cessation advice provision and cessation (both increased), but the intervention also involved implementation strategy categories which involved training and educating stakeholders and the effectiveness was attributed to this latter domain by the study authors.

Overall, I found some evidence for interventions which utilized financial strategies having a beneficial effect on smoking cessation.

My review also involved extracting perceived facilitators and barriers from the 49 included studies, and mapping these to the determinants in the Consolidated Framework for Implementation Research (CFIR). Some key facilitators which I identified were the simplicity of the intervention (VBA) and external policies/incentives which were complementary to the smoking cessation aims of the intervention, such as, wider tobacco control measures and funding for public health and cessation clinics, and having the ability for physicians to refer people who smoke to cessation programmes or community-based support. Some of the key barriers included time and financial constraints, lack of free cessation medications and follow-up, deprioritisation and unclear targets in primary care, lack of knowledge of healthcare professionals, and insufficient messaging to patients about available cessation support options.

Findings in context

My review of the literature in *Chapter 1* found that there is evidence showing that health professionals providing VBA (asking patients about their smoking behaviour, advising about the consequences of smoking and smoking cessation, and acting: offering cessation support options to assist patients' quit attempts) can increase the proportion of patients who make quit attempts, increase the proportion who use cessation aids in their quit attempts, and increase the likelihood of smoking cessation success. However, studies have found that the rate that health professionals provide VBA in clinical practice in the 'real world' is suboptimal [231].

My systematic review [1] complements the findings of the Cochrane review by Lindson et al. [239], which evaluated randomised and cluster-randomised trials of similar implementation strategies but in controlled environments. There were some differences between the findings from RCTs and findings from observational studies which evaluated implementation strategies which were 'rolled out' in the 'real world' on a national/state-wide scale. I highlight some of the differences here.

Adjunctive counselling and tailored print materials were found to be efficacious at increasing quit rates in RCTs [239], whereas I found no studies which assessed these strategies in national/state-wide implementation [1].

The Cochrane review [239] also found that adding cost-free medications to standard cessation support increased smoking quit rates and quit attempts. In my review [1], I found that, where access to health insurance which included coverage for smoking cessation treatment was increased in the 'real world', this improved smoking status recording, the provision of cessation advice and cessation medications, and quit rates – in contrast, the one study which assessed quit attempts found no effect. My review found studies where the implementation strategy was the introduction of new free cessation medications – here, prescribing of the new medication increased, but overall cessation medication prescribing stayed the same (and other outcomes were not assessed) [1].

There was no clear evidence that provider incentives can increase smoking quit rates in RCTs [239]. However, my systematic review [1] found that, in the 'real world', where primary care practices received funding to deliver national cardiovascular disease prevention programmes (including health checks), this increased smoking status recording, cessation advice and cessation medication provision, and cessation. I [1] also found evidence that a nationally implemented financial incentive scheme for GPs (e.g., the QOF in the UK) was effective in increasing the recording of smoking status and cessation advice, and referral to cessation services. However, there was a mixed effect on cessation medication prescribing and smoking cessation – but cessation outcomes were only assessed in two out of 16 studies (one found an increase and one found no effect) [1].

Lastly, the Cochrane review [239] found some evidence for provider training, as a single- and multi-component strategy: the former increased smoking status recording, cessation

advice provision, cessation counselling, and providing self-help materials; the latter increased quit rates, setting a quit date, providing self-help materials, and arranging patient follow-up. In my review, I [1] identified some low-quality evidence (three studies, at serious risk of bias) of provider training as a strategy implemented in the 'real world' – this increased smoking status recording, cessation advice recording, and cessation.

Objective 2 – Vaping recording in electronic health records

Chapter 4 presented my exploratory analysis of primary care electronic health records from UK general practices which contribute to Clinical Practice Research Datalink (CPRD) [2]. My study aimed to describe and characterise the extent to which vaping has been recorded in UK primary care electronic health records, in order to assess the current utility of population-level EHR vaping status data.

I aimed to conduct a descriptive analysis of the primary care electronic health records of adult patients in CPRD. CPRD contains primary care electronic health records of 25% of the UK population, and previous research has found that CPRD can be considered representative of the UK population in terms of geography, relative social deprivation, age, gender, ethnicity and smoking prevalence. I obtained all electronic health records of all patients (aged ≥18 years at index date) who received a medical code related to vaping at any point ('incidence') from 1 September 2006 to 31 March 2022, using the CPRD GOLD April 2023 build and the CPRD Aurum March 2023 build. Using descriptive statistics, I aimed to report the frequency of vaping codes; their distribution by patient age, gender, and ethnicity; trends over time in first-time incidence of vaping codes between 2006–2022; and transitions in patient smoking status. Also, by plotting the trend over time, I aimed to investigate if there was a change in the incidence of vaping codes in the UK following the EVALI outbreak in the US in 2019.

Key findings

Between September 2006 and March 2022, I found seven medical codes which were indicative of current vaping or former vaping, with the first instance on 13 October 2011 [2]:

- Current vaping: 'Electronic cigarette user' (Aurum), 'User of electronic cigarette' (GOLD), 'User of electronic cigarette' (Aurum), 'e-cigarette user' (Aurum), 'Vaper with nicotine' (Aurum).
- Former vaping: 'Ex user of electronic cigarette' (Aurum), 'Ex user of electronic cigarette' (GOLD).

Overall, 150,114 unique patients received vaping medical codes; of these 107,901 (71.9%) unique patients received only one code. There were 219,478 consultations where a patient received a current vaping code and 5,633 consultations where a patient received a former vaping code. There were 2,163 (1.4%) unique patients who had ever received both a current vaping and former vaping code – of these, 1,677 patients received a current vaping code before they received a former vaping code, and 486 vice versa. There were 152,277 observations of patient-level first-time incidence of vaping codes: 147,130 patients ever received a current vaping code, and 5,147 patients ever received a former vaping code.

The mean age of patients when they received their first vaping medical code was 50.2 years. The gender distribution in the sample was approximately balanced between male and female patients, and most (>80%) of the patients who received a vaping medical code were White.

The incidence of vaping medical codes increased from September 2013 onwards. Peak first-time incidence of current vaping codes was in November 2021: 17.8 per 100,000 patients contributing data to CPRD. Peak first-time incidence of former vaping codes was in October 2019: 0.9 per 100,0000 patients. Interrupted time series analyses indicated that the EVALI outbreak in the US (proxy time point: peak media coverage about EVALI in September 2019) was significantly associated with a reduction in new records of current vaping, manifested as a declining trend over a period of seven months (September 2019 to March 2020); additionally, there was an immediate increase in new records of former vaping, followed by a declining trend over the subsequent seven-month period. Interrupted time series analyses

also found that after the implementation of the first COVID-19 pandemic lockdown in the UK, there was an immediate decrease in monthly new current vaping records and new former vaping records (most likely due to the significant reduction in GP consultation frequency). After March 2020, there was a significant increase in the trend for new current vaping records, and a significant decrease in the trend for new former vaping records.

The majority of patients, when they received their first vaping code, were either smoking or had quit smoking in the past, with less than 2% being recorded as having never smoked. Among those currently vaping, 98.9% had documented previous smoking status, and 55.0% had records of their >12 months smoking status. Over a year after being recorded as vaping, 34.2% of people who were smoking prior to being recorded as vaping were still smoking, 23.7% quit smoking, 1.7% received a 'never smoked' status, and 40.4% lacked a recorded smoking status. Over a year after being recorded as vaping, 11.9% of people who had quit smoking prior to being recorded as vaping had returned to smoking, over a third (37.3%) were indicated to still be quit smoking, 2.7% received a 'never smoked' status, and there was no smoking status record for 48.0%. Over a year after being recorded as vaping, 7.7% of people who had never smoked prior to being recorded as vaping had initiated smoking, 18.8% were indicated to have quit smoking, 8.4% still had a 'never smoked' status, and there was no smoking status record for 65.1%.

Findings in context

My review of the literature in *Chapter 1* found that there was sparse literature on how health professionals are documenting NVP use in EHRs, and the extent to which vaping has been recorded over time in UK EHRs was not known. Similar to the few studies (all but one based in the USA) which have examined the documentation of NVP use in EHRs [208–212,214–216], my study also found that vaping documentation in primary care in the UK is low but has increased over time [2]. However, if the EHR was used to estimate national vaping prevalence, it would be significantly lower than national vaping prevalence estimates calculated using population surveys: 150,144 unique patients out of the estimated ~16 million patients registered in CPRD have ever received a vaping medical code, which is 0.9% as a proportion [2]. In comparison, the recent Action on Smoking and Health (ASH) survey

estimated that 9.1% of adults in Great Britain regularly used NVPs in 2023 [172]. Also, I found no medical codes which specifically indicate 'never vaping', or if the patient has had their vaping status screened/checked [2].

The changes associated with the EVALI outbreak could be attributable to increasing numbers of patients quitting vaping due to negative media coverage of potential health harms or GPs paying greater attention to asking and recording about (former) vaping. To my knowledge, no other study has examined the effect of EVALI on vaping documentation in EHRs.

Unlike US studies [212,213], where patients with vaping documentation were more likely to be younger, the mean age of patients in my study [2] when they first received a vaping code was 50 years; this may reflect the NVP prevalence in Great Britain (that 10% of 45–55-year-olds used NVPs in 2022 [263]), that I excluded patients <18 years, and that older people may be more likely to visit a health professional, and hence have more opportunities to receive a vaping code. The gender distribution in my sample [2] was similar to the 2021 England and Wales Census [264]; however, ASH Great Britain vaping surveys [263] found that a higher proportion of males use NVPs compared to females, similar to two US studies [212,213]. Similar to US studies [212,213], I found that most patients who received a vaping code were White (82.1%) [2], which reflects the UK population ethnicity proportions [265].

Regarding smoking status, my study [2] found that, of those who had concurrent smoking status documentation, a high proportion of those with a vaping medical code were indicated to be currently smoking (47%) or formerly smoked (51%) when they first received their current or former vaping medical code. This is relatively similar to previous studies in the US, where at the time of first-documented vaping product use, patients were: currently smoking (57% [212,214], 52.4% [215]) or formerly smoked (35% [212,214]).

In my study [2], I examined smoking status transitions: investigating changes in smoking status between the smoking status that the patient had recorded before they received their first-time vaping medical code, and the smoking status that the patient had recorded >12 months after they received their first-time vaping medical code. Almost all (98.9%) of patients had a recording for their 'previous smoking status' record, but only just over half (55.0%) had a recording for their '>12-month smoking status' record.

I was able to compare some of the findings of my smoking status transition analyses [2] to the findings of two US studies which performed similar analyses on their US EHR datasets. Interestingly, my findings are broadly similar to the US studies' findings. Where there are comparable figures, I report my findings (as reported above) followed by the finding(s) of the US studies in brackets. In my study, over a year after being recorded as vaping, 34.2% of people who were smoking prior to being recorded as vaping were still smoking; 23.7% (compared to: 20.8% [213] and 23.0% [214]) quit smoking; 1.7% received a 'never smoked' status; and there was no smoking status for 40.4%. I also found that 11.9% (compared to: 14.0% [214]) of people who had quit smoking before they received the vaping code had returned to smoking after 12 months. Lastly, I found that among those who had never smoked before they received their vaping code, 7.7% (compared to: 8.0% [214]) had initiated smoking after >12 months after receiving the current vaping code.

Objective 3 – Mental health and health professional interactions

Chapter 5 presented my cross-sectional analysis of Wave 2 (2018) ITC Four Country survey data from Australia, Canada, England, and the US [3]. My study aimed to investigate if there were any associations between adults ≥18 years who currently smoke or recently quit smoking and who self-report currently being treated for, or have been diagnosed (current diagnosis) with, depression and/or anxiety and their interactions with healthcare professionals about smoking cessation (visiting a HP in last 18 months; receiving advice to quit smoking from a HP) and NVPs (discussing NVPs with a HP; receiving a positive recommendation to use NVPs). I also aimed to investigate if the association between depression and/or anxiety and each outcome varied by country.

Key findings

Most (74.6%) respondents reported visiting a HP in the last 18 months and those who had depression alone, anxiety alone or both depression and anxiety were more likely to have visited their HP, compared to those with no depression/anxiety.

Among those who indicated that they had visited their HP in the last 18 months, less than half (47.9%) reported receiving advice to quit smoking; those who had depression alone had a higher likelihood of receiving advice, compared to those with no depression/anxiety; while the likelihood was equal for those with anxiety alone and those with both depression and anxiety (compared to those with no depression/anxiety).

Among those who reported visiting their HP, 6.1% reported that their HP discussed NVPs with them. Those who had both depression and anxiety had a higher likelihood of discussing NVPs with their HP, compared to those with no depression/anxiety.

Among those who visited a HP and their HPs discussed NVPs with them, one-third of respondents (33.5%) reported receiving a positive recommendation to use NVPs and the odds did not differ by mental health condition (but the sample size was small).

There may also be a significant interaction between mental health condition and country regarding visiting a HP and receiving advice to quit smoking.

Findings in context

My review of the literature in *Chapter 1* identified several studies which found that those who smoke and have mental health conditions are more likely to have visited their HP and more likely to have received smoking cessation advice. However, the one study [165] which was able to adjust for the number of consultations patients have (in a given time period) found that the proportion of consultations in which cessation advice was given was lower in patients with mental health conditions. This suggested that given equal opportunity to do so, HPs appear less likely to intervene with people who smoke with indicators of poor mental health compared to those without. Additionally, the proportion of patients who smoke and have mental health conditions who were offered cessation advice varied between studies – some found that over 80% were offered cessation advice [66,164], while some studies found that the proportion was as low as 33% [165]. My study [3] found that those with depression alone were more likely to receive cessation advice (57.0%), compared to those with no depression/anxiety (47.2%) – but could not explore whether this was due to a higher consultation rate. However, although those with anxiety either alone or with

depression were more likely to visit a HP, they were not more likely to receive cessation advice from their doctor (compared to those with no depression/anxiety), which suggests lower overall rates of intervention per visit among these groups.

Nevertheless, the overall proportion receiving advice to quit is not optimal. Indeed, my concerning finding (that overall, only 47.9% of those who visited a HP received cessation advice) is similar to the findings that recent studies have reported regarding the proportion of those who smoke and visited a HP: for example, in 2016 in Australia, Canada, England and the US, only 48% reported receiving advice to quit smoking from their HP in the last 12 months [232], and 2016–2019 Smoking Toolkit Study survey data from England found that only 47% reported receiving advice on smoking in the last 12 months [229].

Regarding NVPs, my review of the literature in *Chapter 1* generally found that up to a third of people who smoke (in the general population) who visited their HP in the last year reported talking about NVPs with their HP [232–234], and most studies found that less than 40% of those who talked to their HP about NVPs actually received a positive recommendation from their HP to use NVPs [229,232,233]. The highest proportion was in England, where in 2020, among respondents who discussed NVPs with their HPs, nearly 56% reported receiving a recommendation from their HP to use a NVP [233].

I only identified one past study [232] which examined if there were differences between people who smoke with and without mental health conditions and their interactions with HPs, regarding discussing NVPs and receiving recommendations to use NVPs. Gravely et al. [232] found no significant difference between those who visited a HP in the last year and discussed NVPs with their HP with depression (3.0%) and without depression (2.6%) (OR: 1.15, 95% CI: 0.82–1.62), and those with anxiety (2.1%) and without anxiety (3.0%) (OR: 0.69, 95% CI: 0.48–1.00). The proportion of people who visited a HP and reported discussing NVPs with their HP was higher in my study than in Gravely et al.'s [232] study which used 2016 data. In my study [3], using 2018 data, overall, 6.1% reported that their HP discussed NVPs with them; those with both depression and anxiety (8.0%) were more likely to report this, compared to those with no depression/anxiety (5.4%), but there was no significant difference for those with depression alone (7.4%) and those with anxiety alone (6.9%).

Lastly, for receiving recommendations from HPs to use NVPs, the only past study to investigate this (Gravely et al. [232]) did not find a significant difference between those who visited a HP in the last year and were recommended by their HP to use an NVP with depression (0.5%) and without depression (0.4%), OR: 1.40, 95% CI: 0.87–2.26. However, there was a difference between those who visited a HP in the last year and were recommended by their HP to use an NVP – those with anxiety (0.2%) were less likely than those without anxiety (0.5%) to receive a positive recommendation to use NVPs, OR: 0.48, 95% CI: 0.29–0.81 [232]. In my study [3], using 2018 data, I did not find an association between depression or anxiety and receiving a positive recommendation from a HP to use NVPs, overall approximately 2% (6.1% x 32.7% = 2.0%) of those who visited a HP reported receiving a positive recommendation to use NVPs – but the sample size was small, and perhaps between 2016 and 2018, HPs increased the rate of recommendation of NVPs to their patients who have anxiety, so that it was in line with their recommendation rate to patients who smoke without mental health conditions.

Objective 4 – Mental health and smoking cessation support option use

Chapter 6 presented a second cross-sectional analysis of Wave 2 (2018) ITC Four Country survey data from Australia, Canada, England, and the US. This study aimed to investigate if there were any associations between adults ≥18 years who had made at least one attempt to quit smoking in the past 18 months and who were currently smoking cigarettes (at least monthly) or not smoking cigarettes at the time of the 2018 survey and who self-report currently being treated for, or have been diagnosed (current diagnosis) with, depression and/or anxiety and what cessation support option they used in their last smoking quit attempt. It also aimed to investigate if the association between depression and/or anxiety and each outcome varied by country.

Key findings

Of those who had made a quit attempt in the last 18 months, 59.8% reported using any cessation aid (NVP, NRT, varenicline or bupropion, or behavioural support [cessation programmes or face-to-face advice from a health professional]) in their last smoking quit attempt – 40.5% reported using none of these. Despite making at least one quit attempt, at the time of the 2018 survey, 75.7% reported that they were currently smoking, suggesting that their quit attempt was unsuccessful.

In their last quit attempt, 31.0% reported using NVPs, 29.0% used NRT, 12.1% used varenicline or bupropion, and 11.0% used behavioural support.

Those with anxiety alone and those with both depression and anxiety were more likely to use any cessation aid, compared to those with no depression/anxiety.

Compared to those with no depression/anxiety, those with depression and/or anxiety were equally likely to use NVPs, or varenicline or bupropion, in their last quit attempt.

Compared to those with no depression/anxiety, only those with both depression and anxiety were more likely to use NRT, and all those with depression alone, anxiety alone, or with both depression and anxiety were more likely to use behavioural support.

There may also be a significant interaction between mental health condition and country regarding using behavioural support.

Findings in context

My review of the literature in *Chapter 1* identified only a few studies which have investigated the rate of cessation support use during quit attempts in this population. The studies found that people who smoke and have mental health conditions are either equally likely [66–68,162,163] or more likely [68,71,155,158,164] to use cessation support in quit attempts, compared to people who smoke and do not have mental health conditions. However, the full picture is not clear. Again, the one study [165] which was able to adjust for the number of consultations patients have (in a given time period) found that because the

proportion of consultations in which cessation medication was prescribed was lower in patients with mental health conditions, this suggests that given equal opportunity to do so, HPs appear less likely to intervene with people who smoke with poor mental health compared to those without. Additionally, some studies, such as Brose et al. [84], found mixed findings where those with mental health conditions were less likely to use over-the-counter NRT, but more likely to use prescription medication and/or behavioural support, and equally likely to use NVPs.

My findings add to this evidence base, using cessation aid utilisation survey data from 2018. My finding that using NVPs to quit smoking was similar among adults with and without depression and/or anxiety was similar to past research [68,84,163]. In contrast to my finding that the use of varenicline/bupropion was similar among adults with depression and/or anxiety and those without, some studies found that a higher proportion of people who smoke with mental health conditions use prescription cessation medications than those without [68,71,84,158,165]. For NRT, I found that those with both depression and anxiety were more likely to use NRT, compared to those with no depression/anxiety – the findings regarding NRT in previous studies have been mixed, potentially due to differentiating between over-the-counter NRT and NRT that is prescribed. Lastly, I found that those with depression and/or anxiety were more likely to use behavioural support, compared to those with no depression/anxiety – two previous studies found similar results [68,84], while one found that they were equally likely to use it [67].

Importantly, I found that a large proportion (40%) of respondents did not use any cessation aid in their last quit attempt and there was a high rate of unsuccessful quit attempts: 76%. These highlight the challenges of quitting smoking. These reflect the findings I identified in *Chapter 1*: in England, around 50% of quit attempts have been aided between 2007 and 2023 [26] and although more recent studies have found that the proportion of quit attempts which are aided has increased over time, at least 35% were still unaided in 2020 in Australia, Canada, England and the US [161].

Strengths and limitations of this research

Strengths

Diverse methodology

A strength of this thesis is that it used diverse methodologies to provide different perspectives regarding the provision and uptake of smoking cessation support options. My research combined a systematic review, an analysis of primary care electronic health record data, and secondary analyses of survey data from multiple countries.

The systematic review provided a comprehensive synthesis of existing evidence around the effectiveness of implementation strategies which have been implemented on a national/state-wide scale in the 'real world'. It highlighted important gaps in the way practitioner-level and patient-level outcomes are recorded, and the discrepancy between findings from RCTs and observational studies.

To my knowledge, the analysis of electronic health records was the first study which aimed specifically to describe and characterise the extent to which vaping has been recorded in UK primary care electronic health records over time. It highlighted important gaps in the completeness of data, and the examination of transitions in smoking status over time provided some interesting findings. The study allowed me to make some recommendations on how the utility may be improved, in order to enable the use of EHRs to investigate the long-term health effects and smoking cessation outcomes of vaping. Also, I found that CPRD vaping record data were sufficiently sensitive to be able to detect statistically significant effects of events (EVALI, COVID-19 lockdown) on vaping record incidence.

The analysis of survey data from Australia, Canada, England and the US, collected in 2018, allowed me to provide an update to the existing evidence regarding whether there are differences between people who smoke with and without mental health conditions in their receipt of smoking cessation advice and advice about NVPs, and in their use of cessation support options in smoking quit attempts.

Generalisability

The systematic review included studies which were conducted internationally – overall, the studies were from 9 countries.

The electronic health records included a substantial proportion of the UK (~25%), and the dataset (CPRD) is considered representative of the UK population in terms of geography, relative social deprivation, age, gender, ethnicity and smoking prevalence. The study covers 16 years (2006 to 2022), which includes the time point when NVPs started to appear in England (NVPs started to appear in England in 2006/7, increasing rapidly by 2010 [103]).

My analyses of survey data from Australia, Canada, England and the US were weighted using cross-sectional weightings derived by the ITC Project analysts. These aim to make the data representative of people who smoke, or vape at least weekly, in each country. Hence, the findings should be generalisable to these four countries.

Open Science approach

The systematic review had a pre-registered protocol and a comprehensive search strategy. The search terms from the complementary Cochrane review [239] were consulted, the search strategy was piloted, and I conducted backward and forward citation tracking of included studies.

I completed a thorough study protocol document for CPRD before I gained access to the data, but I did not pre-register a formal analysis plan because this study, which aimed to describe and characterise the extent to which vaping has been recorded in UK primary care electronic health records, was considered an 'exploratory analysis', which did not initially aim to test pre-determined hypotheses. To be transparent, I included information about the medical codes I used for my analyses, and my sensitivity analyses, in the supplementary materials (Appendices).

The analyses I planned to conduct using the Australia, Canada, England and US survey data were pre-registered on the Open Science Framework (OSF) – I detailed the minor

amendments I made to the analysis plan in *Chapter 2*. To test for associations between my independent variable and outcome variables, I used various logistic regression models, which controlled for various potential confounders. To be transparent, I presented all the results in the supplementary materials (Appendices).

Limitations

Generalisability

Although the systematic review had an international scope, most (36 out of 49) studies were set in the UK and USA, and only articles in English were included.

While CPRD data have been shown to be largely representative of the UK population, CPRD may be less representative for specific subgroups, such as people who vape. Vaping status and smoking status may not be accurately captured in EHRs; for example, some patients were recorded to be smoking or have quit smoking before receiving a vaping code, but they received a 'never smoked' record >12 months after. The interpretation of the smoking status transition analyses is limited regarding the smoking cessation rate following receiving a vaping code because a high proportion of patients (45%) did not have a >12 months follow-up smoking status recording.

Although my survey data analyses are representative of people who smoke, or vape at least weekly, in Australia, Canada, England and the US, they may not be generalisable to other countries. My findings may not be generalisable to more recent years. The survey data I analysed was collected in 2018, because not all survey waves included survey questions about mental health and the 2018 wave was the most recent ITC 4CV survey wave accessible to me which contained survey questions about depression and anxiety. The year 2018 was before the COVID-19 pandemic – during the peak years of the pandemic (2020 to 2022), many countries experienced disruption to primary care health service provision. Additionally, policies around NVPs have changed in these four countries: for example, the 2021 NICE clinical guideline in the UK recommended that NVPs should be accessible to adults who smoke, alongside other smoking cessation interventions [95]; since 2021,

Australia has prohibited the sale of nicotine-containing vaping products, unless on prescription from a licensed health professional [179,180]. Comparison between my findings and other studies may be hampered by methodological differences between studies. Firstly, the way that 'people who currently smoke' is defined varies between studies: some only include people who currently smoke daily [233], some include those who smoke daily and weekly [232], and some include those who smoke daily and non-daily (weekly or monthly) [71,163] – similar to my studies. Secondly, the way that mental health is defined varies between studies, it may be that findings which apply to those who have received a formal diagnosis of depression or anxiety from a health professional may not be directly applicable to those who have undiagnosed depression or anxiety, or have different mental health conditions (such as more severe conditions, such as schizophrenia).

Other limitations

In my CPRD study, I could not analyse free text comments that GPs can log for consultations because these are not currently available for research purposes. Also, I could not characterise consultation-level incidence of vaping medical codes because CPRD does not supply consultation-level denominator files.

The analyses I conducted using survey data from Australia, Canada, England and the US were cross-sectional. Hence, I could only identify associations between depression and/or anxiety and the outcome measures; I could not determine if the mental health conditions *caused* the outcomes. Also, although I was able to control for various potential confounders in my logistic regression models, there may still be unmeasured or residual confounding variables that have an effect on the outcome variables which have not been accounted for.

Survey studies are limited by the fact that the data are self-reported – respondents may provide inaccurate information, e.g., about their smoking status or mental health conditions they have been diagnosed with, which were not verified biochemically or with electronic health records. Responses may also be affected by recall bias. Survey responses can be affected by social desirability bias, where respondents give certain answers to questions due to social pressure, however, previous research has shown that self-reported smoking

abstinence in surveys is usually accurately reported [266,267]. The independent variable (current treatment/diagnosis of depression and/or anxiety) was assessed with a single-item measure, similar to past research [71,72,163,232]. It was not possible to know when a respondent was first diagnosed with depression and/or anxiety and the question used was not intended as a diagnostic tool. Other studies (e.g., [47]) have questioned the best approach to ask about mental health in surveys (a lengthier symptom assessment versus self-report items that ask for the current presence of the condition), so this may be a consideration for future research.

The sample size was small for some of the outcome measures, so further investigation of differences between the four countries was not possible.

For my study examining health professional interactions, it would have been interesting to be able to account for the frequency of consultations respondents had with their health professional in the last 12 months – to calculate the proportion of consultations where cessation advice and discussions about NVPs is provided – however, the survey I used did not capture this information.

Implications for clinical practice, policy and research

Here I consider the implications of my findings for clinical practice, policy and research.

Provision of cessation advice and support in primary care

Although recording patients' smoking status has been a practitioner-level outcome which has been improving over time, the rate of health professionals delivering smoking cessation advice and support is still suboptimal. For example, echoing the findings of previous literature [56,229,231,232], the third study in my PhD [3] found that in 2018 in Australia, Canada, England and the US, overall, only 47.9% of those who visited a HP in the last 18 months received smoking cessation advice. Previous research found that GPs believed that smoking cessation was too time-consuming and ineffective, and some felt that they lacked

confidence in their ability to discuss smoking and cessation options [268,269]. My systematic review [1] found some low-quality evidence regarding implementation strategies which involved training and educating stakeholders. Considering that the Cochrane review also found some evidence of efficacy for provider training [239], in clinical practice, I recommend that health professionals conduct continued professional development/training to ensure that they are up to date with the smoking cessation support options that are available, and the guidance regarding their use. This would hopefully reinforce the need for health professional intervention on smoking and ensure that any interactions are evidence-informed.

Next, I discuss some policy implications. Firstly, I recommend that cessation support options be made available to people who smoke free of charge. This is supported by both my systematic review [1] and the Cochrane review [239] finding some evidence that cost-free medications/insurance coverage which included cessation medications improved cessation rates. It is noteworthy to mention here that the UK government recently announced that they are going to implement a national 'swap to stop' programme, where people will be able to switch cigarettes for NVPs [24], whereby the NVPs will be provided free of charge to all people taking part in the scheme.

Secondly, I recommend that providing financial incentives for healthcare providers to deliver smoking cessation is considered by policy-makers. Overall, the evidence for the effectiveness of provider incentives on smoking cessation is uncertain. RCTs found no clear evidence for the effectiveness of provider incentives on cessation [239]. However, my systematic review [1] found evidence that national cardiovascular disease prevention programmes (e.g., NHS Health Checks) increased cessation rates, but the evidence that my review found for altering incentive structures (via schemes such as the QOF) was uncertain, because only two studies assessed cessation rates (one found an increase, and one found no effect) [1]. I recommend that if health professionals continue to be provided financial incentives to perform certain clinical behaviours, it is important to communicate clearly the intended clinical behaviour that is being incentivised [6,245]. For example, I agree with the recommendation made in the Khan review [18], that "offer of treatment" (i.e., to offer behavioural support, pharmacotherapy or NVPs) should be the QOF indicator, rather than

"offer of support", as the latter is ambiguous and could be interpreted to be synonymous with "offer of cessation advice".

Based on some of the barriers and facilitators I identified in my review, I recommend that future implementation strategies attempt to better align with the existing technologies and the routine systems in place. The recommendations of some other researchers in this area (Pipe et al. [269]) align with this: they recently recommended that electronic medical-record integration and adjunct follow-up support and counselling (in the form of digital and telephone follow-up scripts and materials) may help to facilitate the implementation of VBA in primary care. Although my review did not find studies which assessed adjunctive counselling, the Cochrane review [239] found that this was efficacious in the RCT setting.

Future research could explore interventions which involve implementation strategies which were not identified by my systematic review: from the 'Use of evaluative and iterative strategies', 'Provide interactive assistance', 'Adapt and tailor to context', 'Develop stakeholder inter-relationships', and 'Support clinicians' domains, or ones which encompass adjunctive counselling and tailored print materials, given these were shown to be efficacious in RCTs [239]. Also, given that past research found that the 3As/VBA is more effective than the 5As, researchers could explore if there are any ways to optimise 3As/VBA further [270] – i.e., instead of merely looking at what implementation strategies can increase delivery of the intervention (VBA), they could consider whether the intervention itself (VBA) could be optimised any further. In terms of research methodology, my systematic review found that many of the studies did not measure patient-level outcomes, hence I advise that in the future, hybrid effectiveness-implementation designs [2] are used, where studies assess the effectiveness of implementation strategies on both (practitioner-level) provider performance as well as (patient-level) smoking outcomes. Also, in studies and evaluations, I recommend that providing advice about or access to NVPs is considered as a practitioner-level outcome, given that NVPs are included as a smoking cessation support option in guidelines such as the NICE 2021 clinical guidelines [95] in the UK.

Recording vaping in electronic health records

My study found that vaping documentation in primary care UK EHRs is low [2]. In clinical practice, I strongly recommend that health professionals increase the completeness, accuracy and consistency of vaping status recording to enable longitudinal population-level data for vaping surveillance, which is linkable to other electronic health information. In clinical practice, vaping screening could be assigned to specific clinical team members or integrated into existing processes, such as alongside routine smoking screening during annual health checks [209].

In terms of policy, existing medical codes should be refined to enable health professionals to unambiguously record current vaping, former vaping or never vaping. This should be in the form of a practical, discrete EHR field [212,215,271–273] or a checkbox/dropdown menu [210], containing few options for health professionals to choose from: 'current vaping', 'former vaping', 'never vaping' [188,209], in comparison to the multitude of options I found in the UK and in the two quality improvement studies conducted in the USA [208,274].

Given that I found in my systematic review [1] that in the 'real world' setting, financially incentivising health professionals has increased smoking status recording, in the UK, I propose that a QOF indicator could be introduced for recording vaping status. This could be considered in line with the Khan review [18] recommendations regarding "system change … improving data and evidence", because "good quality data, monitoring and evaluation are essential to achieving positive outcomes for individuals who smoke".

Future research will be able to use EHRs to investigate the long-term health effects and smoking cessation outcomes of vaping. Findings from my study [2] have contributed information to aid sample size calculations of future observational study research investigating the long-term effects of vaping on smoking cessation or health. Although I found that vaping documentation in primary care UK EHRs is low, I found that nearly all patients with a first-time incidence of vaping recording had a previous smoking status recording, but only around half had a subsequent long-term (>12 months) smoking status recording [2]. If the quality of EHR documentation of vaping remains at the current level, this will pose a limitation to future studies aiming to assess the effect of vaping on smoking

status outcomes. However, with more complete recording of vaping status, future studies could employ matched control samples to investigate if there are any differences between longer-term smoking cessation outcomes or health outcomes between patients who vape and those who do not vape (evidence on which is currently lacking).

Smoking cessation advice and NVP discussions for those with mental health conditions

The finding [3] that people who smoke with mental health conditions had higher odds of visiting a HP, but the likelihood of receiving cessation advice was equal for those with anxiety alone and those with both depression and anxiety, compared to those with no depression/anxiety, suggests that there are missed opportunities for HPs to deliver cessation advice. As a recommendation for clinical practice, because overall, only 47.9% of those who visited a HP received cessation advice [3], I advise that HPs increase the rate at which they provide cessation advice and support to all their patients who smoke; however, this is particularly important for those who have mental health conditions to close the inequality gap of differential smoking rates.

Similarly, it is concerning that only 6.1% of respondents who visited their HP reported their HP discussing NVPs with them, and only 2% received a positive recommendation to use NVPs [3]. Given that evidence suggests that using NVPs is substantially less harmful than smoking combustible tobacco [104] and that NVPs have been shown to be an effective smoking cessation aid [102], I recommend that HPs provide accurate information about NVPs to their patients who smoke (with and without mental health conditions) when advising them about smoking cessation. Again, given that the likelihood of receiving a positive recommendation to use NVP did not differ by mental health condition [3], in order to close the disparity in smoking prevalence between those with and without mental health conditions, I recommend that HPs particularly focus on discussing evidence-based treatments, including NVPs, with people who smoke who have mental health conditions.

In terms of policy recommendations, my study [3] provided an update to the existing evidence base regarding if there are differences between people who smoke with and without mental health conditions in their receipt of smoking cessation advice and advice

about NVPs, but my study has not been able to explore reasons behind why HPs do not provide more cessation support to people with mental health conditions. The recent Khan review [18] recommended that smoking be made a key part of mental health treatment in primary care (as well as acute and community mental health services) and that people with mental health conditions are considered a specific target group for interventions due to their high smoking prevalence rates. The Khan review [18] recommended public-facing campaigns and more training for health professionals which spread awareness about research findings which demonstrate that quitting smoking improves long-term mental and physical health [33].

Regarding NVPs specifically, as well as recommending that health professionals receive more training and accurate information, I support the Khan review's [18] recommendation that a national mass media campaign is implemented to direct people who smoke to cessation support, and to educate them about the cessation support options which are available, including vaping. Additionally, I endorse the proposed recommendation that a vaping facts website be launched [18] (which is similar to the one that exists in New Zealand) – which will aim to combat harm misperceptions [173,174] regarding NVPs for both health professionals and people who smoke/members of the general public.

Future research could explore the reasons behind why HPs provide differing care regarding smoking cessation to people with mental health conditions, and investigate if recommendation of other forms of cessation support options (such as cessation medications) differ by mental health status. Also, the effect of other mental health conditions should be investigated, and it would be impactful to be able to explore country differences further, but an adequate sample of respondents with mental health conditions will be required.

I recommend that future research on health professional interactions with people who smoke includes specific outcome measures, such as, the rate of cessation advice and cessation support options provided per consultation. This, in addition to the overall proportion of patients who have received these behaviours, will enhance our understanding of the context of patients' interactions with health professionals. However, it is noteworthy to mention here that although electronic health records make it possible to capture

consultation frequency, cessation medication prescribing and health professionals providing cessation advice [165], the latter outcome measure may be less accurate because it is arguably less objectively operationalised/quantifiable. Regarding cessation advice provision, Szatkowski et al.'s [246] previous research – which compared patient recall of receiving cessation advice to the recording of cessation advice provision in electronic health records – found that more patients had cessation advice recorded in their medical records than recalled receiving advice. Szatkowski et al. [246] attributed the discrepancy to health professionals not adequately communicating cessation advice to patients, or to health professionals misrepresenting the provision of cessation advice due to financial incentives.

Smoking cessation support options for those with mental health conditions

In clinical practice, it is important for health professionals to systematically identify their patients who smoke and offer ongoing cessation support, to all patients regardless of mental health status. Across Australia, Canada, England and the US, my study found that approximately 40% of last smoking quit attempts in 2018 did not use any cessation aid, and 76% of those who made a quit attempt did not succeed at stopping smoking. This reflects previous research, which suggests that it can take 30 or more quit attempts for a person who smokes before they are able to successfully quit smoking long term [74]. Research has shown that the efficacy of cessation aids is moderate (see *Chapter 1*, sections *Smoking cessation support options – Efficacy in RCTs* and *Smoking cessation support options – Effectiveness in the 'real world'*), meaning that although using these aids in quit attempts does increase smoking cessation likelihood, even if cessation aid utilisation is 100%, the majority of people will not successfully quit smoking.

Smoking cessation may be more challenging for people with mental health conditions because they are more likely to smoke heavily and be highly dependent on cigarettes. Given that using cessation support in quit attempts can increase the likelihood of successful smoking cessation, my finding that people with anxiety, and both anxiety and depression were more likely to use support than those without either condition is promising. Additionally, my finding that those with anxiety and/or depression may be more likely to use certain cessation aids (NRT and behavioural support) is also promising. Overall, this may

help to narrow the disparity in smoking prevalence that exists between those with and without these mental health conditions. However, we also found evidence of missed opportunities for health professionals to provide cessation support for those with mental health conditions: people with depression alone were only equally likely to use any cessation support, compared to those with no depression/anxiety; and the use of NVPs and varenicline/bupropion in quit attempts was similar among adults with and without depression/anxiety. Given that varenicline [105] and bupropion [106] are currently unavailable, and that NVPs have shown to be more effective in achieving smoking cessation than NRT [102], NVPs are potentially the most effective smoking cessation support option currently available. In clinical practice, I recommend that health professionals provide accurate information about and access to NVPs to people who smoke, especially for individuals with mental health conditions.

In terms of policy, as I mentioned above under *Provision of cessation advice and support*, the UK government recently announced that they are going to implement a national 'swap to stop' programme, where people will be able to switch cigarettes for NVPs [24]. Given my finding that those with and without mental health conditions were equally likely to use NVPs in their last quit attempt, to address the disparity in smoking prevalence between those with and without mental health conditions, I recommend that people with mental health conditions be specifically targeted as a priority population for participation in the upcoming 'swap to stop' scheme. Additionally, one of the other recommendations that the Khan review [18] made is also important and relevant here: the implementation of public-facing campaigns and more training for health professionals which spread awareness about the benefits that smoking cessation can have on the mental and physical health of those who have mental health conditions [33].

Future research could explore what factors influence what cessation aid (if any) a person who smokes decides to use to support their quit attempt. Again, the effect of mental health conditions other than depression and anxiety should also be investigated, and it would be impactful to be able to explore country differences further, but an adequate sample of respondents with mental health conditions will be required. Lastly, as other tobacco harm reduction products on the market, such as heated tobacco products [275] and nicotine

pouches, may be becoming more popular, it is important to monitor their use and whether they are effective as a smoking cessation tool.

Conclusions

The four studies in this thesis represent a substantial contribution to the evidence base regarding how the provision and uptake of smoking cessation support options (including NVPs) in the UK could be improved, to aim to meet the national smoke-free target.

The rate at which health professionals deliver smoking cessation advice and support is suboptimal. My systematic review found evidence for the adoption and effectiveness of implementation strategies on a national/state-wide scale regarding smoking cessation treatment provision and patient smoking outcomes in 'real world' primary care settings. I found evidence towards the effectiveness of utilizing financial strategies, and some (limited) evidence towards training and educating stakeholders, on increasing smoking cessation rates.

Given that using NVPs has been demonstrated to be a smoking cessation tool, it is important to assess how NVP use is recorded in population-level EHRs because EHRs could be employed to investigate the long-term health effects and smoking cessation outcomes of vaping. My analysis of EHRs described the state of play of how NVP use has been recorded since 2006 in UK primary care. Vaping documentation is low but increasing over time. I proposed recommendations to improve the completeness, accuracy and consistency of vaping status recording, by refining medical codes for vaping, and introducing a QOF indicator for recording vaping status.

Smoking prevalence is significantly higher in those with mental health conditions compared to those without, and depression and anxiety are two of the most common mental health conditions among people who smoke. My analysis of survey data from Australia, Canada, England and the US, collected in 2018, provided an update to the existing evidence regarding whether there are differences between people who smoke with and without common mental health conditions (depression and/or anxiety) in their receipt of smoking

cessation advice and advice about NVPs, and in their use of cessation support options in smoking quit attempts. I found that there are missed opportunities for health professionals to provide cessation advice and recommendations about using NVPs to quit smoking, and to offer cessation support. In particular, to address the disparity in smoking prevalence between those with and without mental health conditions, health professionals need to increase the rate of smoking cessation support provision to those who smoke and have mental health conditions (above the rate of provision to people who smoke without mental health conditions). To achieve this, people with mental health conditions could be specifically targeted as a priority population in some of the policy recommendations recently made in the Khan review and the initiatives recently announced by the UK government, such as the national 'swap to stop' programme.

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Appendices

Appendix A. Supplementary material for Chapter 2

Appendix 1: Pre-registered analysis plan for ITC Study 1 (Chapter 5) and ITC Study 2 (Chapter 6)

Registered on 30 August 2022.

Also available at: https://osf.io/y72cj/

Discussions between health professionals and current smokers/recent quitters with self-reported depression and anxiety, and cessation support used in last or current quit attempt: Findings from the ITC Four Country Smoking and Vaping Survey (Australia, Canada, England, and US) (2018).

Bernadett Tildy, Ann McNeill, Shannon Gravely, Hua Yong, Katherine East, Leonie Brose

Study Information

Background:

Health practitioners can trigger and aid quit attempts, increasing cessation likelihood by up to three times (West & Papadakis, 2019). However, previous research has shown that the rate at which health professionals provide advice to quit smoking and offer cessation support or aids, is suboptimal, internationally (Bartsch et al., 2016; Gravely et al., 2019).

Smoking prevalence is considerably higher in disadvantaged groups, including people who have mental health conditions (Smokefree Action Coalition, 2020). For example, a third of people who smoke in England have mental health conditions (Brose et al., 2020), and more than a third of people with a mental health condition smoke (Smokefree Action Coalition, 2020). People with mental health conditions are more likely to smoke, more likely to be heavy smokers, and more likely to be highly dependent on cigarettes (Richardson et al., 2019). Depression and anxiety are two of the most common mental health conditions globally (Ferrari et al., 2022). Smoking cessation is associated with reduced depression and anxiety (Taylor et al, 2014), thus contact with healthcare professionals and guidance and encouragement for smoking cessation is critical for this population.

Few studies have explored whether the rate of health professionals providing advice to quit smoking, offering cessation support or aids, or recommending switching to a vaping product differs between smokers with and without a self-reported current diagnosis of depression, anxiety or both.

Research questions:

Using cross-sectional 2018 survey data in England, US, Canada and Australia, this study will investigate:

RQ1: Visiting a health professional: Do the odds of current smokers and recent quitters who have visited a health professional in the last 18 months differ between those with and without a current diagnosis of depression/anxiety?

RQ2: Advice to quit smoking from health professional: Among current smokers and recent quitters who visited a health professional, do the odds of receiving advice to quit smoking from health professionals in the last 18 months differ between those with and without a current diagnosis of depression/anxiety?

RQ3: Positive recommendation to use vaping products: Among current smokers and recent quitters who visited a health professional, do the odds of receiving a positive recommendation to use a vaping product from health professionals in the last 18 months differ between those with and without a current diagnosis of depression/anxiety?

RQ4: Use of vaping products or cessation aids in last or current quit attempt: Among current smokers and recent quitters who made a quit attempt in the last 18 months, do the odds of using the following products or aids in their last or current quit attempt differ between those with and without a current diagnosis of depression/anxiety?

a vaping product,

nicotine replacement therapy,

varenicline or bupropion,

behavioural cessation support.

For each of these research questions, this study will also investigate whether any differences exist between countries.

Design Plan

Registration prior to analysis of the data: As of the date of submission, the data exist and we have accessed it, though no analysis has been conducted related to the research plan.

Study type: Observational cross-sectional study.

Survey: This is an analysis of existing data from an ongoing international survey. The data have not been analysed to test the research questions posed in this pre-registration. For this study, data from wave 2 (2018) will be analysed from the International Tobacco Control (ITC) Four-Country Smoking and Vaping Surveys in Australia, Canada, England and the United States. Details on survey methods for each country are available via the ITC website (https://itcproject.org/methods). Briefly, Wave 1 (July–November 2016) participants (these data were not analysed for this study) included adult (aged 18+) smokers either recontacted from the original ITC 4C cohort or newly recruited ('replenished') from online panels using either probability-based sampling frames, non-probability opt-in panels or a combination of these. Participants from Wave 2 (March–June 2018) included those who were re-contacted

from the previous wave and new participants who were recruited to address attrition and maintain sample size over time.

Wave 2 (2018) survey questions:
https://itcproject.s3.amazonaws.com/uploads/documents/ITC_4CV2_Recontact-Replenishment_web_Eng_13Apr2020.pdf

Further information about derived variables:
https://itcproject.s3.amazonaws.com/uploads/documents/Derived_Varia.pdf

Sample selection:

Sample size: The sample sizes in the technical reports for Wave 2 (2018) are n=4848 (England), n=3783 (Canada), n=2828 (US), n=1515 (Australia), total n= 12994. https://itcproject.org/methods/technical-reports/itc-four-country-smoking-and-vaping-survey-wave-2-4cv2-technical-report/ However, as we have not analysed the data, applying exclusions to the sample, the final sample size for this study is not known.

The analyses will include participants in the 2018 survey who answered questions regarding their current frequency of cigarette smoking, number of lifetime cigarettes smoked, smoking status and number of quit attempts they made in the last 24 months/since the last survey; and based on their answers, the respondents will be classified as 'current daily smoker', 'current weekly smoker', 'current monthly smoker', and 'recent quitter' (to VarName FR309v).

VarName: FR309v

Derived variable for all respondents – cigarette smoking status at current wave:

10 Current Daily Smoker (FR225v=1)

20 Current Weekly Smoker (FR225v=2)

31 Current Monthly Smoker (FR225v=3 AND BI345v=1)

40 Recent Quitter: Identifies as quit in last 24M AND has smoked 100+ lifetime cigs [(FR225v=5 AND BI345v=1 AND QA439=1-8) or (QA342=1-2 and QA439=1-8)]

Variables

Independent variable:

Mental health status: self-reported depression and/or self-reported anxiety:

These measures are self-reported, not verified as a clinical diagnosis.

"Are you currently being treated for, or have you been diagnosed (current diagnosis) with, any of the following…?

VarName: HE522: Depression.

1 Selected,

2 Not selected,

8 Refused,

9 Don't know.

VarName: HE524: Anxiety.

1 Selected,

2 Not selected,

8 Refused,

9 Don't know.

Analytic coding:

Variable: Mental health condition with mutually exclusive categories:

No mental health condition: answered 'not selected' to depression and answered 'not selected' to anxiety.

Depression only: answered 'selected' to depression.

Anxiety only: answered 'selected' to anxiety.

Both depression and anxiety: answered 'selected' to depression and answered 'selected' to anxiety.

Those respondents who refused to answer these survey questions, or answered 'don't know' to these survey questions will be excluded.

Outcome variables:

1. Visiting a health professional:

VarName: CH801

C (recontacted sample of participants): Have you visited a doctor or other health professional since [Last Survey Date]?

P (replenished sample of participants): In the last 18 months, since [18M Anchor], have you visited a doctor or other health professional?

1 Yes,

2 No,

8 Refused,

9 Don’t know.

Analytic coding:

Outcome: Visiting a health professional:

Yes: answered ‘yes’ to CH801.

No: answered ‘no’ to CH801.

Those respondents who refused to answer this survey question, or answered ‘don’t know’, will be excluded.

2. Advice to quit smoking from health professional:

For those respondents who answered ‘yes’ to visiting a health professional (CH801)*:

VarName: CH811

C: On any visit to a doctor or health professional since [Last Survey Date], did you receive any advice to quit smoking?

P: On any visit to a doctor or health professional in the last 18 months, did you receive any advice to quit smoking?

1 Yes,

2 No,

8 Refused,

9 Don’t know.

Analytic coding:

Outcome: Advice to quit smoking from health professional:

Yes: answered ‘yes’ to CH811.

No: answered ‘no’ to CH811.

*Only those eligible to answer this survey question will be included; those respondents who refused to answer this survey question, or answered ‘don’t know’, will be excluded.

3. Positive recommendation to use vaping products:

For those respondents who answered ‘yes’ to visiting a health professional (CH801) and ‘yes’ to EK210 (C: On any visit to a doctor or health professional since [Last Survey Date], did the doctor or health professional talk to you about e-cigarettes? P: On any visit to a doctor or health professional in the last 18 months, did the doctor or health professional talk to you about e-cigarettes?)*:

VarName: EK220

What advice did the doctor or health professional give you about e-cigarettes?

1 They specifically recommended that I use e-cigarettes,

2 They advised me against using e-cigarettes,

3 They didn't express a view for or against e-cigarettes,

8 Refused,

9 Don't know.

Analytic coding:

Outcome: Positive recommendation to use vaping products:

Yes: answered ‘1 they specifically recommended that I use e-cigarettes’ to EK220.

No: answered ‘2 they advised me against using e-cigarettes’, ‘3 they didn't express a view for or against e-cigarettes’ to EK220.

*Only those eligible to answer this survey question will be included; those respondents who refused to answer this survey question, or answered ‘don’t know’, will be excluded.

4. Use of vaping products or cessation aids in last or current quit attempt (unrelated to health professional discussions)

For those respondents who had made a quit attempt in the last 18 months*:

Four independent binary outcome variables will be derived: use of a vaping product; use of nicotine replacement therapy; use of varenicline or bupropion; use of behavioural cessation support.

Respondents had the option to answer ‘selected’ to more than one individual option if they used more than one cessation aid. Those respondents who answered ‘selected’ to more than one of the individual options will be included in all of the corresponding regression models (for the different outcome variables) independently.

(E.g.: a respondent who answered ‘selected’ to vaping product (EQ101) and answered ‘selected’ to varenicline (SM942) will be included in the ‘Yes’ category of the (a) Use of

vaping product in last or current quit attempt and the (c) Use of varenicline or bupropion in last or current quit attempt outcomes.)

Outcome: (a) Use of vaping product in last or current quit attempt

For those respondents who had made a quit attempt in the last 18 months and were classified as current e-cigarette status (EC309v): 'current daily vaper', 'current weekly vaper', 'current monthly vaper', 'current less-than-monthly vaper', 'ever quitter: past vaper at least weekly', 'past trier: vaped more than once/occasionally', 'past trier: vaped only once':

VarName: EQ101

Did you use an e-cigarette/ vaping device on your [LAST (FR309v=1-3)/ CURRENT (QA439=1-7)] quit attempt?

1 Yes,

2 No,

8 Refused,

9 Don't know.

Analytic coding:

Outcome: (a) Use of vaping product in last or current quit attempt:

Yes: answered 'yes' to EQ101

No: answered 'no' to EQ101.

*Only those eligible to answer this survey question will be included; those respondents who refused to answer this survey question, or answered 'don't know', will be excluded.

Outcome: (b) Use of nicotine replacement therapy in last or current quit attempt

For those respondents who had made a quit attempt in the last 18 months:

Which of the following forms of help did you receive or use as part of your [LAST (FR309v=1-3)/ CURRENT (QA439=1-7)] quit attempt [apart from the use of e-cigarettes, which you have already told us about (EQ101=1)]?

VarName: SM920: Any type of nicotine replacement product, such as patches, gum, mouth spray, etc.

1 Selected,

2 Not selected,

8 Refused,

9 Don't know

Analytic coding:

Outcome: (b) Use of nicotine replacement therapy in last or current quit attempt:

Yes: answered 'selected' to SM920

Other: answered 'not selected' to SM920.

*Only those eligible to answer this survey question will be included; those respondents who refused to answer this survey question, or answered 'don't know', will be excluded.

Outcome: (c) Use of varenicline or bupropion in last or current quit attempt

For those respondents who had made a quit attempt in the last 18 months:

Which of the following forms of help did you receive or use as part of your [LAST (FR309v=1-3)/ CURRENT (QA439=1-7)] quit attempt [apart from the use of e-cigarettes, which you have already told us about (EQ101=1)]?

VarName: SM942: Varenicline or Chantix or Champix.

1 Selected,

2 Not selected,

8 Refused,

9 Don't know

VarName: SM940: Bupropion or Zyban or Wellbutrin.

1 Selected,

2 Not selected,

8 Refused,

9 Don’t know

Analytic coding:

Outcome: (c) Use of varenicline or bupropion in last or current quit attempt:

Yes: answered ‘selected’ to SM942 or answered ‘selected’ to SM940, or answered ‘selected’ to both SM942 and SM940.

No: answered ‘not selected’ to SM942 and answered ‘not selected’ to SM940.

*Only those eligible to answer this survey question will be included; those respondents who refused to answer this survey question, or answered ‘don’t know’, will be excluded.

Outcome: (d) Use of behavioural cessation support in last or current quit attempt

For those respondents who had made a quit attempt in the last 18 months:

Which of the following forms of help did you receive or use as part of your [LAST (FR309v=1-3)/ CURRENT (QA439=1-7)] quit attempt [apart from the use of e-cigarettes, which you have already told us about (EQ101=1)]?

VarName: CH969: *‘Cessation service’*

CA, US: Clinic, individual or group counselling, stop-smoking course, or behaviour therapy.

UK: Local stop smoking service (e.g. clinics or specialists)

AU: Face-to-face specialised stop smoking program.

1 Selected,

2 Not selected,

8 Refused,

9 Don’t know

VarName: CH966: Face-to-face advice from a doctor or other health care professional (dentist, pharmacist, etc.).

1 Selected,

2 Not selected,

8 Refused,

9 Don’t know

Analytic coding:

Outcome: (d) Use of behavioural cessation support in last or current quit attempt:

Yes: answered ‘selected’ to CH969 or answered ‘selected’ to CH966 or answered ‘selected’ to both CH969 and CH966.

No: answered ‘not selected’ to CH969 and answered ‘not selected’ to CH966.

*Only those eligible to answer this survey question will be included; those respondents who refused to answer this survey question, or answered ‘don’t know’, will be excluded.

Covariates

sex [VarName: gender]

Derived variable by ITC Project analytics team.

1 Male

2 Female

‘Refused’ or ‘don’t know’ responses will be excluded from analyses.

country of residence [VarName: country]

Australia

Canada

England

United States

‘Refused’ or ‘don’t know’ responses will be excluded from analyses.

age [VarName: AgeGroup]

Derived variable – current age (categories) for all respondents.

1 18-24

2 25-39

3 40-54

4 55 and up

'Refused' or 'don't know' responses will be excluded from analyses.

education [VarName: DE312v]

Derived variable – highest level of education (all countries)

1 Low

2 Moderate

3 High

Australia:

Low = Completed high school or less

Moderate = Technical school/some university (no degree)

High = Completed university or post-graduate

Canada and United States:

Low = Completed high school or less

Moderate = Community college/trade/technical school/some university (no degree)

High = Completed university or post-graduate

England:

Low = Secondary/vocational 3 or less

Moderate = College/university (no degree)

High = Completed university or post-graduate

‘Refused’ or ‘don’t know’ responses will be excluded from analyses.

ethnicity [VarName: ethnic]

Derived variable

1 Majority group

2 Minority group

Australia:

1 Majority group = Speaks only English at home

2 Minority group = English & one of: Italian, Greek, Cantonese, Mandarin, Arabic, Vietnamese, Other

Canada:

1 Majority group = White

2 Minority group = Chinese, South Asian, Black, Filipino, Latin American, South East Asian, Arab, West Asian, Korean, Aboriginal, Other.

England:

1 Majority group = White

2 Minority group = Asian/Asian-British, Black/Black-British, Chinese, Mixed, Other

United States:

1 Majority group = White

2 Minority group = Black, Hispanic, Asian, Native, Other

‘Refused’ or ‘don’t know’ responses will be excluded from analyses.

income [VarName: DE212v]

Derived variable

Low

Moderate

High

No answer

Australia, Canada and United States:

Low = Less than $30,000

Moderate = $30,000 - 59,999

High = $60,000 or greater

No answer

England:

Low = Less than £15,000

Moderate = £15,001 - 30,000

High = £30,001 or greater

No answer

The ‘No answer’ category in the derived income variable consisted of ‘refused’ or ‘don’t know’ responses. Previous research suggests that the frequency of these responses may be high, so these respondents will be included in analyses in a separate category.

smoking status [VarName: FR309v]

Derived variable for all respondents: cigarette smoking status at current wave.

10 Current Daily Smoker (FR225v=1)

20 Current Weekly Smoker (FR225v=2)

31 Current Monthly Smoker (FR225v=3 AND BI345v=1)

40 Recent Quitter: Identifies as quit in last 24M AND has smoked 100+ lifetime cigs [(FR225v=5 AND BI345v=1 AND QA439=1-8) or (QA342=1-2 and QA439=1-8)]

Analytic coding:

Outcome: smoking status (collapsed):

Daily: answer '10' to FR309v.

Non-daily: answer '20' and '31' to FR309v.

Former: answer '40' to FR309v.

'Refused' or 'don't know' responses will be excluded from analyses.

problematic alcohol use [VarName: DI712, DI703, DI706]

A derived variable will be created, based on the Alcohol use disorders identification test consumption (AUDIT C).

DI712: How often do you have a drink containing alcohol?

0 Never → 0 points

1 Once a month or less → 1 point

2 2-4 times a month → 2 points

3 2-3 times a week → 3 points

4 4 or more times a week → 4 points

8 Refused

9 Don't know

For those respondents who answered 1-4 to DI712:

DI703: On days that you drink, how many standard drinks of alcohol do you have on a typical day?

0 1-2 → 0 points

1 3-4 → 1 point

2 5-6 → 2 points

3 7-9 → 3 points

4 10 or more → 4 points

8 Refused

9 Don't know

For those respondents who answered 1-4 to DI712:

DI706: How often do you have 6 or more drinks on one occasion?

0 Never → 0 points

1 Less than monthly → 1 point

2 Monthly → 2 points

3 Weekly → 3 points

4 Daily or almost daily → 4 points

8 Refused

9 Don't know

Analytic coding:

Each question (DI712, DI703, DI706) had five response options (plus 'refused' and 'don't know') which were valued from 0 to 4 points. A sum of the points gave a score out of 12. Respondents who scored 5 or more were considered to have problematic alcohol use.

Those respondents who answered 'Never' to DI712 were not asked DI703 and DI706. These respondents will be derived a total score of 0 and will be in the 'No' category for the problematic alcohol use variable.

Outcome: Problematic alcohol use:

Yes: respondents who scored 5 or more.

No: respondents who score 4 or less.

Those respondents who refused to answer either of the three questions, or answered 'don't know', will not be derived a total score. Previous research suggests that the frequency of this may be high, so these respondents will be included in analyses in a separate category.

Analysis plan

Description of sample:

Number and weighted proportion of 2018 survey respondents included in the analysis sample, who are classified as 'current daily smoker', 'current weekly smoker', 'current monthly smoker', and 'recent quitter'.

Among these respondents, the number and weighted proportions of respondents who:

had neither self-reported depression nor anxiety,

had self-reported depression only,

had self-reported anxiety only,

had both self-reported depression and anxiety.

Number and weighted proportion of respondents stratified by country (Australia, Canada, England, US).

Number and weighted proportion of respondents for each of the outcome variables of the research questions, broken down by sociodemographics and mental health status.

Analyses:

To assess the association between mental health status and the outcomes, the regression analyses will use weighted data.

RQ1: Visiting a health professional:

RQ1: Do the odds of current smokers and recent quitters visiting a health professional differ between those with and without depression/anxiety?

Independent variable: mental health status

Outcome variable: Visiting a health professional

If there are at least 10 cases with the least frequent outcome for each predictor variable, unadjusted and adjusted regression models will be run:

Unadjusted (bivariate) logistic regression: outcome regressed onto mental health status.

Adjusted (multivariate) logistic regression: outcome regressed onto mental health status and the sociodemographic covariates: country of residence, sex, age, education, ethnicity, income.

Adjusted (multivariate) logistic regression: outcome regressed onto mental health status and the sociodemographic covariates: country of residence, sex, age, education, ethnicity,

income, and other proposed covariates: smoking status, problematic alcohol use.

RQ2: Advice to quit smoking from health professional:

RQ2: Among current smokers and recent quitters who visited a health professional, do the odds of receiving advice to quit smoking from health professionals differ between those with and without depression/anxiety?

Independent variable: mental health status

Outcome variable: Advice to quit smoking from health professional

Of those eligible for this question, if there are at least 10 cases with the least frequent outcome for each predictor variable, unadjusted and adjusted regression models will be run:

Unadjusted logistic regression: outcome regressed onto mental health status.

Adjusted logistic regression: outcome regressed onto mental health status and the sociodemographic covariates: country of residence, sex, age, education, ethnicity, income.

Adjusted logistic regression: outcome regressed onto mental health status and the sociodemographic covariates: country of residence, sex, age, education, ethnicity, income, and other proposed covariates: smoking status, problematic alcohol use.

RQ3: Positive recommendation to use vaping products:

RQ3: Among current smokers and recent quitters who visited a health professional, do the odds of receiving a positive recommendation to use a vaping product from health professionals differ between those with and without depression/anxiety?

Independent variable: mental health status

Outcome variable: Positive recommendation to use vaping products

Of those eligible for this question, if there are at least 10 cases with the least frequent outcome for each predictor variable, unadjusted and adjusted regression models will be run:

Unadjusted logistic regression: outcome regressed onto mental health status.

Adjusted logistic regression: outcome regressed onto mental health status and the sociodemographic covariates: country of residence, sex, age, education, ethnicity, income.

Adjusted logistic regression: outcome regressed onto mental health status and the sociodemographic covariates: country of residence, sex, age, education, ethnicity, income, and other proposed covariates: smoking status, problematic alcohol use.

RQ4: Use of vaping products or cessation aids in last or current quit attempt:

RQ4: Among current smokers and recent quitters who made a quit attempt in the last 18 months, do the odds of using the following products or aids in their last or current quit attempt differ between those with and without a current diagnosis of depression/anxiety?

a vaping product,

nicotine replacement therapy,

varenicline or bupropion,

behavioural cessation support.

Independent variable: mental health status

Outcome variable: four independent binary outcome variables that will be derived.

Use of vaping product in last or current quit attempt

Use of nicotine replacement therapy in last or current quit attempt

Use of varenicline or bupropion in last or current quit attempt

Use of behavioural cessation support in last or current quit attempt

Respondents had the option to answer 'selected' to more than one individual option. Those respondents who answered 'selected' to more than one of the individual options will be included in all of the corresponding regression models (for the different outcome variables) independently.

(E.g.: a respondent who answered 'selected' to vaping product (EQ101) and answered 'selected' to varenicline (SM942) will be included in the 'Yes' category of the (a) Use of vaping product in last or current quit attempt and the (c) Use of varenicline or bupropion in last or current quit attempt outcomes.)

Of those eligible for this question, if there are at least 10 cases with the least frequent outcome for each predictor variable, unadjusted and adjusted regression models will be run:

Unadjusted logistic regression: outcome regressed onto mental health status.

Adjusted logistic regression: outcome regressed onto mental health status and the sociodemographic covariates: country of residence, sex, age, education, ethnicity, income.

Adjusted logistic regression: outcome regressed onto mental health status and the sociodemographic covariates: country of residence, sex, age, education, ethnicity, income, and other proposed covariates: smoking status, problematic alcohol use.

Inference criteria

95% confidence intervals and exact p-values will be reported.

Data exclusion and Missing data

A respondent will be excluded from the sample population if they have a 'refused' or 'don't know' response to a variable included in the above analyses, except for the covariate 'income' and 'problematic alcohol use' (where we anticipate that the frequency of 'No answer' responses will be high, so these respondents will be included in analyses in a separate category).

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Appendix B. Supplementary material for Chapter 3

Appendix 1. 5As and 3As/Very Brief Advice

A table outlining and comparing the steps involved in the 5As and 3As/Very Brief Advice process for delivering 'brief advice' about smoking cessation to service users.

5As	**Very Brief Advice (VBA)**
Ask about tobacco use	Ask about current/past smoking behaviour
Advise to quit	Advise about the consequences of smoking and smoking cessation
Assess willingness to make a quit attempt	
Assist in quit attempt (provide general assistance, prescribe cessation medications, set quit date, provide counselling, provide self-help materials)	Act: Provide options for later/additional support, and advise on stop smoking medications.
Arrange follow-up appointment to address smoking	

Appendix 2: Implementation strategies

The implementation strategies in the included studies were coded using the definitions based on the Expert Recommendations for Implementing Change (ERIC) programme (1) which defined 73 individual implementation strategies, which were subsequently grouped into 9 domains (2).

The 9 domains (and number of individual implementation strategies identified per domain) are:

- Domain 1. Use of evaluative and iterative strategies (10)
- Domain 2. Provide interactive assistance (4)
- Domain 3. Adapt and tailor to context (4)
- Domain 4. Develop stakeholder inter-relationships (17)
- Domain 5. Train and educate stakeholders (11)
- Domain 6. Support clinicians (5)
- Domain 7. Engage consumers (5)
- Domain 8. Utilize financial strategies (9)
- Domain 9. Change infrastructure (8)

The 73 distinct implementation strategies and definitions (1) grouped into 9 domains (2):

Implementation strategy	**Definition**
Domain 1: Use of evaluative and iterative strategies	
1. Assess for readiness and identify barriers and facilitators	Assess various aspects of an organization to determine its degree of readiness to implement, barriers that may impede implementation, and strengths that can be used in the implementation effort
2. Audit and provide feedback	Collect and summarize clinical performance data over a specified time period and give it to clinicians and administrators to monitor, evaluate, and modify provider behavior
3. Purposefully reexamine the implementation	Monitor progress and adjust clinical practices and implementation strategies to continuously improve the quality of care
4. Develop and implement tools for quality monitoring	Develop, test, and introduce into quality-monitoring systems the right input—the appropriate language, protocols, algorithms, standards, and measures (of processes, patient/consumer outcomes, and implementation outcomes) that are often specific to the innovation being implemented

5. Develop and organize quality monitoring systems	Develop and organize systems and procedures that monitor clinical processes and/or outcomes for the purpose of quality assurance and improvement
6. Develop a formal implementation blueprint	Develop a formal implementation blueprint that includes all goals and strategies. The blueprint should include the following: 1) aim/purpose of the implementation; 2) scope of the change (e.g., what organizational units are affected); 3) timeframe and milestones; and 4) appropriate performance/progress measures. Use and update this plan to guide the implementation effort over time
7. Conduct local need assessment	Collect and analyze data related to the need for the innovation
8. Stage implementation scale up	Phase implementation efforts by starting with small pilots or demonstration projects and gradually move to a system wide rollout
9. Obtain and use patients/consumers and family feedback	Develop strategies to increase patient/consumer and family feedback on the implementation effort
10. Conduct cyclical small tests of change	Implement changes in a cyclical fashion using small tests of change before taking changes system-wide. Tests of change benefit from systematic measurement, and results of the tests of change are studied for insights on how to do better. This process continues serially over time, and refinement is added with each cycle
Domain 2: Provide interactive assistance	
11. Facilitation	A process of interactive problem solving and support that occurs in a context of a recognized need for improvement and a supportive interpersonal relationship
12. Provide local technical assistance	Develop and use a system to deliver technical assistance focused on implementation issues using local personnel
13. Provide clinical supervision	Provide clinicians with ongoing supervision focusing on the innovation. Provide training for clinical supervisors who will supervise clinicians who provide the innovation
14. Centralize technical assistance	Develop and use a centralized system to deliver technical assistance focused on implementation issues
Domain 3: Adapt and tailor to context	

15. Tailor strategies	Tailor the implementation strategies to address barriers and leverage facilitators that were identified through earlier data collection
16. Promote adaptability	Identify the ways a clinical innovation can be tailored to meet local needs and clarify which elements of the innovation must be maintained to preserve fidelity
17. Use data experts	Involve, hire, and/or consult experts to inform management on the use of data generated by implementation efforts
18. Use data warehousing techniques	Integrate clinical records across facilities and organizations to facilitate implementation across systems
Domain 4: Develop stakeholder interrelationships	
19. Identify and prepare champions	Identify and prepare individuals who dedicate themselves to supporting, marketing, and driving through an implementation, overcoming indifference or resistance that the intervention may provoke in an organization
20. Organize clinician implementation team meetings	Develop and support teams of clinicians who are implementing the innovation and give them protected time to reflect on the implementation effort, share lessons learned, and support one another's learning
21. Recruit, designate, and train for leadership	Recruit, designate, and train leaders for the change effort
22. Inform local opinion leaders	Inform providers identified by colleagues as opinion leaders or "educationally influential" about the clinical innovation in the hopes that they will influence colleagues to adopt it
23. Build a coalition	Recruit and cultivate relationships with partners in the implementation effort
24. Obtain formal commitments	Obtain written commitments from key partners that state what they will do to implement the innovation
25. Identify early adopters	Identify early adopters at the local site to learn from their experiences with the practice innovation
26. Conduct local consensus discussions	Include local providers and other stakeholders in discussions that address whether the chosen problem is important and whether the clinical innovation to address it is appropriate
27. Capture and share local knowledge	Capture local knowledge from implementation sites on how implementers and clinicians made something work in their setting and then share it with other sites

28. Use advisory boards and workgroups	Create and engage a formal group of multiple kinds of stakeholders to provide input and advice on implementation efforts and to elicit recommendations for improvements
29. Use an implementation advisor	Seek guidance from experts in implementation
30. Model and simulate change	Model or simulate the change that will be implemented prior to implementation
31. Visit other sites	Visit sites where a similar implementation effort has been considered successful
32. Involve executive boards	Involve existing governing structures (e.g., boards of directors, medical staff boards of governance) in the implementation effort, including the review of data on implementation processes
33. Develop an implementation glossary	Develop and distribute a list of terms describing the innovation, implementation, and stakeholders in the organizational change
34. Develop academic partnerships	Partner with a university or academic unit for the purposes of shared training and bringing research skills to an implementation project
35. Promote network weaving	Identify and build on existing high-quality working relationships and networks within and outside the organization, organizational units, teams, etc. to promote information sharing, collaborative problem-solving, and a shared vision/goal related to implementing the innovation
Domain 5: Train and educate stakeholders	
36. Conduct ongoing training	Plan for and conduct training in the clinical innovation in an ongoing way
37. Provide ongoing consultation	Provide ongoing consultation with one or more experts in the strategies used to support implementing the innovation
38. Develop educational materials	Develop and format manuals, toolkits, and other supporting materials in ways that make it easier for stakeholders to learn about the innovation and for clinicians to learn how to deliver the clinical innovation
39. Make training dynamic	Vary the information delivery methods to cater to different learning styles and work contexts, and shape the training in the innovation to be interactive

40. Distribute educational materials	Distribute educational materials (including guidelines, manuals, and toolkits) in person, by mail, and/or electronically
41. Use train-the-trainer strategies	Train designated clinicians or organizations to train others in the clinical innovation
42. Conduct educational meetings	Hold meetings targeted toward different stakeholder groups (e.g., providers, administrators, other organizational stakeholders, and community, patient/consumer, and family stakeholders) to teach them about the clinical innovation
43. Conduct educational outreach visits	Have a trained person meet with providers in their practice settings to educate providers about the clinical innovation with the intent of changing the provider's practice
44. Create a learning collaborative	Facilitate the formation of groups of providers or provider organizations and foster a collaborative learning environment to improve implementation of the clinical innovation
45. Shadow other experts	Provide ways for key individuals to directly observe experienced people engage with or use the targeted practice change/innovation
46. Work with educational institutions	Encourage educational institutions to train clinicians in the innovation
Domain 6: Support clinicians	
47. Facilitate relay of clinical data to providers	Provide as close to real-time data as possible about key measures of process/outcomes using integrated modes/channels of communication in a way that promotes use of the targeted innovation
48. Remind clinicians	Develop reminder systems designed to help clinicians to recall information and/or prompt them to use the clinical innovation
49. Develop resource sharing agreements	Develop partnerships with organizations that have resources needed to implement the innovation
50. Revise professional roles	Shift and revise roles among professionals who provide care, and redesign job characteristics
51. Create new clinical teams	Change who serves on the clinical team, adding different disciplines and different skills to make it more likely that the clinical innovation is delivered (or is more successfully delivered)
Domain 7: Engage consumers	

52. Involve patients/consumers and family members	Engage or include patients/consumers and families in the implementation effort
53. Intervene with patients/consumers to enhance uptake and adherence	Develop strategies with patients to encourage and problem solve around adherence
54. Prepare patients/consumers to be active participants	Prepare patients/consumers to be active in their care, to ask questions, and specifically to inquire about care guidelines, the evidence behind clinical decisions, or about available evidence-supported treatments
55. Increase demand	Attempt to influence the market for the clinical innovation to increase competition intensity and to increase the maturity of the market for the clinical innovation
56. Use mass media	Use media to reach large numbers of people to spread the word about the clinical innovation
Domain 8: Utilize financial strategies	
57. Fund and contract for the clinical innovation	Governments and other payers of services issue requests for proposals to deliver the innovation, use contracting processes to motivate providers to deliver the clinical innovation, and develop new funding formulas that make it more likely that providers will deliver the innovation
58. Access new funding	Access new or existing money to facilitate the implementation
59. Place innovation on fee for service lists/formularies	Work to place the clinical innovation on lists of actions for which providers can be reimbursed (e.g., a drug is placed on a formulary, a procedure is now reimbursable)
60. Alter incentive/allowance structures	Work to incentivize the adoption and implementation of the clinical innovation
61. Make billing easier	Make it easier to bill for the clinical innovation
62. Alter patient/consumer fees	Create fee structures where patients/consumers pay less for preferred treatments (the clinical innovation) and more for less-preferred treatments
63. Use other payment schemes	Introduce payment approaches (in a catch-all category)
64. Develop disincentives	Provide financial disincentives for failure to implement or use the clinical innovations
65. Use capitated payments	Pay providers or care systems a set amount per patient/consumer for delivering clinical care

Domain 9: Change infrastructure	
66. Mandate change	Have leadership declare the priority of the innovation and their determination to have it implemented
67. Change record systems	Change records systems to allow better assessment of implementation or clinical outcomes
68. Change physical structure and equipment	Evaluate current configurations and adapt, as needed, the physical structure and/or equipment (e.g., changing the layout of a room, adding equipment) to best accommodate the targeted innovation
69. Create or change credentialing and/or licensure standards	Create an organization that certifies clinicians in the innovation or encourage an existing organization to do so. Change governmental professional certification or licensure requirements to include delivering the innovation. Work to alter continuing education requirements to shape professional practice toward the innovation
70. Change service sites	Change the location of clinical service sites to increase access
71. Change accreditation or membership requirements	Strive to alter accreditation standards so that they require or encourage use of the clinical innovation. Work to alter membership organization requirements so that those who want to affiliate with the organization are encouraged or required to use the clinical innovation
72. Start a dissemination organization	Identify or start a separate organization that is responsible for disseminating the clinical innovation. It could be a for-profit or non-profit organization
73. Change liability laws	Participate in liability reform efforts that make clinicians more willing to deliver the clinical innovation

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Appendix 3. PRISMA guidelines for reporting

Section and Topic	Item #	Checklist item	Location where item is reported
TITLE			
Title	1	Identify the report as a systematic review.	Page 1,7
ABSTRACT			
Abstract	2	See the PRISMA 2020 for Abstracts checklist.	Followed
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of existing knowledge.	Page 6-7
Objectives	4	Provide an explicit statement of the objective(s) or question(s) the review addresses.	Page 7-8
METHODS			
Eligibility criteria	5	Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses.	Page 9-12
Information sources	6	Specify all databases, registers, websites, organisations, reference lists and other sources searched or consulted to identify studies. Specify the date when each source was last searched or consulted.	Page 9
Search strategy	7	Present the full search strategies for all databases, registers and websites, including any filters and limits used.	Appendix 4
Selection process	8	Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many reviewers screened each record and each report retrieved, whether they worked independently, and if applicable, details of automation tools used in the process.	Page 11-13
Data collection process	9	Specify the methods used to collect data from reports, including how many reviewers collected data from each report, whether they worked independently, any processes for obtaining or confirming data from study investigators, and if applicable, details of automation tools used in the process.	Page 11-13
Data items	10a	List and define all outcomes for which data were sought. Specify whether all results that were compatible with each outcome domain in each study were sought (e.g. for all measures, time points, analyses), and if not, the methods used to decide which results to collect.	Protocol, Page 11. Table 1, 2. Appendix 8.
	10b	List and define all other variables for which data were sought (e.g. participant and intervention characteristics, funding sources). Describe any assumptions made about any missing or unclear information.	Protocol, Page 12.
Study risk of bias assessment	11	Specify the methods used to assess risk of bias in the included studies, including details of the tool(s) used, how many reviewers assessed each study and whether they worked independently, and if applicable, details of automation tools used in the process.	Page 12-13, Appendix 6
Effect measures	12	Specify for each outcome the effect measure(s) (e.g. risk ratio, mean difference) used in the synthesis or presentation of results.	Table 2, Appendix 8.

Section and Topic	Item #	Checklist item	Location where item is reported
Synthesis methods	13a	Describe the processes used to decide which studies were eligible for each synthesis (e.g. tabulating the study intervention characteristics and comparing against the planned groups for each synthesis (item #5)).	Page 13
	13b	Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or data conversions.	Page 13
	13c	Describe any methods used to tabulate or visually display results of individual studies and syntheses.	Page 13. Table 2. Appendix 8.
	13d	Describe any methods used to synthesize results and provide a rationale for the choice(s). If meta-analysis was performed, describe the model(s), method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used.	Page 13
	13e	Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup analysis, meta-regression).	N/A
	13f	Describe any sensitivity analyses conducted to assess robustness of the synthesized results.	N/A
Reporting bias assessment	14	Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).	Page 13, Appendix 6
Certainty assessment	15	Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome.	N/A
RESULTS			
Study selection	16a	Describe the results of the search and selection process, from the number of records identified in the search to the number of studies included in the review, ideally using a flow diagram.	Figure 1, Page 12
	16b	Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded.	Reasons for exclusion summarised in Figure 1
Study characteristics	17	Cite each included study and present its characteristics.	Page 14-15. Table 1.
Risk of bias in studies	18	Present assessments of risk of bias for each included study.	Appendix 6.
Results of individual studies	19	For all outcomes, present, for each study: (a) summary statistics for each group (where appropriate) and (b) an effect estimate and its precision (e.g. confidence/credible interval), ideally using structured tables or plots.	Table 2. Appendix 8.
Results of syntheses	20a	For each synthesis, briefly summarise the characteristics and risk of bias among contributing studies.	Page 16-28
	20b	Present results of all statistical syntheses conducted. If meta-analysis was done, present for each the summary estimate and its precision (e.g. confidence/credible interval) and measures of statistical heterogeneity. If comparing groups, describe the direction of the effect.	N/A
	20c	Present results of all investigations of possible causes of heterogeneity among study results.	N/A

Section and Topic	Item #	Checklist item	Location where item is reported
	20d	Present results of all sensitivity analyses conducted to assess the robustness of the synthesized results.	N/A
Reporting biases	21	Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed.	Appendix 6
Certainty of evidence	22	Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed.	N/A
DISCUSSION			
Discussion	23a	Provide a general interpretation of the results in the context of other evidence.	Page 28-31
	23b	Discuss any limitations of the evidence included in the review.	Page 31
	23c	Discuss any limitations of the review processes used.	Page 31
	23d	Discuss implications of the results for practice, policy, and future research.	Page 32
OTHER INFORMATION			
Registration and protocol	24a	Provide registration information for the review, including register name and registration number, or state that the review was not registered.	Page
	24b	Indicate where the review protocol can be accessed, or state that a protocol was not prepared.	Page 8
	24c	Describe and explain any amendments to information provided at registration or in the protocol.	Page 8
Support	25	Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the review.	'Funding' section
Competing interests	26	Declare any competing interests of review authors.	'Competing interests' section
Availability of data, code and other materials	27	Report which of the following are publicly available and where they can be found: template data collection forms; data extracted from included studies; data used for all analyses; analytic code; any other materials used in the review.	Data extraction variables are in the protocol and in Appendix 5. As not all the included studies are available Open Access, the completed data extraction form and PDFs of the 49 included studies are available from the corresponding author on reasonable request.

From: Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021;372:n71. doi: 10.1136/bmj.n71 For more information, visit: http://www.prisma-statement.org/

Appendix 4: Systematic review search terms and the search strategy

Records identified from*:
Databases total (n = 12532)
Embase (n = 4964)
Medline (n = 2863)
APA PsycInfo (n = 955)
CINAHL (n = 1861)
Global Health (n = 652)
Social Policy and Practice (n = 28)
Applied Social Sciences Index and Abstracts (ASSIA) (n = 830)
OpenGrey (n = 11)
Social Care Online (n = 15)
Healthcare Management Information Consortium (HMIC) Database (n = 353)

Search and export: 7 April 2021

'Citation, abstract, subject headings' in RIS.

Embase 7 April 2021

Via Ovid

Database: Embase <1974 to 2021 Week 13>

Search Strategy:

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1 exp smoking/ (405134)

2 exp cigarette smoking/ (57862)

3 exp tobacco consumption/ (3011)

4 exp tobacco/ (47678)

5 exp tobacco dependence/ (21693)

6 tobacco.mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word, candidate term word] (161193)

7 smoking.mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word, candidate term word] (506719)

8 cigarett*.mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word, candidate term word] (126082)

9 exp smoking cessation/ (61774)

10 smoking cessation.mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word, candidate term word] (68962)

11 exp smoking cessation program/ (3482)

12 quit* smoking.mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word, candidate term word] (11181)

13 stop* smoking.mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word, candidate term word] (6500)

14 tobacco cessation.mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word, candidate term word] (3388)

15 smoking abstinence.mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word, candidate term word] (1997)

16 quit attempt*.mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word, candidate term word] (3178)

17 quit date*.mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word, candidate term word] (748)

18 exp primary medical care/ (111688)

19 primary care.mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word, candidate term word] (169863)

20 primary medic*.mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word, candidate term word] (114080)

21 primary health*.mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word, candidate term word] (89046)

22 exp general practice/ (79786)

23 general practi*.mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word, candidate term word] (205510)

24 general medic*.mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word, candidate term word] (22708)

25 exp family medicine/ (11673)

26 family medic*.mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word, candidate term word] (20287)

27 family practi*.mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word, candidate term word] (12825)

28 family physician*.mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word, candidate term word] (19317)

29 family doctor*.mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word, candidate term word] (6797)

30 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 (591107)

31 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 (73395)

32 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 (437307)

33 30 and 31 and 32 (5451)

34 limit 33 to randomized controlled trial (487)

35 33 not 34 (4964)

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Medline 7 April 2021

Via Ovid

Database: Ovid MEDLINE(R) and Epub Ahead of Print, In-Process, In-Data-Review & Other Non-Indexed Citations and Daily <1946 to April 06, 2021>

Search Strategy:

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1 exp Smoking/ (150989)

2 exp Tobacco Smoking/ (3969)

3 exp Cigarette Smoking/ (2459)

4 exp Tobacco/ (31718)

5 exp "Tobacco Use"/ (5915)

6 exp "Tobacco Use Disorder"/ (11528)

7 tobacco.mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] (133865)

8 smoking.mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] (294977)

9 cigarett*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] (75715)

10 exp Smoking Cessation/ (29636)

11 smoking cessation.mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] (40497)

12 quit* smoking.mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] (8424)

13 stop* smoking.mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] (4893)

14 tobacco cessation.mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] (2497)

15 smoking abstinence.mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism

supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] (1668)

16 quit attempt*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] (2721)

17 quit date*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] (625)

18 exp Primary Health Care/ (166713)

19 primary care.mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] (124282)

20 primary medic*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] (2138)

21 primary health*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] (102377)

22 exp General Practice/ (75681)

23 general practi*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] (94408)

24 general medic*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] (14767)

25 exp Family Practice/ (65514)

26 family medic*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] (12281)

27 family practi*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary

concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] (70243)

28 family physician*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] (15119)

29 family doctor*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] (4794)

30 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 (369611)

31 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 (45754)

32 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 (388463)

33 30 and 31 and 32 (3356)

34 limit 33 to randomized controlled trial (493)

35 33 not 34 (2863)

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APA PsycInfo 7 April 2021

Via Ovid

Database: APA PsycInfo <1806 to March Week 5 2021>

Search Strategy:

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1 exp Tobacco Smoking/ (34023)

2 exp "Tobacco Use Disorder"/ (239)

3 smoking.mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures, mesh] (59809)

4 tobacco.mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures, mesh] (43684)

5 cigarett*.mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures, mesh] (22468)

6 exp Smoking Cessation/ (13661)

7 smoking cessation.mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures, mesh] (18659)

8 quit* smoking.mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures, mesh] (4301)

9 stop* smoking.mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures, mesh] (1664)

10 tobacco cessation.mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures, mesh] (1113)

11 smoking abstinence.mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures, mesh] (1289)

12 quit attempt*.mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures, mesh] (1952)

13 quit date*.mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures, mesh] (419)

14 exp Primary Health Care/ (18961)

15 primary care.mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures, mesh] (32989)

16 primary medic*.mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures, mesh] (570)

17 primary health*.mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures, mesh] (25808)

18 exp General Practitioners/ (5993)

19 general practi*.mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures, mesh] (15647)

20 general medic*.mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures, mesh] (4741)

21 exp Family Medicine/ (1252)

22 family medic*.mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures, mesh] (2830)

23 exp Family Physicians/ (1557)

24 family practi*.mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures, mesh] (6648)

25 family physician*.mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures, mesh] (3148)

26 family doctor*.mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures, mesh] (769)

27 1 or 2 or 3 or 4 or 5 (68742)

28 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 (20188)

29 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 (61794)

30 27 and 28 and 29 (955)

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CINAHL 7 April 2021

http://search.ebscohost.com/login.aspx?profile=ehost&defaultdb=cin20&authtype=ip,shib&custid=s5003934

'Direct Export in RIS Format (e.g. CITAVI, EasyBib, EndNote, ProCite, Reference Manager, Zotero)'

Wednesday, April 07, 2021 9:13:43 AM

Query Limiters/Expanders Last Run Via Results

S30 S27 AND S28 AND S29 Expanders - Apply equivalent subjects

Search modes - Boolean/Phrase Interface - EBSCOhost Research Databases

Search Screen - Advanced Search

Database - CINAHL 1,861

S29 S15 OR S16 OR S17 OR S18 OR S19 OR S20 OR S21 OR S22 OR S23 OR S24 OR S25 OR S26 Expanders - Apply equivalent subjects

Search modes - Boolean/Phrase Interface - EBSCOhost Research Databases

Search Screen - Advanced Search

Database - CINAHL 163,724

S28 S6 OR S7 OR S8 OR S9 OR S10 OR S11 OR S12 OR S13 OR S14 Expanders - Apply equivalent subjects

Search modes - Boolean/Phrase Interface - EBSCOhost Research Databases

Search Screen - Advanced Search

Database - CINAHL 29,163

S27 S1 OR S2 OR S3 OR S4 OR S5 Expanders - Apply equivalent subjects

Search modes - Boolean/Phrase Interface - EBSCOhost Research Databases

Search Screen - Advanced Search

Database - CINAHL 126,242

S26 "family doctor*" Expanders - Apply equivalent subjects

Search modes - Boolean/Phrase Interface - EBSCOhost Research Databases

Search Screen - Advanced Search

Database - CINAHL 12,882

S25 "family physician*" Expanders - Apply equivalent subjects

Search modes - Boolean/Phrase Interface - EBSCOhost Research Databases

Search Screen - Advanced Search

Database - CINAHL 16,195

S24 "family practi*" Expanders - Apply equivalent subjects

Search modes - Boolean/Phrase Interface - EBSCOhost Research Databases

Search Screen - Advanced Search

Database - CINAHL 27,402

S23 "family medic*" Expanders - Apply equivalent subjects

Search modes - Boolean/Phrase Interface - EBSCOhost Research Databases

Search Screen - Advanced Search

Database - CINAHL 4,964

S22 "general medic*" Expanders - Apply equivalent subjects

Search modes - Boolean/Phrase Interface - EBSCOhost Research Databases

Search Screen - Advanced Search

Database - CINAHL 5,173

S21 "general practi*" Expanders - Apply equivalent subjects

Search modes - Boolean/Phrase Interface - EBSCOhost Research Databases

Search Screen - Advanced Search

Database - CINAHL 31,588

S20 (MH "Family Practice") Expanders - Apply equivalent subjects

Search modes - Boolean/Phrase Interface - EBSCOhost Research Databases

Search Screen - Advanced Search

Database - CINAHL 25,431

S19 "primary health*" Expanders - Apply equivalent subjects

Search modes - Boolean/Phrase Interface - EBSCOhost Research Databases

Search Screen - Advanced Search

Database - CINAHL 73,983

S18 "primary medic*" Expanders - Apply equivalent subjects

Search modes - Boolean/Phrase Interface - EBSCOhost Research Databases

Search Screen - Advanced Search

Database - CINAHL 684

S17 (MH "Physicians, Family") Expanders - Apply equivalent subjects

Search modes - Boolean/Phrase Interface - EBSCOhost Research Databases

Search Screen - Advanced Search

Database - CINAHL 20,676

S16 "primary care"Expanders - Apply equivalent subjects

Search modes - Boolean/Phrase Interface - EBSCOhost Research Databases

Search Screen - Advanced Search

Database - CINAHL 89,309

S15 (MH "Primary Health Care") Expanders - Apply equivalent subjects

Search modes - Boolean/Phrase Interface - EBSCOhost Research Databases

Search Screen - Advanced Search

Database - CINAHL 66,100

S14 "quit date*" Expanders - Apply equivalent subjects

Search modes - Boolean/Phrase Interface - EBSCOhost Research Databases

Search Screen - Advanced Search

Database - CINAHL 334

S13 "quit attempt*" Expanders - Apply equivalent subjects

Search modes - Boolean/Phrase Interface - EBSCOhost Research Databases

Search Screen - Advanced Search

Database - CINAHL 1,752

S12 "smoking abstinence" Expanders - Apply equivalent subjects

Search modes - Boolean/Phrase Interface - EBSCOhost Research Databases

Search Screen - Advanced Search

Database - CINAHL 874

S11 "stop* smoking" Expanders - Apply equivalent subjects

Search modes - Boolean/Phrase Interface - EBSCOhost Research Databases

Search Screen - Advanced Search

Database - CINAHL 15,000

S10 "quit* smoking" Expanders - Apply equivalent subjects

Search modes - Boolean/Phrase Interface - EBSCOhost Research Databases

Search Screen - Advanced Search

Database - CINAHL 15,979

S9 "smoking cessation" Expanders - Apply equivalent subjects

Search modes - Boolean/Phrase Interface - EBSCOhost Research Databases

Search Screen - Advanced Search

Database - CINAHL 27,315

S8 "tobacco cessation" Expanders - Apply equivalent subjects

Search modes - Boolean/Phrase Interface - EBSCOhost Research Databases

Search Screen - Advanced Search

Database - CINAHL 1,626

S7 (MH "Smoking Cessation Programs") Expanders - Apply equivalent subjects

Search modes - Boolean/Phrase Interface - EBSCOhost Research Databases

Search Screen - Advanced Search

Database - CINAHL 2,479

S6 (MM "Smoking Cessation") Expanders - Apply equivalent subjects

Search modes - Boolean/Phrase Interface - EBSCOhost Research Databases

Search Screen - Advanced Search

Database - CINAHL 14,065

S5 "tobacco" Expanders - Apply equivalent subjects

Search modes - Boolean/Phrase Interface - EBSCOhost Research Databases

Search Screen - Advanced Search

Database - CINAHL 35,423

S4 "cigarett*" Expanders - Apply equivalent subjects

Search modes - Boolean/Phrase Interface - EBSCOhost Research Databases

Search Screen - Advanced Search

Database - CINAHL 24,757

S3 "smoking" Expanders - Apply equivalent subjects

Search modes - Boolean/Phrase Interface - EBSCOhost Research Databases

Search Screen - Advanced Search

Database - CINAHL 111,904

S2 (MH "Tobacco") Expanders - Apply equivalent subjects

Search modes - Boolean/Phrase Interface - EBSCOhost Research Databases

Search Screen - Advanced Search

Database - CINAHL 7,850

S1 (MH "Smoking+") Expanders - Apply equivalent subjects

Search modes - Boolean/Phrase Interface - EBSCOhost Research Databases

Search Screen - Advanced Search

Database - CINAHL 73,196

Global Health 7 April 2021
Via Ovid

Database: Global Health <1973 to 2021 Week 13>

Search Strategy:

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1 exp smoking/ (1417)

2 exp tobacco smoking/ (51559)

3 exp tobacco/ (21785)

4 tobacco.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes] (60470)

5 smoking.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes] (82809)

6 cigarett*.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes] (26193)

7 exp smoking cessation/ (6536)

8 smoking cessation.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes] (9629)

9 quit* smoking.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes] (3067)

10 stop* smoking.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes] (1177)

11 tobacco cessation.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes] (873)

12 smoking abstinence.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes] (492)

13 quit attempt*.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes] (1199)

14 quit date*.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes] (165)

15 exp primary health care/ (16265)

16 primary care.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes] (19465)

17 primary medic*.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes] (324)

18 primary health*.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes] (23841)

19 general pract*.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes] (11543)

20 general medic*.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes] (1509)

21 exp general practitioners/ (4458)

22 family medic*.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes] (1404)

23 family practi*.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes] (820)

24 family physician*.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes] (1718)

25 family doctor*.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes] (653)

26 1 or 2 or 3 or 4 or 5 or 6 (91239)

27 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 (11400)

28 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 (45313)

29 26 and 27 and 28 (652)

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Social Policy and Practice 7 April 2021
Via Ovid

Database: Social Policy and Practice <202101>

Search Strategy:

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1 smoking.mp. [mp=abstract, title, publication type, heading word, accession number] (1675)

2 tobacco.mp. [mp=abstract, title, publication type, heading word, accession number] (566)

3 cigarett*.mp. [mp=abstract, title, publication type, heading word, accession number] (261)

4 smoking cessation.mp. [mp=abstract, title, publication type, heading word, accession number] (162)

5 quit* smoking.mp. [mp=abstract, title, publication type, heading word, accession number] (24)

6 stop* smoking.mp. [mp=abstract, title, publication type, heading word, accession number] (56)

7 tobacco cessation.mp. [mp=abstract, title, publication type, heading word, accession number] (3)

8 smoking abstinence.mp. [mp=abstract, title, publication type, heading word, accession number] (3)

9 quit attempt*.mp. [mp=abstract, title, publication type, heading word, accession number] (5)

10 quit date*.mp. [mp=abstract, title, publication type, heading word, accession number] (2)

11 primary care.mp. [mp=abstract, title, publication type, heading word, accession number] (5457)

12 primary medic*.mp. [mp=abstract, title, publication type, heading word, accession number] (44)

13 primary health*.mp. [mp=abstract, title, publication type, heading word, accession number] (1050)

14 general practi*.mp. [mp=abstract, title, publication type, heading word, accession number] (3962)

15 general medic*.mp. [mp=abstract, title, publication type, heading word, accession number] (198)

16 family medic*.mp. [mp=abstract, title, publication type, heading word, accession number] (37)

17 family practi*.mp. [mp=abstract, title, publication type, heading word, accession number] (200)

18 family physician*.mp. [mp=abstract, title, publication type, heading word, accession number] (55)

19 family doctor*.mp. [mp=abstract, title, publication type, heading word, accession number] (73)

20 1 or 2 or 3 (1906)

21 4 or 5 or 6 or 7 or 8 or 9 or 10 (209)

22 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 (8793)

23 20 and 21 and 22 (28)

****

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ASSIA Applied Social Sciences Index and Abstracts 7 April 2021

Via ProQuest

(ab,ti,su(smoking) OR ab,ti,su(cigarett[*20]) OR ab,ti,su(tobacco) OR MAINSUBJECT.EXACT.EXPLODE("Smoking"))

AND (ab,ti,su(smoking cessation) OR ab,ti,su(quit[*20] smoking) OR ab,ti,su(stop[*20] smoking) OR ab,ti,su(tobacco cessation) OR ab,ti,su(smoking abstinence) OR ab,ti,su(quit attempt[*20]) OR ab,ti,su(quit date[*20]) OR MAINSUBJECT.EXACT.EXPLODE("Cessation"))

AND (ab,ti,su(primary care) OR ab,ti,su(primary medic[*20]) OR ab,ti,su(primary health[*20]) OR ab,ti,su(general medic[*20]) OR ab,ti,su(general practi[*20]) OR ab,ti,su(family practi[*20]) OR ab,ti,su(family medic[*20]) OR ab,ti,su(family physician[*20]) OR ab,ti,su(family doctor[*20]) OR MAINSUBJECT.EXACT.EXPLODE("Primary health care"))

830 results

****

OpenGrey 7 April 2021

http://www.opengrey.eu/

“GreyNet has recently archived OpenGrey in its collection of research data housed in the DANS EASY Archive https://doi.org/10.17026/dans-xtf-47w5. OpenGrey will be shutdown before summer.”

(smoking OR tobacco OR cigarett*) AND (general medic* OR general practi* OR primary care OR primary health* OR primary medic* OR family practi* OR family medic* OR family physician* OR family doctor*)

➔ Exclude ‘thesis’

11 results (other 272 results were PhD theses)

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Social Care Online 7 April 2021

https://www.scie-socialcareonline.org.uk/

(smoking OR tobacco OR cigarett*) 748

(general medic* OR general practi* OR primary care OR primary health* OR primary medic* OR family practi* OR family medic* OR family physician* OR family doctor*) 10,809

(smoking cessation OR quit* smoking OR stop* smoking OR tobacco cessation OR smoking abstinence OR quit attempt* OR quit date* OR cessation) 178

Current search (with results shown below)

- **(New Combined Search:**

  - Smoking concept [
    - AllFields:'smoking'
    - OR AllFields:'tobacco'
    - OR AllFields:'cigarett*'
    ]
    AND
  - Primary care concept [
    - AllFields:'general medic*'
    - OR AllFields:'general practi*'
    - OR AllFields:'primary care'
    - OR AllFields:'primary health*'
    - OR AllFields:'primary medic*'
    - OR AllFields:'family practi*'
    - OR AllFields:'family medic*'
    - OR AllFields:'family physician*'
    - OR AllFields:'family doctor*'
    ]
    AND
  - Smoking cessation concept [
    - AllFields:'smoking cessation'
    - OR AllFields:'quit* smoking'
    - OR AllFields:'stop* smoking'
    - OR AllFields:'tobacco cessation'
    - OR AllFields:'smoking abstinence'
    - OR AllFields:'quit attempt*'
    - OR AllFields:'quit date*'
    - OR AllFields:'cessation'
    ]

)

15 results

****

Healthcare Management Information Consortium Database 7 April 2021
Via Ovid

Database: HMIC Health Management Information Consortium <1979 to January 2021>

Search Strategy:

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1 exp Smoking/ (3747)

2 exp Tobacco/ (725)

3 exp Cigarette tobacco/ (6)

4 exp Tobacco consumption/ (169)

5 smoking.mp. [mp=title, other title, abstract, heading words] (8418)

6 tobacco.mp. [mp=title, other title, abstract, heading words] (2746)

7 cigarett*.mp. [mp=title, other title, abstract, heading words] (1730)

8 exp Smoking cessation/ (1895)

9 exp Smoking treatment/ (218)

10 smoking cessation.mp. [mp=title, other title, abstract, heading words] (2208)

11 quit* smoking.mp. [mp=title, other title, abstract, heading words] (329)

12 stop* smoking.mp. [mp=title, other title, abstract, heading words] (511)

13 tobacco cessation.mp. [mp=title, other title, abstract, heading words] (36)

14 smoking abstinence.mp. [mp=title, other title, abstract, heading words] (42)

15 quit attempt*.mp. [mp=title, other title, abstract, heading words] (122)

16 quit date*.mp. [mp=title, other title, abstract, heading words] (51)

17 exp primary care/ (22774)

18 primary care.mp. [mp=title, other title, abstract, heading words] (24846)

19 primary medic*.mp. [mp=title, other title, abstract, heading words] (261)

20 primary health*.mp. [mp=title, other title, abstract, heading words] (3603)

21 exp Primary care teams/ (659)

22 exp General practice/ (9229)

23 general practi*.mp. [mp=title, other title, abstract, heading words] (26625)

24 general medic*.mp. [mp=title, other title, abstract, heading words] (2586)

25 family medic*.mp. [mp=title, other title, abstract, heading words] (201)

26 family practi*.mp. [mp=title, other title, abstract, heading words] (1147)

27 exp General practitioners/ (10304)

28 family physician*.mp. [mp=title, other title, abstract, heading words] (267)

29 family doctor*.mp. [mp=title, other title, abstract, heading words] (388)

30 1 or 2 or 3 or 4 or 5 or 6 or 7 (9309)

31 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 (2428)

32 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 (48184)

33 30 and 31 and 32 (353)

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Appendix 5: Pre-piloted data extraction form fields

- Authors' information
- Year of publication
- Year(s) the data analysed was collected in
- Country in which intervention was delivered
- Details of the intervention (including duration)
- Description of comparator/control
- Description of the setting/context (e.g. environmental and cultural factors)
- Study design type
- Data collection method (interview, telephone, mail survey, electronic health records)
- Respondent (patient, provider, other: specify)
- Inclusion criteria, including sub-populations
- Characteristics of study participants (age, sex, co-morbidities, readiness to quit)
- Outcome measures and definitions used (including self-reported or biochemically verified etc), and time point at which they were assessed.
    - Quantitative outcomes:
        - number of participants included in analysis
        - number of people in each group
        - estimate effect with confidence interval
    - Explanation offered to explain why certain strategies to increase the provision and uptake of smoking cessation treatment in primary care settings were/were not effective
    - Cost effectiveness estimates or economic indicators
- Methods for managing missing data
- Funding and declaration of interest for primary investigators
- Authors' conclusions

Appendix 6: Risk of bias assessment

As outlined in the manuscript, The ROBINS-I (Risk Of Bias In Non-randomized Studies of Interventions) tool was used to evaluate the risk of bias in non-randomised observational studies (23–25).

BT performed the risk of bias assessments. After the first five studies were assessed, LB also assessed these, and BT and LB compared ratings. The risk of bias assessment ratings and justifications are included below.

The tool assesses risk of bias in seven domains (23):

- Pre-intervention: (1) bias due to confounding, (2) bias in selection of participants into the study.
- At intervention: (3) bias in classification of interventions.
- Post-intervention: (4) bias due to deviations from intended interventions, (5) bias due to missing data, (6) bias in measurement of outcomes, (7) bias in selection of the reported result.

Then an overall risk of bias rating is decided for each study (23):

- Low risk of bias: The study is comparable to a well performed randomised trial.
- Moderate risk of bias: The study provides sound evidence for a non-randomised study but cannot be considered comparable to a well performed randomised trial.
- Serious risk of bias: The study has some important problems.
- Critical risk of bias: The study is too problematic to provide any useful evidence and should not be included in any synthesis.
- No information: No information on which to base a judgement about risk of bias.

References:

23. Sterne JA, Hernán MA, Reeves BC, Savović J, Berkman ND, Viswanathan M, et al. ROBINS-I: a tool for assessing risk of bias in non-randomised studies of interventions. BMJ. 2016 Oct;355:i4919.

24. Mueller M, D'Addario M, Egger M, Cevallos M, Dekkers O, Mugglin C, et al. Methods to systematically review and meta-analyse observational studies: a systematic scoping review of recommendations. BMC Med Res Methodol. 2018;18(1):44.

25. Sterne JAC, Hernán MA, McAleenan A, Reeves BC, Higgins JPT. Chapter 25: Assessing risk of bias in a non-randomized study. In: Higgins J, Thomas J, Chandler J, Cumpston M, Li T, Page M, et al., editors. Cochrane Handbook for Systematic Reviews of Interventions version 62 (updated February 2021) [Internet]. 2021 [cited 2022 Feb 3]. Available from: https://training.cochrane.org/handbook

Please find the risk of bias assessment table here:

https://static-content.springer.com/esm/art%3A10.1186%2Fs12875-023-01981-2/MediaObjects/12875_2023_1981_MOESM6_ESM.pdf

Appendix 7: Consolidated Framework for Implementation Research (CFIR) determinants

The facilitators and barriers proposed by the authors of the included studies were coded to the specific Consolidated Framework for Implementation Research (CFIR) domains and constructs.

The CFIR (1) https://cfirguide.org/constructs/ comprises five major domains which interact in complex ways to influence the implementation effectiveness of an intervention:

1. Intervention characteristics
2. Outer setting,
3. Inner setting,
4. Characteristic of individuals,
5. Implementation process.

Construct	Definition
Domain 1. Intervention characteristics	**The features of an intervention that might influence implementation.**
Intervention Source	Perception of key stakeholders about whether the intervention is externally or internally developed.
Evidence Strength & Quality	Stakeholders' perceptions of the quality and validity of evidence supporting the belief that the intervention will have desired outcomes.
Relative Advantage	Stakeholders' perception of the advantage of implementing the intervention versus an alternative solution.
Adaptability	The degree to which an intervention can be adapted, tailored, refined, or reinvented to meet local needs.
Trialability	The ability to test the intervention on a small scale in the organization, and to be able to reverse course (undo implementation) if warranted.
Complexity	Perceived difficulty of implementation, reflected by duration, scope, radicalness, disruptiveness, centrality, and intricacy and number of steps required to implement.
Design Quality & Packaging	Perceived excellence in how the intervention is bundled, presented, and assembled.
Cost	Costs of the intervention and costs associated with implementing the intervention including investment, supply, and opportunity costs.
Domain 2. Outer setting	**The features of the external context or environment that might influence implementation.**
Patient Needs & Resources	The extent to which patient needs, as well as barriers and facilitators to meet those needs, are

	accurately known and prioritized by the organization.
Cosmopolitanism	The degree to which an organization is networked with other external organizations.
Peer Pressure	Mimetic or competitive pressure to implement an intervention; typically because most or other key peer or competing organizations have already implemented or are in a bid for a competitive edge.
External Policy & Incentives	A broad construct that includes external strategies to spread interventions, including policy and regulations (governmental or other central entity), external mandates, recommendations and guidelines, pay-for-performance, collaboratives, and public or benchmark reporting.
Domain 3. Inner setting	**The features of the implementing organization that might influence implementation.**
Structural Characteristics	The social architecture, age, maturity, and size of an organization.
Networks & Communications	The nature and quality of webs of social networks and the nature and quality of formal and informal communications within an organization.
Culture	Norms, values, and basic assumptions of a given organization.
Implementation Climate	The absorptive capacity for change, shared receptivity of involved individuals to an intervention, and the extent to which use of that intervention will be rewarded, supported, and expected within their organization.
(i) Tension for Change	The degree to which stakeholders perceive the current situation as intolerable or needing change.
(ii) Compatibility	The degree of tangible fit between meaning and values attached to the intervention by involved individuals, how those align with individuals' own norms, values, and perceived risks and needs, and how the intervention fits with existing workflows and systems.
(iii) Relative Priority	Individuals' shared perception of the importance of the implementation within the organization.
(iv) Organizational Incentives & Rewards	Extrinsic incentives such as goal-sharing awards, performance reviews, promotions, and raises in salary, and less tangible incentives such as increased stature or respect.
(v) Goals and Feedback	The degree to which goals are clearly communicated, acted upon, and fed back to staff, and alignment of that feedback with goals.

(vi) Learning Climate	A climate in which: a) leaders express their own fallibility and need for team members' assistance and input; b) team members feel that they are essential, valued, and knowledgeable partners in the change process; c) individuals feel psychologically safe to try new methods; and d) there is sufficient time and space for reflective thinking and evaluation.
Readiness for Implementation	Tangible and immediate indicators of organizational commitment to its decision to implement an intervention.
(i) Leadership Engagement	Commitment, involvement, and accountability of leaders and managers with the implementation.
(ii) Available Resources	The level of resources dedicated for implementation and on-going operations, including money, training, education, physical space, and time.
(iii) Access to Knowledge & Information	Ease of access to digestible information and knowledge about the intervention and how to incorporate it into work tasks.
Domain 4. Characteristics of individuals	**Features of individuals involved in implementation that might influence implementation.**
Knowledge & Beliefs about the Intervention	Individuals' attitudes toward and value placed on the intervention as well as familiarity with facts, truths, and principles related to the intervention.
Self-efficacy	Individual belief in their own capabilities to execute courses of action to achieve implementation goals.
Individual Stage of Change	Characterization of the phase an individual is in, as he or she progresses toward skilled, enthusiastic, and sustained use of the intervention.
Individual Identification with Organization	A broad construct related to how individuals perceive the organization, and their relationship and degree of commitment with that organization.
Other Personal Attributes	A broad construct to include other personal traits such as tolerance of ambiguity, intellectual ability, motivation, values, competence, capacity, and learning style.
Domain 5. Implementation process	**Strategies or tactics that might influence implementation.**
Planning	The degree to which a scheme or method of behaviour and tasks for implementing an intervention are developed in advance, and the quality of those schemes or methods.

Engaging	Attracting and involving appropriate individuals in the implementation and use of the intervention through a combined strategy of social marketing, education, role modelling, training, and other similar activities.
(i) Opinion Leaders	Individuals in an organization who have formal or informal influence on the attitudes and beliefs of their colleagues with respect to implementing the intervention.
(ii) Formally Appointed Internal Implementation Leaders	Individuals from within the organization who have been formally appointed with responsibility for implementing an intervention as coordinator, project manager, team leader, or other similar role.
(iii) Champions	"Individuals who dedicate themselves to supporting, marketing, and 'driving through' an [implementation]" [101] (p. 182), overcoming indifference or resistance that the intervention may provoke in an organization.
(iv) External Change Agents	Individuals who are affiliated with an outside entity who formally influence or facilitate intervention decisions in a desirable direction.
Executing	Carrying out or accomplishing the implementation according to plan.
Reflecting & Evaluating	Quantitative and qualitative feedback about the progress and quality of implementation accompanied with regular personal and team debriefing about progress and experience.

References

1. Damschroder LJ, Aron DC, Keith RE, Kirsh SR, Alexander JA, Lowery JC. Fostering implementation of health services research findings into practice: a consolidated framework for advancing implementation science. Implement Sci. 2009 Aug;4:50.

Appendix 8. Supplementary table containing long-form quantitative outcome measures for RQ2 effectiveness

First author, year	Location	Implementation strategy category	Study design	Outcome measures
Domain 5. Train and educate stakeholders				
Mullins, 1999 (70)	Victoria, Australia	40. Distribute educational materials	Repeated cross-sectional study. Analytical.	**Recall of asking about smoking status** (GP "asked if smoked/no advice given"): 1990: 22.4%, 95% CI: 19.2 to 25.7. 1992: 21.3%, 95% CI: 18.0 to 24.6. 1994: 15.6%, 95% CI: 12.7 to 18.5. 1996: 19.2%, 95% CI: 15.9 to 22.4. **Recall of receiving cessation advice** (GP "advised to stop smoking"): 1990: 34.8%, 95% CI: 31.0 to 38.5. 1992: 37.2%, 95% CI: 33.4 to 41.1. 1994: 37.4%, 95% CI: 33.6 to 41.3. 1996: 35.2%, 95% CI: 31.2 to 39.1. **Recall of GP assisting to quit** (GP gave "information or help to stop"): 1990: 10.7%, 95% CI: 8.3 to 13.2. 1992: 13.1%, 95% CI: 10.4 to 15.8. 1994: 17.2%, 95% CI: 14.2 to 20.2. 1996: 20.6%, 95% CI: 17.3 to 23.9. Statistically significant increase "over time": X^2=17.58, p<0.001. "In 1996, 9% of smokers said their doctor had advised them to contact Quit (this response was subsumed into the category “information or help to stop”). **Recall of advise to cut down** (GP "advised to cut down"): 1990: 11.4%, 95% CI: 8.9 to 13.9. 1992: 10.2%, 95% CI: 7.8 to 12.7.

First author, year	Location	Implementation strategy category	Study design	Outcome measures
				1994: 11.0%, 95% CI: 8.5 to 13.5. 1996: 9.2%, 95% CI: 6.8 to 11.6.
Vasankari, 2011 (74)	Finland	42. Conduct educational meetings	Repeated cross-sectional study. Analytical.	**Record of smoking status:** All patients with respiratory symptoms: 1997: 16.6% of all patients "had written information on smoking habits". (n = 178/1,072) 2002: 53.2%. (n = 875/1,645) Statistically significant increase: p<0.001. In patients with COPD: 1997: 45.0% of all patients "had written information on smoking habits". (n = 45/100) 2002: 84.3%. (n = 182/216) Statistically significant increase: p<0.001.
Domain 7. Engage consumers				
Szatkowski, 2011 (33)	England	54. Prepare patients/consumers to be active participants	Repeated cross-sectional study. Interrupted time series analysis (no control).	**Prescription for NRT:** 9 months before: 4.0% change, 95% CI: -1.3 to 9.3, p=0.135 6 months before: 6.2% change, 95% CI: 1.4 to 11.0, p=0.012 3 months before: 10.4% change, 95% CI: 5.0 to 15.7, p<0.001 2 months before: 13.6% change, 95% CI: 8.1 to 19.1, p<0.001 1 month before: 17.5% change, 95% CI: 11.1 to 24.0, p<0.001 1 month after: -1.1% change, 95% CI: -32.2 to 30.0, p=0.945 2 months after: -6.9% change, 95% CI: -0.3 to -13.4, p=0.040 3 months after: -9.0% change, 95% CI: -3.9 to -14.2, p=0.001 6 months after: -6.7% change, 95% CI: -2.1 to -11.2, p=0.004 9 months after: -5.5% change, 95% CI: -2.3 to -8.7, p=0.001

First author, year	Location	Implementation strategy category	Study design	Outcome measures
				Permanent change: -1.7% change, 95% CI: -4.4 to 1.0, p=0.229 **Prescription for bupropion:** 9 months before: 5.2% change, 95% CI: -1.8 to 12.3, p=0.147 6 months before: 7.1% change, 95% CI: -0.4 to 14.5, p=0.062 3 months before: 13.2% change, 95% CI: 4.3 to 22.2, p=0.004 2 months before: 18.9% change, 95% CI: 9.2 to 28.6, p<0.001 1 month before: 44.7% change, 95% CI: 20.4 to 69.0, p<0.001 1 month after: -6.8% change, 95% CI: -40.1 to 26.6, p=0.691 2 months after: -25.3% change, 95% CI: -4.9 to -45.7, p=0.015 3 months after: -21.1% change, 95% CI: -2.1 to -40.1, p=0.029 6 months after: -19.7% change, 95% CI: -5.5 to -34.0, p=0.007 9 months after: -13.7% change, 95% CI: -4.6 to -22.8, p=0.003 Permanent change: -3.5% change, 95% CI: -8.8 to 1.9, p=0.206 **Prescription for all medications:** 9 months before: 6.4% change, 95% CI: 0.7 to 12.1, p=0.027 6 months before: 11.1% change, 95% CI: 5.5 to 16.7, p<0.001 3 months before: 9.9% change, 95% CI: 5.2 to 14.6, p<0.001 2 months before: 14.7% change, 95% CI: 10.4 to 19.1, p<0.001 1 month before: 22.3% change, 95% CI: 17.9 to 26.8, p<0.001 1 month after: 7.7% change, 95% CI: -13.0 to 28.4, p=0.468 2 months after: -5.3% change, 95% CI: -17.2 to 6.7, p=0.387 3 months after: -10.0% change, 95% CI: -0.2 to -19.9, p=0.046 6 months after: -7.4% change, 95% CI: -16.3 to 1.5, p=0.101 9 months after: -6.4% change, 95% CI: -1.1 to -11.7, p=0.019 Permanent change: -2.2% change, 95% CI: -5.6 to 1.2, p=0.209

First author, year	Location	Implementation strategy category	Study design	Outcome measures
Langley, 2012 (46)	England (and Wales)	56. Use mass media	Repeated cross-sectional study. Interrupted time series analysis (no control).	**Prescription for NRT:** Intervention: Tobacco control TVRs: In both the seasonally adjusted and unadjusted models, tobacco control campaign advertising had no statistically significant effect on NRT prescribing (January 2002 to June 2009) in the same month. Unadjusted model: 0.034 Orthogonalised Impulse Response Function (OIRF); 95% CI: -0.008 to 0.077, p=0.121. Seasonally adjusted model: 0.012 OIRF; 95% CI: -0.007 to 0.031, p=0.220. Intervention: Pharmaceutical company TVRs: In both the seasonally adjusted and unadjusted models, pharmaceutical company advertising had no statistically significant effect on NRT prescribing (January 2005 to June 2009) in the same month. Unadjusted model: 0.028 Orthogonalised Impulse Response Function (OIRF); 95% CI: -0.023 to 0.080, p=0.285. Seasonally adjusted model: 0.020 OIRF; 95% CI: -0.004 to 0.044, p=0.121.
Domain 8. Utilize financial strategies				
Alageel, 2019 (31)	England	57. Fund and contract for the clinical innovation	Cohort study. Interrupted time series analysis (with control).	**Record of referral to smoking cessation advisor or stop smoking clinic:** Health check participants: 19,818 (90%); Controls: 48,900 (61%). Adjusted HR: 3.13; 95% CI: 3.07 to 3.20, p<0.001. **Prescription for NRT:** Health check participants: 3,956 (18%); Controls: 8,630 (11%). Adjusted HR: 1.63; 95% CI: 1.57 to 1.69, p<0.001.

First author, year	Location	Implementation strategy category	Study design	Outcome measures
				Record of all smoking cessation interventions: Health check participants: 19,927 (91%); Controls: 42,282 (61%). Adjusted HR: 3.20; 95% CI: 3.13 to 3.27, p<0.001. **Smoking prevalence:** 'Current smoking' OR: Mean difference between cases and controls: 0.70, 95% CI: 0.69 to 0.71, p<0.001. Mean change per year for cases and controls: 0.97, 95% CI: 0.96 to 0.97, p<0.001. 1st year following the health check: 0.97, 95% CI: 0.96 to 0.98, p<0.001. 2nd year following the health check: 0.93, 95% CI: 0.92 to 0.94, p<0.001. 3rd year following the health check: 0.91, 95% CI: 0.89 to 0.93, p<0.001. 4th year following the health check: 0.91, 95% CI: 0.89 to 0.93, p<0.001. 5th year following the health check: 0.92, 95% CI: 0.90 to 0.94, p<0.001. 6th year following the health check: 0.90, 95% CI: 0.87 to 0.94, p<0.001.
Bennett, 2008 (65)	Ireland	57. Fund and contract for the clinical innovation	Cohort study.	**Smoking prevalence:** **1-year follow up cohort:** n (with data at both visits) = 7,097. Baseline: 14.8% smoking. 1-year: 12.0% smoking. Statistically significant difference between 1-year and baseline: -2.8%, p<0.0001. **2-year follow up cohort:** n (with data at all visits) = 4,011. Baseline: 13.7% smoking.

First author, year	Location	Implementation strategy category	Study design	Outcome measures
				1-year: 11.3% smoking. 2-year: 10.1% smoking. Statistically significant difference between 2-year and baseline: -3.6%, p<0.0001.
Fitzpatrick, 2011 (66)	Ireland	57. Fund and contract for the clinical innovation	Cohort study.	**Smoking prevalence:** **2-year follow up cohort:** n (with data at baseline and 2-years) = 5,430. Baseline: 13.9% smoking. 1-year: 11.2% smoking. 2-year: 10.4% smoking. Statistically significant difference between 2-year and baseline: -3.5%, p<0.0001. **3.5-year follow up cohort:** n (with data at baseline and 3.5-years) = 2,078. Baseline: 12.8% smoking. 1-year: 11.7% smoking. 2-year: 9.8% smoking. 3-year: 10.0% smoking. 3.5-year: 9.9% smoking. Statistically significant difference between 3.5-year and baseline: -2.9%, p<0.0001. **Proportions of 'nonsmokers':** Proportion (%) read off the graph, Figure 1a. Baseline: 85%. 1-year: 88%. 2-year: 90%. 3-year: 90%.

First author, year	Location	Implementation strategy category	Study design	Outcome measures
				3.5-year: 90.1%. Relative increase of 22.7% in proportion of nonsmokers from baseline (to 90.1%, p<0.0001). **Prescription for smoking cessation medication:** 3.5-year: "23.5% of smokers were prescribed smoking cessation medication."
Forster, 2016 (48)	England	57. Fund and contract for the clinical innovation	Cohort study.	**Record of smoking status:** NHS health check: 0% of men (n=20) and 0% of women (n=10) did not have smoking status recorded. Controls: 7% of men (n=6,321) and 2% of women (n=1,473) did not have smoking status recorded. Net reduction in proportion with no smoking status: 7% in men and 2% in women (p<0.001). Reduction in deprivation inequality was greater for men (4% for smoking records), compared to 1% for women. **Smoking prevalence:** NHS health check: 21% of men (n=7,775) and 16% of women (n=6,300) had 'current smoking detected'. Controls: 26% of men (n=26,841) and 21% of women (n=19,071) had 'current smoking detected'. Deprivation inequality reduced by 1% in men and by 4% in women.
Frijling, 2003 (69)	Netherlands	57. Fund and contract for the clinical innovation	Controlled before-and-after trial.	**Record of smoking status:** **Results not available for 'smoking habits' only. **Record of cessation counselling:**

First author, year	Location	Implementation strategy category	Study design	Outcome measures
				Intervention practices: Baseline: 27.3% (n=84/308) Post-intervention: 37% (n=114/308) Difference: 9.7%, 95% CI: 3.2 to 16.3. Control practices: Baseline: 23.2% (n = 69/297) Post-intervention: 28.3% (n = 84/297) Difference: 5.1%, 95% CI: -0.6 to 10.7. Adjusted odds ratio: 1.45, 95% CI: 1.02 to 2.07.
Pajak, 2010 (73)	Poland	57. Fund and contract for the clinical innovation	Cohort study.	**Record of smoking status:** Before screening period: 12.3% (95% CI: 7.2 to 20.1) of patients had this information available in their medical records before the PCVDP, at the active clinics (n=3,940). Before screening period: 8.0% (95% CI: 4.6 to 13.6) of patients had this information available in their medical records before the PCVDP, at the non-active clinics (n=3,162). Difference between the two groups: non-significant, p=0.82. After screening period: 32.9% (95% CI: 22.8 to 45.0) of patients had this information available in their medical records after the PCVDP, at the active clinics (n=3,940). After screening period: 10.1% (95% CI: 6.3 to 15.8) of patients had this information available in their medical records after the PCVDP, at the non-active clinics (n=3,162). Difference between the two groups: significant, p<0.001. **Recall of receiving any cessation intervention ("tobacco cessation"):**

First author, year	Location	Implementation strategy category	Study design	Outcome measures
				Percentage of participants who received advice to change lifestyle prior to final examination (adjusted for age, sex and design effects): Active clinics (n=2,314): 41.0% (95% CI: 31.0 to 51.7) Non-active clinics (n=2,107): 34.6% (95% CI: 25.5 to 44.9) Difference between the two groups: non-significant, p=0.35. **Recall of verbal advice or receipt of leaflets:** Percentage of participants who received advice to change lifestyle prior to final examination (adjusted for age, sex and design effects): Active clinics (n=2,314): 37.7% (95% CI: 27.6 to 49.0) Non-active clinics (n=2,107): 29.8% (95% CI: 21.1 to 40.3) Difference between the two groups: non-significant, p=0.25. **Recall of referral to specialist clinic:** Percentage of participants who received advice to change lifestyle prior to final examination (adjusted for age, sex and design effects): Active clinics (n=2,314): 2.5% (95% CI: 1.2 to 5.1) Non-active clinics (n=2,107): 4.4% (95% CI: 2.3 to 8.2) Difference between the two groups: non-significant, p=0.25. **Recall of prescription for pharmacotherapy:** Percentage of participants who received advice to change lifestyle prior to final examination (adjusted for age, sex and design effects): Active clinics (n=2,314): 5.8% (95% CI: 3.4 to 9.7) Non-active clinics (n=2,107): 5.8% (95% CI: 3.4 to 9.8) Difference between the two groups: non-significant, p=0.97. **Recall of discussion about "other methods":**

First author, year	Location	Implementation strategy category	Study design	Outcome measures
				Percentage of participants who received advice to change lifestyle prior to final examination (adjusted for age, sex and design effects): Active clinics (n=2,314): 3.8% (95% CI: 2.1 to 6.7) Non-active clinics (n=2,107): 3.5% (95% CI: 1.9 to 6.3) Difference between the two groups: non-significant, p=0.84. **Non-smoking prevalence:** Percentage of participants who were "not smoking" at the final examination (adjusted for age, sex and design effects): Active clinics (n=2,314): 73.9% (95% CI: 65.7 to 80.7) Non-active clinics (n=2,107): 65.4% (95% CI: 56.6 to 73.2) Difference between the two groups: non-significant, p=0.29.
Wright, 2018 (71)	Australia	57. Fund and contract for the clinical innovation	Cohort study.	**Record of smoking status:** TIS-funded services: 2014: 85% of clients asked about their tobacco use. 2016: 88% of clients asked about their tobacco use. Non-TIS-funded services: 2014: 84% of clients asked about their tobacco use. 2016: 80% of clients asked about their tobacco use. Among TIS-funded services, the tobacco use reporting ratio (RR) was 1.58-fold higher (95% CI: 1.30 to 1.91; p<0.001) after controlling for remoteness, year of funding, and interactions. **Smoking prevalence:** 53% of all clients attending all services in 2014, 2015, 2016 were reported as current

First author, year	Location	Implementation strategy category	Study design	Outcome measures
				smokers. 14% in 2014 and 2015, 15% in 2016 were reported as ex-smokers. 33% in 2014, 32% in 2015 and 2016 were reported as non-smokers. TIS funding was not associated with any change in reporting of clients as current smokers, ex-smokers or non-smokers across the three reporting periods (2014, 2015, 2016).
Bailey, 2016 (54)	Oregon, USA	59. Place innovation on fee for service lists/formularies	Cohort study.	**Prescription of cessation medication (NRT, varenicline, bupropion):** Gained Medicaid: 26.9% (n=1,115/4,140) of smokers had a cessation medication ordered. Uninsured: 11.5% (n=477/4,140) of smokers had a cessation medication ordered. Statistically significant difference, p<0.001. The odds of having medication ordered were almost 3 times higher for patients who gained Medicaid relative to the uninsured cohort (aOR: 2.94, 95% CI: 2.61 to 3.32). **Cessation:** Gained Medicaid: 16.6% (n=686/4,140) of smokers quit smoking during the study periods. Uninsured: 13.3% (n=550/4,140) of smokers quit smoking during the study periods. Statistically significant difference, p<0.001. The newly insured (gained Medicaid) had 40% increased odds of quitting compared to their uninsured counterparts (aOR: 1.40, 95% CI: 1.24 to 1.58). Among patients without a smoking medication ordered, the gained Medicaid group had significantly higher odds of quitting compared to the group of uninsured smokers (aOR: 1.23, 95% CI: 1.06 to 1.41). Among patients with medication ordered, the odds of quitting was also higher for

First author, year	Location	Implementation strategy category	Study design	Outcome measures
				those who gained Medicaid, but the difference was not significant in this smaller group (aOR: 1.29, 95% CI: 0.99 to 1.67). Among patients with more follow-up visits, the odds of quitting were 22% higher for those who gained Medicaid (aOR: 1.22, 95% CI: 1.05 to 1.42); there were no significant between-group differences in quit rates among patients with <6 follow-up visits. Within-group analyses: Having a smoking cessation medication order resulted in higher odds of quitting smoking for both groups (newly insured: aOR: 2.00, 95% CI: 1.69 to 2.37; uninsured: aOR: 1.90, 95% CI: 1.50 to 2.41). Patients with more visits had higher odds of quitting than patients with fewer visits (newly insured: aOR: 2.86, 95% CI: 2.36 to 3.45; uninsured: aOR: 2.60, 95% CI: 2.16 to 3.12).
Bailey, 2020 (60)	United States (multi-state)	59. Place innovation on fee for service lists/formularies	Cohort study.	**Prescription of cessation medication (NRT, varenicline, bupropion):** Adjusted odds ratio (over 24 months): Non-expansion: 1.00 (reference group). Expansion: 1.53, 95% CI: 1.44 to 1.62 (p<0.001). **Cessation:** Adjusted odds ratio (over 24 months): Non-expansion: 1.00 (reference group). Expansion: 1.35, 95% CI: 1.28 to 1.43 (p<0.001).

First author, year	Location	Implementation strategy category	Study design	Outcome measures
				"Among patients with a cessation medication ordered, those from expansion states had 65% higher odds of quitting compared to those from non-expansion states (aOR: 1.65, 95% CI: 1.48 to 1.84); the odds of quitting among those without a cessation medication ordered were 29% higher for patients in expansion versus non-expansion states." "For patients in expansion states, the odds of quitting were higher regardless of follow-up visit numbers or percent of federal poverty level (FPL) at baseline, compared to those in non-expansion states." Follow-up visits (<6): (aOR: 1.30, 95% CI: 1.21 to 1.40); Follow-up visits (6+): (aOR: 1.25, 95% CI: 1.16 to 1.34); FPL ≤138%: (aOR: 1.32, 95% CI: 1.23 to 1.41); FPL >138%: (aOR: 1.21, 95% CI: 1.07 to 1.37). "Among patients who were uninsured at baseline, those in expansion states had 51% higher odds of quitting than those from states that did not expand (aOR: 1.51, 95% CI: 1.39 to 1.64); the odds of quitting among those that were insured at baseline were also higher for patients in expansion versus non-expansion states, although of lesser magnitude (aOR: 1.29, 95% CI: 1.21 to 1.37)."
Li, 2018 (61)	United States (multi-state)	59. Place innovation on fee for service lists/formularies	Repeated cross-sectional study. Descriptive.	Proportion (%) read off the graph, Figure 2. **Record of smoking status:** 2010: 59.2% (of patients who had a documentation of smoking history). 2011: 64.3% 2012: 67.8% 2013: 70.3% 2014: 73.6%

First author, year	Location	Implementation strategy category	Study design	Outcome measures
				2015: 76.5% 2016: 77.8%
Marino, 2016 (62)	Oregon, USA	59. Place innovation on fee for service lists/formularies	Cohort study.	**Record of smoking status** ('screening for smoking'): "Individuals randomly selected to apply for insurance did not always follow through, and thus remained uninsured." Both 'selected to apply for coverage' and 'gained coverage' results outlined. Intervention: 'Selected to apply for coverage'. Selected: 59.2% (n=4,049) Not selected (ref): 56.9% (n=6,594) Difference: 2.3%. OR: 1.07, 95% CI: 1.04 to 1.10. AOR: 1.04, 95% CI: 1.02 to 1.06. Intervention: 'Gained coverage', n=1,718 (44% of n=4,049). Mean value in control group: 56.4%, 95% CI: 53.0 to 59.7. 6.2% change with Medicaid coverage, 95% CI: 5.3 to 7.1, p<0.001.
Miraldo, 2018 (57)	Massachusetts, USA	59. Place innovation on fee for service lists/formularies	Repeated cross-sectional study with control. Difference-in-differences	**Quit attempt** ("attempted to quit smoking"): DD coefficient for whole sample: 0.001 (standard error: 0.018). Not statistically significant. DDD coefficient for whole sample vs adults above 300% FPL: 0.004 (standard error: 0.029). Not statistically significant.

First author, year	Location	Implementation strategy category	Study design	Outcome measures
			(DD) and triple differences (DDD) design.	
Parnes, 2002 (58)	Colorado, USA	59. Place innovation on fee for service lists/formularies	Cross-sectional study (with control group). Analytical.	**Smoking prevalence:** Total number of smokers: n=351/1,443 (24%). OR for smoking. Uninsured: 1.00 (reference group). Medicaid: 1.01, 95% CI: 0.73 to 1.4 (p=0.937). Private/Health Maintenance Organisation (HMO): 0.55, 95% CI: 0.41 to 0.73 (p<0.001). **Record of cessation counselling:** Total number of smokers who received smoking cessation counselling: n=129/351 (37%). OR of receiving cessation counselling. Uninsured: 1.00 (reference group). Medicaid: 2.1, 95% CI: 1.2 to 3.7 (p=0.011). Private/Health Maintenance Organisation (HMO): 3.0, 95% CI: 1.8 to 5.3 (p<0.001).
Tilson, 2004 (63)	Ireland	59. Place innovation on fee for service lists/formularies	Repeated cross-sectional study. Descriptive.	**Prescription for NRT (dispensed?):** May 2001 (free prescriptions for NRT were introduced in April 2001): 6 per 1,000 patients were prescribed NRT. 2002: n=47,147/49,826 (94.6%) patients who received smoking cessation products in 2002 were prescribed NRT. **More detailed outcome data is missing in the paper.

First author, year	Location	Implementation strategy category	Study design	Outcome measures
				Prescription for bupropion (dispensed?): January 2001 (before introduction of free prescriptions for NRT in April 2001): 6 per 1,000 patients were prescribed bupropion. June 2001: 1 per 1,000 patients were prescribed bupropion. 2002: n=2,679/49,826 (5.4%) patients who received smoking cessation products in 2002 were prescribed bupropion. **More detailed outcome data is missing in the paper.
Williams, 2004 (64)	Ireland	59. Place innovation on fee for service lists/formularies	Repeated cross-sectional study. Descriptive.	Proportion read off the graph, Figure 1. **Prescription for bupropion (dispensed?):** Sept 2000: 3.1 per 1,000 patients. Oct 2000: 6.1 per 1,000 patients. Nov 2000: 4.8 per 1,000 patients. Dec 2000: 3 per 1,000 patients. Jan 2001: 6 per 1,000 patients. Feb 2001: 5 per 1,000 patients. Mar 2001: 2.5 per 1,000 patients. Apr 2001: 1.8 per 1,000 patients. May 2001: 1 per 1,000 patients. Jun to Dec 2001: <1 per 1,000 patients. **Prescription for NRT (dispensed?)** (Introduction of NRT to GMS: Apr 2001): Sept 2000 to March 2001: 0 per 1,000 patients. Apr 2001: 6.1 per 1,000 patients. May 2001: 7.2 per 1,000 patients. Jun 2001: 7 per 1,000 patients. Jul 2001: 6.2 per 1,000 patients.

First author, year	Location	Implementation strategy category	Study design	Outcome measures
				Aug 2001: 5.9 per 1,000 patients. Sept 2001: 6.5 per 1,000 patients. Oct 2001: 7.5 per 1,000 patients. Nov 2001: 7.2 per 1,000 patients. Dec 2001: 7.2 per 1,000 patients.
Coleman, 2007 (32)	UK	60. Alter incentive/allowance structures	Repeated cross-sectional study. Analytical.	**Record of smoking status:** "Compared to the first quarter of 2003, there was an increase up to the first quarter of 2004 in recording of smoking status (RR 1.88, 95% CI 1.87–1.89), which was sustained until the first quarter of 2005." **Record of cessation advice:** "Compared to the first quarter of 2003, there was an increase up to the first quarter of 2004 in brief advice to smokers (RR 3.03, 95% CI 2.98–3.09), which was sustained until the first quarter of 2005." **Prescription for NRT/bupropion:** "The incidence of receiving nicotine addiction treatments increased after the year in which these became available on prescription from UK GPs (2000 for bupropion and 2001 for nicotine replacement therapy), but there was no consistent change in this index of smoking cessation activity in the period leading up to or following the introduction of the contract." "for all patients, temporary increases in the recording of smoking status and (for smokers) brief advice between 1993 and 1995 and sustained increases from around the turn of the millennium with an acceleration in this trend from 2003." "The absolute increase in the annual incidence of recording smoking status from the

First author, year	Location	Implementation strategy category	Study design	Outcome measures
				year 2000 was more marked in the disease-specific cohorts (those with a diagnosis of COPD, ischaemic heart disease or diabetes). This was slightly lower for those with a diagnosis of stroke/TIA, hypertension and asthma." "the absolute increase is seen to be much greater in those with one of these conditions than in all patients, but was nevertheless also increased in patients who did not have a diagnosis of the six conditions listed in the GP contract." "prescriptions for nicotine addiction treatments increased steadily in all six 'diseased' cohorts and also in the 'healthy' cohort from 2001, without any acceleration around the introduction of the new contract in any cohort."
Dhalwani, 2013 (38)	UK	60. Alter incentive/allowance structures	Repeated cross-sectional study. Descriptive.	Proportion (%) read off the graph, Figure 1. **Record of smoking status** (imputing data based on QOF): 2000: ~11% of pregnancies with recording of smoking status during gestation. 2001: ~13% 2002: ~15% 2003: ~21% 2004: ~36% 2005: ~39% 2006: ~38% 2007: ~44% 2008: ~43% 2009: ~49%
Farley, 2017 (40)	UK	60. Alter incentive/allowance structures	Cohort study.	**Updating of smoking status:** "Cancer patients were significantly less likely to have their smoking status updated during the first year after diagnosis than control patients (37% vs 78%)." (All cancer patients vs CHD controls, OR: 0.18, (95% CI: 0.17 to 0.19.)

First author, year	Location	Implementation strategy category	Study design	Outcome measures
				All cancers: Pre-QOF: 19% (n=398/2,057) of all cancer patients had a smoking status update within the first year after diagnosis. Post-QOF: 40% (n=4,143/10,336) of all cancer patients had a smoking status update within the first year after diagnosis. CHD control: Pre-QOF: 61% (n=1,282/2,116) of all CHD patients had a smoking status update within the first year after diagnosis. Post-QOF: 81% (n=8,345/10,277) of all CHD patients had a smoking status update within the first year after diagnosis. Adjusted OR for post-QOF/pre-QOF for cancer patients and CHD control patients combined: 2.71; 95% CI: 2.44 to 2.99. No statistically significant difference between the change for cancer patients vs the change for CHD patients: p=0.86. **Record of cessation advice:** "Cancer patients were significantly less likely to have a recording of advice to quit (all cancer patients vs CHD controls, OR: 0.38, (95% CI: 0.36 to 0.40))." All cancers: Pre-QOF: 8% (n=166/2,057) of all cancer patients had a record of cessation advice within the first year after diagnosis. Post-QOF: 25% (n=2,628/10,336) of all cancer patients had a record of cessation advice within the first year after diagnosis. CHD control: Pre-QOF: 24% (n=509/2,116) of all CHD patients had a record of cessation advice within the first year after diagnosis. Post-QOF: 49% (n=5,092/10,277) of all CHD patients had a record of cessation advice within the first year after diagnosis.

First author, year	Location	Implementation strategy category	Study design	Outcome measures
				Adjusted OR for post-QOF/pre-QOF for cancer patients and CHD control patients combined: 3.04; 95% CI: 2.73 to 3.38. Statistically significant difference between the change for cancer patients vs the change for CHD patients: p=0.02. **Prescription of smoking cessation medications:** "Cancer patients were significantly less likely to be prescribed smoking cessation medications (all cancer patients vs CHD controls, OR: 0.67, (95% CI: 0.63 to 0.73)." All cancers: Pre-QOF: 13% (n=285/2,116) of all cancer patients received a prescription for smoking cessation medication within the first year after diagnosis. Post-QOF: 22% (n=2,275/10,277) of all cancer patients received a prescription for smoking cessation medication within the first year after diagnosis. CHD control: Pre-QOF: 8% (n=165/2,057) of all CHD patients received a prescription for smoking cessation medication within the first year after diagnosis. Post-QOF: 13% (n=1,339/10,336) of all CHD patients received a prescription for smoking cessation medication within the first year after diagnosis. Adjusted OR for post-QOF/pre-QOF for cancer patients and CHD control patients combined: 1.79; 95% CI: 1.56 to 2.05. No statistically significant difference between the change for cancer patients vs the change for CHD patients: p=0.89. **Smoking cessation 1 year-post cancer/CHD diagnosis:** "Of the 3,706 cancer and CHD patients who smoked at diagnosis and had at least 1 smoking status update in the year following diagnosis, 1,359 (36.7%) of patients with cancer and 1,645 (44.4%) of patients with CHD stopped smoking (OR: 0.76; 95% CI: 0.69 to 0.84). Among 2,253 pairs, both of whom had smoking status updated and

First author, year	Location	Implementation strategy category	Study design	Outcome measures
				survived at least 1 year, 863 (38.3%) with cancer and 1,004 (44.6%) with CHD stopped smoking (OR: 0.82; 95% CI: 0.72 to 0.93)." All cancers: Pre-QOF: 33.95% (n=110/324) of all cancer patients quit smoking within the first year after diagnosis. Post-QOF: 36.9% (n=1,249/3,382) of all cancer patients quit smoking within the first year after diagnosis. CHD control: Pre-QOF: 40.9% (n=139/340) of all CHD patients quit smoking within the first year after diagnosis. Post-QOF: 44.7% (n=1,506/3,366) of all CHD patients quit smoking within the first year after diagnosis. Adjusted OR for post-QOF/pre-QOF for cancer patients and CHD control patients combined: 1.18; 95% CI: 0.94 to 1.49. No statistically significant difference between the change for cancer patients vs the change for CHD patients: p=0.95.
Fichera, 2016 (45)	England	60. Alter incentive/allowance structures	Repeated cross-sectional study. Regression discontinuity design (with control).	**Number of cigarettes smoked per day** (n=10,924): Before: 3.80 After: 3.20 Statistically significant difference, p=0.004 Local linear regression, optimal bandwidth (3.4 years): coefficient: -0.70 (SD: 0.29), p<0.01. (n=19,663). **Recall of receiving cessation advice:** Polynomial regression, Model 1 (with best polynomial order): coefficient 0.02 (SD: 0.02), not statistically significant. (n=21,418)

First author, year	Location	Implementation strategy category	Study design	Outcome measures
				Recall of receiving prescription for cessation medication: Polynomial regression, Model 1 (with best polynomial order): coefficient -0.04 (SD: 0.04), not statistically significant. (n=23,346)
Hardy, 2014 (39)	UK	60. Alter incentive/allowance structures	Repeated cross-sectional study. Descriptive.	Proportion (%) read off the graph, Figure 1. **Record of cessation advice:** 2000: ~7% of pregnant smokers recorded to be given smoking cessation advice. 2001: ~8% 2002: ~11% 2003: ~15% 2004: ~33% 2005: ~37% 2006: ~26% 2007: ~29% 2008: ~26% 2009: ~29%
McGovern, 2008 (43)	Scotland	60. Alter incentive/allowance structures	Repeated cross-sectional study. Analytical.	**Record of smoking status:** Pre-contract (March 2004): 69.5% (n=35,095) of patients had smoking status recorded. Post-contract (March 2005): 95.7% (n=71,747) of patients had smoking status recorded. Statistically significant increase, $p<0.05$. **Patients with missing data (e.g. smoking status) were excluded from the analysis of that factor.

First author, year	Location	Implementation strategy category	Study design	Outcome measures
				Record of cessation advice: Pre-contract (March 2004): 81.0% (n=9,904) of smokers given advice. Post-contract (March 2005): 96.2% (n=31,881) of smokers given advice. Statistically significant increase, p<0.05. **Patients with missing data (e.g. smoking status) were excluded from the analysis of that factor.
Millett, 2007 (44)	UK	60. Alter incentive/allowance structures	Cohort study.	**Record of smoking status:** 2003: 90.0% of patients with diabetes had ever had smoking status recorded. 2005: 98.8% of patients with diabetes had ever had smoking status recorded. Statistically significant increase, p<0.001. 2003: 67.6% of patients with diabetes whose smoking status was recorded in the 15 months before the 2003 study period. 2005: 86.7% of patients with diabetes whose smoking status was recorded in the 15 months before the 2005 study period. Statistically significant increase, p<0.001. **Record of cessation advice:** 2003: 48.0% of patients with diabetes who were given smoking cessation advice in the 15 months before the 2003 study period. 2005: 83.5% of patients with diabetes who were given smoking cessation advice in the 15 months before the 2005 study period. Statistically significant increase, p<0.001. **Smoking prevalence:** 2003: 20.0% of patients with diabetes who were smokers during the 2003 study period.

First author, year	Location	Implementation strategy category	Study design	Outcome measures
				2005: 16.2% of patients with diabetes who were smokers during the 2005 study period. Statistically significant decrease, p<0.001.
Simpson, 2006 (49)	Scotland	60. Alter incentive/allowance structures	Repeated cross-sectional study. Analytical.	**Record of smoking status:** Precontract: 41.1% (n=8,990) of patients with a history of stroke/TIA who had a recording of smoking status. Postcontract: 90.6% (n=27,019) of patients with a history of stroke/TIA who had a recording of smoking status. Difference: 49.4%, 95% CI: 48.7 to 50.2. **Record of cessation advice:** Precontract: 79.0% (n=3,081) of patients with a history of stroke/TIA who smoke who had a record of cessation advice. Postcontract: 95.9% (n=13,021) of patients with a history of stroke/TIA who smoke who had a record of cessation advice. Difference: 17.0%, 95% CI: 15.7 to 18.3.
Sutton, 2010 (47)	Scotland	60. Alter incentive/allowance structures	Repeated cross-sectional study. Analytical.	**Record of smoking status:** "Rates of recording are higher than the reference risk factor (alcohol consumption) for blood pressure, smoking status and BMI." Model 1: Coefficient of 'smoking status' is 0.480 (z: 202.2), where the reference category is 'alcohol status' (which was not incentivised by the QOF scheme). However: The coefficient on the dummy variable indicating that a disease-factor is incentivised is reduced when a variable is introduced to reflect the higher rates of recording of the incentivised disease-factor combinations prior to the introduction of the QOF (Model (2)) (Smoking status coefficient becomes -0.132 (z: -32.4)). The effect

First author, year	Location	Implementation strategy category	Study design	Outcome measures
				is further reduced when the variables capturing the dynamic process are introduced (Model (3)) (Smoking status coefficient becomes -0.138 (z: -33.8)).
Szatkowski, 2010 (29)	UK	60. Alter incentive/allowance structures	Repeated cross-sectional study. Descriptive.	**Record of smoking status:** The proportion of new patients annually who have their smoking status recorded within 90 days of registration has steadily increased between 1990 and 2006. 1990: 25.8% of patients had their smoking status recorded at registration, but 63.1% of patients lacked a recording of smoking status 1 year after registration. 2006: 73.3% of new patients had their smoking status recorded within 90 days of registering, but 16.6% patients (19.4% men and 14.1% women) lacked a recording of smoking status 1 year after registration. "In all years, there was considerable variation between practices in the recording of recently registered patients' smoking status; e.g. in 2006, while one practice recorded the smoking status of all its new patients, the worst performer did so in just 7.8% of cases (IQR: 62.5% to 88.2%)."
Szatkowski, 2011 (28)	England	60. Alter incentive/allowance structures	Repeated cross-sectional study. Descriptive.	Proportion (%) read off the graph, Figure 1. THIN: **Record of cessation advice:** 2000-2003: <3% of patients had a record of cessation advice. 2004: ~7% of patients had a record of cessation advice. 2005-2009: ~10% of patients had a record of cessation advice. (10.9% in 2009.) "Majority of increase occurred between 2003 and 2005." PCT Patient Survey: **Recall of receiving cessation advice:**

First author, year	Location	Implementation strategy category	Study design	Outcome measures
				2004: 6.6% of patients had recalled receiving cessation advice. 2005: ~7% of patients had recalled receiving cessation advice. 2008: 8.3% of patients had recalled receiving cessation advice.
Szatkowski, 2016 (27)	England	60. Alter incentive/allowance structures	Repeated cross-sectional study. Interrupted time series analysis (no control).	Two analyses reported: Pre: Apr 2004 to Mar 2012, Post: Apr 2012 to Apr 2013. **Record of cessation advice:** 19.6% change, 95% CI: 7.9 to 31.4, p<0.001. **Referral to NHS Stop Smoking Service:** 38.8% change, 95% CI: 15.2 to 62.4, p<0.001. **Prescription for pharmacotherapy (NRT/bupropion/varenicline):** -7.7% change, 95% CI: -21.6 to 6.2, p=0.280. Pre: Apr 2010 to Mar 2012, Post: Apr 2012 to Apr 2013. **Record of cessation advice:** 18.9% change, 95% CI: 9.9 to 27.9, p<0.001. **Referral to NHS Stop Smoking Service:** 38.1% change, 95% CI: 19.3 to 57.0, p<0.001. **Prescription for pharmacotherapy (NRT/bupropion/varenicline):** -13.8% change, 95% CI: -21.0 to -6.5, p<0.001.
Taggar, 2012 (30)	UK	60. Alter incentive/allowance structures	Repeated cross-sectional study. Descriptive.	Proportion (%) read off the graph, Figure 1. **Record of smoking status:** 2000: ~19% of patients had a record of smoking status. 2001: ~20% 2002: ~26% 2003: ~31% 2004: ~45% 2005: ~57% 2006: ~59%

First author, year	Location	Implementation strategy category	Study design	Outcome measures
				2007: ~63% 2008: 64.5% **Record of cessation advice:** 2000: ~6% of current smoker patients had a record of cessation advice. 2001: ~9% 2002: ~11% 2003: ~12% 2004: ~32% 2005: ~45% 2006: ~42% 2007: ~49% 2008: 50.5% "A substantial acceleration in recording of both smoking status and cessation advice was observed between 2003 and 2005, although rates of increase plateaued after 2006. "
Tahrani, 2007 (42)	England	60. Alter incentive/allowance structures	Repeated cross-sectional study. Analytical.	**Record of smoking status:** April 2004 (pre-intervention): mean 44% (SD: 14). March 2005 (post-intervention): mean 96% (SD: 4). March 2006 (post-intervention): mean 95% (SD: 4). Difference in means between (April 2004) and (March 2006): 95% CI: -54.7 to -47.3, p<0.001. **Record of cessation advice:** April 2004 (pre-intervention): N/A. March 2005 (post-intervention): mean 95% (SD: 7).

First author, year	Location	Implementation strategy category	Study design	Outcome measures
				March 2006 (post-intervention): mean 96% (SD: 5). Difference in means between (October 2004) and (March 2006), as data for April 2004 was not available: 95% CI: -15.2 to -9.2, p<0.001. **Missing: October 2004 value.
Donner-Banzhoff, 1996 (75)	Germany vs UK	65. Use capitated payments	Cross-sectional study (comparing two groups). Analytical.	**Recall receiving "any cessation intervention":** Germany (Fee-For-Service): 55.7% of current and ex-smokers (n=103/185). UK (Capitation): 51.7% of current and ex-smokers (n=108/209). Not statistically significant difference, OR: 1.17, 95% CI: 0.79 to 1.75. Germany (Fee-For-Service): 64.8% of current smokers (n=68/105). UK (Capitation): 64.7% of current smokers (n=77/119). Not statistically significant difference, OR: 1.0, 95% CI: 0.58 to 1.74. **Recall of receiving cessation "advice once":** OR: 1.9, 95% CI: 1.2 to 3.1. (n=386 smokers and ex-smokers in Germany and the UK). **Recall of receiving cessation "advice several times":** OR: 0.7, 95% CI: 0.4 to 1.0. (n=386 smokers and ex-smokers in Germany and the UK). **Recall of receiving "nicotine patch/gum":** OR: 1.0, 95% CI: 0.4 to 2.6. (n=386 smokers and ex-smokers in Germany and the UK).
Domain 9. Change infrastructure				

First author, year	Location	Implementation strategy category	Study design	Outcome measures
Szatkowski, 2021 (36)	England	66. Mandate change	Repeated cross-sectional study. Segmented regression analysis, no control.	**Prescription for any NRT:** Absolute annual percentage change in prescribing 2005 to 2012: -0.25, 95% CI: -0.36 to -0.15, p<0.001. Percentage change in trend from 2012 to 2013: -1.125, 95% CI: -1.35 to -0.88, p<0.001. Absolute annual percentage change in prescribing 2013 to 2017 (annual change 2005 to 2012 + change in trend 2012 to 2013): -1.37, 95% CI: -1.52 to -1.21, p<0.001. **Prescription for dual NRT:** Absolute annual percentage change in prescribing 2005 to 2012: 0.34, 95% CI: 0.26 to 0.42, p<0.001. Percentage change in trend from 2012 to 2013: -0.76, 95% CI: -0.93 to -0.60, p<0.001. Absolute annual percentage change in prescribing 2013 to 2017 (annual change 2005 to 2012 + change in trend 2012 to 2013): -0.42, 95% CI: -0.53 to -0.31, p<0.001.
Dhalwani, 2014 (41)	UK	69. Create or change credentialing and/or licensure standards	Repeated cross-sectional study. Descriptive.	Proportion (%) read off the graph, Figure 2. **Prescription for NRT in all pregnancies, during pregnancy:** 2001: ~0% (prescribing prevalence of NRT in all pregnancies) 2002: ~0.5% 2003: ~1% 2004: ~1.8% 2005: ~2.6% 2006: ~2.7% 2007: ~2.6% 2008: ~2.4% 2009: ~2.5% 2010: ~2.3%

First author, year	Location	Implementation strategy category	Study design	Outcome measures
				2011: ~2.5% 2012: ~2.3% **Prescription for NRT in all pregnant smokers, during pregnancy:** 2001: ~0.7% (prescribing prevalence of NRT in pregnant smokers) 2002: ~7% 2003: ~10% 2004: ~11% 2005: ~11.4% 2006: ~12% 2007: ~11.4% 2008: ~10% 2009: ~11.3% 2010: ~10% 2011: ~10.5% 2012: ~10%
Langley, 2011 (34)	England	69. Create or change credentialing and/or licensure standards	Repeated cross-sectional study. Segmented regression analysis (no control).	Baseline trend (monthly change in number of prescriptions per 100,000 adolescents before licensing change); level change (step change in the monthly level of prescribing immediately after licensing change); trend change (absolute change in trend in monthly numbers of prescriptions per 100,000 adolescents after licensing change, compared with baseline trend). **Prescription for NRT:** All: Baseline trend: 1.36, 95% CI: 1.16 to 1.55, p<0.001. Level change: N/A. Trend change: -1.16, 95% CI: -1.52 to -0.79, p<0.001. 12-13 year olds: Baseline trend: 0.09, 95% CI: 0.07 to 0.12, p<0.001. Level change: N/A. Trend change: N/A.

First author, year	Location	Implementation strategy category	Study design	Outcome measures
				14-15 year olds: Baseline trend: 1.08, 95% CI: 0.82 to 1.34, p<0.001. Level change: 19.29, 95% CI: 9.02 to 29.59, p<0.001. Trend change: -1.13, 95% CI: -1.51 to -0.74, p<0.001. 16-17 year olds: Baseline trend: 2.62, 95% CI: 2.16 to 3.08, p<0.001. Level change: N/A. Trend change: -2.73, 95% CI: -3.59 to -1.88, p<0.001. Females: Baseline trend: 1.66, 95% CI: 1.42 to 1.91, p<0.001. Level change: N/A. Trend change: -1.65, 95% CI: -2.10 to -1.20, p<0.001. Males: Baseline trend: 0.87, 95% CI: 0.59 to 1.16, p<0.001. Level change: 13.37, 95% CI: 2.21 to 24.52, p=0.02. Trend change: -0.76, 95% CI: -1.19 to -0.33, p<0.001.
Langley, 2012 (35)	England	69. Create or change credentialing and/or licensure standards	Repeated cross-sectional study. Segmented regression analysis (no control).	Baseline trend (monthly change in number of prescriptions per 100,000 patients before licensing change); level change (step change in the monthly level of prescribing immediately after licensing change); trend change (absolute change in trend in monthly numbers of prescriptions per 100,000 patients after licensing change, compared with baseline trend). **Prescription for NRT:** CHD: Baseline trend: 3.18, 95% CI: 2.15 to 4.21, p<0.0001. Level change: N/A. Trend change: -6.45, 95% CI: -8.36 to -4.53, p<0.0001. Stroke: Baseline trend: 3.37, 95% CI: 2.31 to 4.43, p<0.0001. Level change: N/A. Trend change: -5.99, 95% CI: -7.96 to -4.01, p<0.0001. **Prescription for all licensed smoking cessation medications (NRT, varenicline, bupropion):** CHD: Baseline trend: 2.73, 95% CI: 1.23 to 4.25, p<0.001. Level change: N/A. Trend change: -3.07, 95% CI: -5.87 to -0.26, p=0.035.

First author, year	Location	Implementation strategy category	Study design	Outcome measures
				Stroke: Baseline trend: 3.29, 95% CI: 1.81 to 4.76, p<0.0001. Level change: N/A. Trend change: -3.76, 95% CI: -6 to -1.02, p=0.009.
Li, 2020 (55)	United States (multi-state)	69. Create or change credentialing and/or licensure standards	Repeated cross-sectional study. Analytical.	**Record of assist to quit (1)** ("referrals to smoking cessation programs" or "informal smoking cessation counselling"): **these outcome measures were grouped by the authors. Pre-guideline (2010-2013): 27.1% (n=1,513/5,580). Post-guideline (2014-2017): 27.0% (n=1,916/7,098). Not statistically significant change, p=0.87881. Model A (after controlling for age, sex, race/ethnicity, and level of smoking), post- versus pre-guideline OR: 1.29, 95% CI: 1.15 to 1.46, p<0.05. **Record of assist to quit (2)** ("formal in-visit smoking cessation counselling"): Pre-guideline (2010-2013): 0.9% (n=49/5,580). Post-guideline (2014-2017): 2.7% (n=194/7,098). Statistically significant change, p<0.0001. Model A (after controlling for age, sex, race/ethnicity, and level of smoking), post- versus pre-guideline OR: 5.03, 95% CI: 3.05 to 8.30, p<0.05. **Prescription for smoking cessation pharmacotherapy (bupropion, varenicline, NRT)** ("medication orders for pharmacotherapy"): Pre-guideline (2010-2013): 4.3% (n=238/5,580). Post-guideline (2014-2017): 5.2% (n=371/7,098). Statistically significant change, p=0.01196. Model A (after controlling for age, sex, race/ethnicity, and level of smoking), post- versus pre-guideline OR: 1.24, 95% CI: 1.02 to 1.50, p<0.05. **Receipt of any smoking cessation intervention(s):**

First author, year	Location	Implementation strategy category	Study design	Outcome measures
				Pre-guideline (2010-2013): 30.6% (n=1,708/5,580). Post-guideline (2014-2017): 32.7% (n=2,323/7,098). Statistically significant change, p=0.01101. Model A (after controlling for age, sex, race/ethnicity, and level of smoking), post- versus pre-guideline OR: 1.44, 95% CI: 1.28 to 1.61, p<0.05. **Cigarettes smoked per day:** Pre-guideline (2010-2013): 15.2 (SD: 10.5) (n=5,580). Post-guideline (2014-2017): 14.2 (SD: 9.9) (n=7,098). Statistically significant change, p<0.0001.
Thorndike, 2007 (53)	United States (multi-state)	69. Create or change credentialing and/or licensure standards	Repeated cross-sectional study. Analytical.	**Record of smoking status:** 1994-1996: 68% of primary care physicians identified patients' smoking status at all visits (weighted to reflect national estimates). 2001-2003: 70% of primary care physicians identified patients' smoking status at all visits (weighted to reflect national estimates). Adjusted OR: 1.10, 95% CI: 0.94 to 1.32. (Adjusted for patient demographics, physician specialty, and diagnosis.) **Record of cessation counselling:** 1994-1996: Primary care physicians recorded smoking counselling at 30% of smokers' visits (weighted to reflect national estimates). 2001-2003: Primary care physicians recorded smoking counselling at 26% of smokers' visits (weighted to reflect national estimates). Adjusted OR: 0.81, 95% CI: 0.65 to 1.00. (Adjusted for patient demographics, physician specialty, and diagnosis.)

First author, year	Location	Implementation strategy category	Study design	Outcome measures
				Prescription for pharmacotherapy (NRT and bupropion): **Results not available for primary care physicians.
Peterson, 2016 (52)	United States (multi-state)	71. Change accreditation or membership requirements	Repeated cross-sectional study. Analytical.	**Record of cessation counselling** (physician-reported): **Raw data missing. "the rate of physician-reported counseling for ... smoking cessation was above 90% post-intervention." **Recall of receiving cessation counselling** (patient questionnaire): (n=7,319) Pre: 92.5% of patients who smoke report that their "doctor talked to you about quitting". Post: 96.1% of patients who smoke report that their "doctor talked to you about quitting". Statistically significant difference: p<0.05. "Small increases were seen for quality measures that were already at high levels prior to the intervention with the percentage of patients who reported receiving smoking cessation counseling increasing from 92.5% to 96.1%."
Shi, 2017 (59)	United States (multi-state)	71. Change accreditation or membership requirements	Cross-sectional study (with control group). Analytical.	**Record of smoking status:** PCMH recognition in 2012 (n=539 practices): 87.64% (0.69) of adults assessed for tobacco use. No PCMH recognition in 2012 (n=548 practices): 83.85% (0.81) of adults assessed for tobacco use. Statistically significant difference: p<0.001. Regression coefficient: 3.0079 (SE: 1.3256), p<0.05. (n=1,193). PCMH recognition status was positively associated with being assessed for tobacco use. **Record of cessation intervention:**

First author, year	Location	Implementation strategy category	Study design	Outcome measures
				PCMH recognition in 2012 (n=539 practices): 59.9% (1.05) of adults who were known tobacco users that received tobacco cessation counselling and/or pharmacologic intervention. No PCMH recognition in 2012 (n=548 practices): 55.51% (1.14) of adults who were known tobacco users that received tobacco cessation counselling and/or pharmacologic intervention. Statistically significant difference: p<0.01. Regression coefficient: 3.7993 (SE: 1.7852), p<0.05. (n=1,175). PCMH recognition status was positively associated with receiving tobacco cessation intervention.
Van Doorn-Klomberg, 2014 (68)	Netherlands	71. Change accreditation or membership requirements	Cohort study.	**Smoking prevalence:** 1st cohort, 2006-2008: 36.6% (SD: 22.9) of patients with COPD smoked. 1st cohort, 2009-2011: 31.8% (SD: 16.1) of patients with COPD smoked. Difference: -4.9% (95% CI: -11.5 to 1.8), p=0.15. 2nd cohort, 2009-2011: 32.2% (SD: 20.7) of patients with COPD smoked. Difference between 1st cohort 2009-2011 and 2nd cohort 2009-2011: -0.4% (95% CI: -6.9 to 6.2), p=0.92. 1st cohort, 2006-2008: not available. 1st cohort, 2009-2011: 12.6% (SD: 8.5) of patients with CVD smoked. Difference: not available. **"The inclusion criteria for patients with risk for cardiovascular disease changed towards the inclusion of patients with known cardiovascular disease only, which made a within-group comparison of the first cohort not justifiable." 2nd cohort, 2009-2011: 10.5% (SD: 7.8) of patients with CVD smoked. Difference between 1st cohort 2009-2011 and 2nd cohort 2009-2011: 1.9% (95% CI: -

First author, year	Location	Implementation strategy category	Study design	Outcome measures
				1.1 to 4.9), p=0.20. **Record of smoking status:** 1st cohort, 2006-2008: 76.0% (SD: 21.4) of patients with COPD had known smoking status. 1st cohort, 2009-2011: 75.4% (SD: 23.2) of patients with COPD had known smoking status. Difference: -1.3% (95% CI: -8.1 to 5.6), p=0.71. 2nd cohort, 2009-2011: 69.4% (SD: 27.0) of patients with COPD had known smoking status. Difference between 1st cohort 2009-2011 and 2nd cohort 2009-2011: 6.1% (95% CI: -2.8 to 15.0), p=0.18. 1st cohort, 2006-2008: not available. 1st cohort, 2009-2011: 51.7% (SD: 26.6) of patients with CVD had known smoking status. Difference: not available. **"The inclusion criteria for patients with risk for cardiovascular disease changed towards the inclusion of patients with known cardiovascular disease only, which made a within-group comparison of the first cohort not justifiable." 2nd cohort, 2009-2011: 39.8% (SD: 25.5) of patients with CVD had known smoking status. Difference between 1st cohort 2009-2011 and 2nd cohort 2009-2011: 11.3% (95% CI: 1.9 to 20.8), p=0.02. **Record of cessation advice:**

First author, year	Location	Implementation strategy category	Study design	Outcome measures
				1st cohort, 2006-2008: 47.0% (SD: 33.9) of patients with COPD who smoked had a record of stop smoking advice. 1st cohort, 2009-2011: 69.8% (SD: 30.8) of patients with COPD who smoked had a record of stop smoking advice. Difference: 21.9% (95% CI: 8.7 to 34.9), p=0.002. 2nd cohort, 2009-2011: 65.2% (SD: 32.6) of patients with COPD who smoked had a record of stop smoking advice. Difference between 1st cohort 2009-2011 and 2nd cohort 2009-2011: 5.1% (95% CI: -10.1 to 20.2), p=0.51. 1st cohort, 2006-2008: not available. 1st cohort, 2009-2011: 66.7% (SD: 34.2) of patients with CVD had known smoking status. Difference: not available. **"The inclusion criteria for patients with risk for cardiovascular disease changed towards the inclusion of patients with known cardiovascular disease only, which made a within-group comparison of the first cohort not justifiable." 2nd cohort, 2009-2011: 51.1% (SD: 34.0) of patients with CVD had known smoking status. Difference between 1st cohort 2009-2011 and 2nd cohort 2009-2011: 13.2% (95% CI: -4.6 to 30.9), p=0.14.
Multiple domains				

First author, year	Location	Implementation strategy category	Study design	Outcome measures
Akman, 2017 (72)	Turkey	Domain 8. 65. Use capitated payments AND Domain 9. 66. Mandate change, 67. Change record systems, 71. Change accreditation or membership requirements	Repeated cross-sectional study. Analytical.	**Rate of cessation counselling:** Proportion of primary care doctors who report being "usually or almost always involved in smoking counselling during outpatient clinic" (From Supplementary Table 2): 1993: n=146 (82.0%) 2012: n=253 (84.6%) **Denominators are not included in the paper. The total number of respondents were n=199 in 1993 and n=299 in 2012 but it is not stated how many participants responded to the individual survey questions. Percentage change: +3.1 (p>0.05), not statistically significant.
Bailey, 2017 (50)	Oregon, USA	Domain 8. 60. Alter incentive/allowance structures AND	Repeated cross-sectional study. Analytical.	**Record of smoking status:** 2010: 93.90% (n=52,019/55,398) of non-pregnant patients have smoking status assessed. 2012: 96.16% (n=58,282/60,610) of non-pregnant patients have smoking status assessed. 2014: 97.41% (n=64,981/66,712) of non-pregnant patients have smoking status assessed. 2014 vs 2010 (ref), adjusted OR: 2.52, 95% CI: 2.37 to 2.69, p<0.0001.

First author, year	Location	Implementation strategy category	Study design	Outcome measures
		Domain 9. 67. Change record systems		2012 vs 2010 (ref), adjusted OR: 1.54, 95% CI: 1.46 to 1.63, p<0.0001. 2014 vs 2012 (ref), adjusted OR: 1.58, 95% CI: 1.47 to 1.69, p<0.0001. **Smoking prevalence:** 2010: 30.33% (n=16,802/55,398) of non-pregnant patients were current smokers. 2012: 29.09% (n=17,631/60,610) of non-pregnant patients were current smokers. 2014: 27.15% (n=18,111/66,712) of non-pregnant patients were current smokers. 2014 vs 2010 (ref), adjusted OR: 0.81, 95% CI: 0.79 to 0.83, p<0.0001. 2012 vs 2010 (ref), adjusted OR: 0.93, 95% CI: 0.90 to 0.96, p<0.0001. 2014 vs 2012 (ref), adjusted OR: 0.85, 95% CI: 0.79 to 0.82, p<0.0001. **Record of cessation counselling:** 2010: 29.75% (n=4,998/16,802) of non-pregnant smoker patients were given counselling. 2012: 53.88% (n=9,500/17,631) of non-pregnant smoker patients were given counselling. 2014: 69.49% (n=12,585/18,110) of non-pregnant smoker patients were given counselling. 2014 vs 2010 (ref), adjusted OR: 7.76, 95% CI: 7.35 to 8.20, p<0.0001. 2012 vs 2010 (ref), adjusted OR: 3.66, 95% CI: 3.48 to 3.85, p<0.0001. 2014 vs 2012 (ref), adjusted OR: 2.24, 95% CI: 2.13 to 2.35, p<0.0001. **Prescription for cessation medications (NRT, varenicline, bupropion):** 2010: 12.09% (n=2,032/16,802) of non-pregnant smoker patients were ordered cessation medication. 2012: 13.26% (n=2,338/17,631) of non-pregnant smoker patients were ordered

First author, year	Location	Implementation strategy category	Study design	Outcome measures
				cessation medication. 2014: 15.68% (n=2,839/18,110) of non-pregnant smoker patients were ordered cessation medication. 2014 vs 2010 (ref), adjusted OR: 1.15, 95% CI: 1.07 to 1.23, p<0.0001. 2012 vs 2010 (ref), adjusted OR: 1.00, 95% CI: 0.93 to 1.07, not statistically significant. 2014 vs 2012 (ref), adjusted OR: 1.1, 95% CI: 1.03 to 1.17, p<0.01. **Record of cessation medication "ordered and/or discussed":** 2010: 27.60% (n=4,638/16,802) of non-pregnant smoker patients were ordered cessation medication and/or discussed cessation medication. 2012: 39.63% (n=6,987/17,631) of non-pregnant smoker patients were ordered cessation medication and/or discussed cessation medication. 2014: 48.30% (n=8,747/18,110) of non-pregnant smoker patients were ordered cessation medication and/or discussed cessation medication. 2014 vs 2010 (ref), adjusted OR: 2.25, 95% CI: 2.14 to 2.37, p<0.0001. 2012 vs 2010 (ref), adjusted OR: 1.65, 95% CI: 1.57 to 1.73, p<0.0001. 2014 vs 2012 (ref), adjusted OR: 1.38, 95% CI: 1.32 to 1.45, p<0.0001.
Fortmann, 2020 (56)	United States (multi-state)	Domain 8. 60. Alter incentive/allowance structures AND	Cohort study. Interrupted time series analysis (no control).	Proportion (%) read off the graph, Figure 1. **Record of smoking status:** Smoking status documentation for all CHCs combined. 2006: ~30%. 2007: ~42%. 2008: ~45%. 2009: ~50%.

First author, year	Location	Implementation strategy category	Study design	Outcome measures
		Domain 9. 71. Change accreditation or membership requirements		2010: ~50%. 2011: ~50%. 2012: ~80%. 2013: ~90%. "The interrupted time series analysis showed that the increase in documentation rate between 2011 and 2012 of 21.3% (95% CI: 8.2% to 34.4%) from the current trend was statistically significant, p=0.011."
Langley, 2011 (37)	England	Domain 8. 59. Place innovation on fee for service lists/formularies AND Domain 9. 69. Create or change credentialing and/or licensure standards	Repeated cross-sectional study. Interrupted time series analysis (no control).	**Prescription for NRT, varenicline or bupropion (all):** Change in prescribing (%) after the introduction of varenicline: -0.42, 95% CI: -3.10 to 2.27, p=0.760. Change in prescribing (%) after the NICE guidance on varenicline: -1.72, 95% CI: -3.96 to 0.53, p=0.134. **Prescription for NRT:** Change in prescribing (%) after the introduction of varenicline: -0.31, 95% CI: -3.11 to 2.49, p=0.828. Change in prescribing (%) after the NICE guidance on varenicline: -1.78, 95% CI: -4.26 to 0.69, p=0.159. **Prescription for bupropion:** Change in prescribing (%) after the introduction of varenicline: -1.17, 95% CI: -3.90 to 1.56, p=0.401. Change in prescribing (%) after the NICE guidance on varenicline: -2.80, 95% CI: -6.22 to 0.61, p=0.108.

First author, year	Location	Implementation strategy category	Study design	Outcome measures
Mullins, 2009 (51)	Delaware, USA	Domain 5. 40. Distribute educational materials. 42. Conduct educational meetings AND Domain 7. 54. Prepare patients/consumers to be active participants	Repeated cross-sectional study. Analytical.	**Smoking prevalence:** Pre-intervention group: 221 out of 922 patients (24.0%) had 'current smoking status' in their electronic health record. Post-intervention group: 547 out of 3,125 patients (17.3%) had 'current smoking status' in their electronic health record. Statistically significant difference, p=0.001. **Record of cessation advice:** Pre-intervention group: 155 out of 221 current smokers (70.1%) had 'advised to quit', 'yes' in their electronic health record. Post-intervention group: 538 out of 547 current smokers (98.3%) had 'advised to quit', 'yes' in their electronic health record. Statistically significant difference, p=0.001.
Verbiest, 2013 (67)	Netherlands	Domain 8. 59. Place innovation on fee for service lists/formularies	Repeated cross-sectional study. Interrupted time series analysis (no	Interventions: (i): introduction of GP guideline (ii): introduction of health insurance coverage for smoking cessation treatment (iii): abolition of health insurance coverage for smoking cessation treatment **Prescription for all cessation medications (NRT/varenicline/bupropion):** Pre- (i) and (ii) and (iii): 0.02 quarterly change in the number of prescriptions per 1,000 smokers, 95% CI: -0.09 to -1.14, p=0.676.

First author, year	Location	Implementation strategy category	Study design	Outcome measures
		AND Domain 9. 69. Create or change credentialing and/or licensure standards	control) (of three nation-wide representative databases).	Post- (i): 0.84 change in the quarterly level of prescriptions per 1,000 smokers, 95% CI: -2.04 to -3.71, p=0.560. (Immediate, level change) Post- (i): -0.10 change in the trend in quarterly number of prescriptions per 1,000 smokers, 95% CI: -0.40 to -0.20, p=0.499. (Trend change) Post- (ii): 6.31 change in the quarterly level of prescriptions per 1,000 smokers, 95% CI: 2.86 to 9.76, p=0.001. (Immediate, level change) **Prescription for bupropion:** Pre- (i) and (ii) and (iii): 0.02 quarterly change in the number of prescriptions per 1,000 smokers, 95% CI: -0.03 to -0.07, p=0.374. Post- (i): 0.12 change in the quarterly level of prescriptions per 1,000 smokers, 95% CI: -1.13 to -1.37, p=0.845. (Immediate, level change) Post- (i): -0.05 change in the trend in quarterly number of prescriptions per 1,000 smokers, 95% CI: -0.18 to -0.08, p=0.475. (Trend change) Post- (ii): 0.91 change in the quarterly level of prescriptions per 1,000 smokers, 95% CI:-0.59 to 2.41, p=0.227. (Immediate, level change) **Prescription for NRT:** Pre- (i) and (ii) and (iii): -0.00 quarterly change in the number of prescriptions per 1,000 smokers, 95% CI: -0.03 to -0.02, p=0.832. Post- (i): 0.11 change in the quarterly level of prescriptions per 1,000 smokers, 95% CI: -0.52 to -0.73, p=0.735. (Immediate, level change) Post- (i): -0.00 change in the trend in quarterly number of prescriptions per 1,000 smokers, 95% CI: -0.07 to -0.07, p=0.986. (Trend change) Post- (ii): 1.97 change in the quarterly level of prescriptions per 1,000 smokers, 95% CI: 1.23 to 2.72, p<0.000. (Immediate, level change) **Prescription for varenicline:**

First author, year	Location	Implementation strategy category	Study design	Outcome measures
				Pre- (i) and (ii) and (iii): 0.01 quarterly change in the number of prescriptions per 1,000 smokers, 95% CI: -0.03 to -0.05, p=0.644. Post- (i): did not assess. Post- (i): did not assess. Post- (ii): 2.97 change in the quarterly level of prescriptions per 1,000 smokers, 95% CI: 1.30 to 4.64, p=0.0001. (Immediate, level change) **Dispensed prescription for all cessation medications (NRT/varenicline/bupropion):** Pre- (i) and (ii) and (iii): -0.01 quarterly change in the number of (dispensed) prescriptions per 1,000 smokers, 95% CI: -0.16 to -0.15, p=0.924. Post- (i): 2.68 change in the quarterly level of (dispensed) prescriptions per 1,000 smokers, 95% CI: -1.23 to -6.59, p=0.173. (Immediate, level change) Post- (i): 0.39 change in the trend in quarterly number of (dispensed) prescriptions per 1,000 smokers, 95% CI: -0.02 to -0.79, p=0.060. (Trend change) Post- (ii): 17.26 change in the quarterly level of (dispensed) prescriptions per 1,000 smokers, 95% CI: 12.53 to 21.98, p<0.000. (Immediate, level change) Post- (iii): -21.56 change in quarterly level of (dispensed) prescriptions per 1,000 smokers, 95% CI: -25.93 to -17.19, p<0.000. (Immediate, level change) **Dispensed prescription for bupropion:** Pre- (i) and (ii) and (iii): 0.03 quarterly change in the number of (dispensed) prescriptions per 1,000 smokers, 95% CI: -0.03 to -0.08, p=0.292. Post- (i): -0.31 change in the quarterly level of (dispensed) prescriptions per 1,000 smokers, 95% CI: -1.64 to -1.03, p=0.645. (Immediate, level change) Post- (i): -0.02 change in the trend in quarterly number of (dispensed) prescriptions per 1,000 smokers, 95% CI: -1.28 to 1.92, p=0.688. (Trend change) Post- (ii): 0.32 change in the quarterly level of (dispensed) prescriptions per 1,000 smokers, 95% CI: -1.28 to 1.92, p=0.688. (Immediate, level change)

First author, year	Location	Implementation strategy category	Study design	Outcome measures
				Post- (iii): -0.79 change in quarterly level of (dispensed) prescriptions per 1,000 smokers, 95% CI: -2.27 to 0.69, p=0.288. (Immediate, level change) **Dispensed prescription for NRT:** Pre- (i) and (ii) and (iii): 0.06 quarterly change in the number of (dispensed) prescriptions per 1,000 smokers, 95% CI: 0.01 to 0.11, p=0.026. Post- (i): 0.20 change in the quarterly level of (dispensed) prescriptions per 1,000 smokers, 95% CI: -1.15 to -1.55, p=0.768. (Immediate, level change) Post- (i): 0.01 change in the trend in quarterly number of (dispensed) prescriptions per 1,000 smokers, 95% CI: -0.13 to 0.15, p=0.929. (Trend change) Post- (ii): 5.45 change in the quarterly level of (dispensed) prescriptions per 1,000 smokers, 95% CI: 3.82 to 7.08, p<0.000. (Immediate, level change) Post- (iii): -5.86 change in quarterly level of (dispensed) prescriptions per 1,000 smokers, 95% CI: -7.37 to -4.35, p<0.000. (Immediate, level change) **Dispensed prescription for varenicline**: Pre- (i) and (ii) and (iii): 0.02 quarterly change in the number of (dispensed) prescriptions per 1,000 smokers, 95% CI: -0.07 to -0.12, p=0.618. Post- (i): did not assess. Post- (i): did not assess. Post- (ii): 4.72 change in the quarterly level of (dispensed) prescriptions per 1,000 smokers, 95% CI: 0.65 to 8.79, p=0.024. (Immediate, level change) Post- (iii): -11.30 change in quarterly level of (dispensed) prescriptions per 1,000 smokers, 95% CI: -16.05 to -6.55, p<0.000. (Immediate, level change) **Smoking prevalence:** Pre- (i) and (ii) and (iii): -0.14 quarterly change in smoking prevalence (%), 95% CI: -0.20 to -0.09, p<0.000.

First author, year	Location	Implementation strategy category	Study design	Outcome measures
				Post- (i): -0.15 change in the quarterly level of smoking prevalence (%), 95% CI: -1.60 to -1.30, p=0.835. (Immediate, level change) Post- (i): 0.17 change in the trend in quarterly smoking prevalence (%), 95% CI: 0.02 to 0.32, p=0.028. (Trend change) Post- (ii): -2.90 change in the quarterly level of smoking prevalence (%), 95% CI: 4.61 to -1.11, p=0.002. (Immediate, level change) Post- (iii): 1.16 change in quarterly level of smoking prevalence (%), 95% CI: 0.50 to 2.8, p=0.156. (Immediate, level change)

The included studies are ordered by implementation strategy domain (5, 7, 8 and 9 and 'Multiple domains'). Within the domains, the studies are ordered by implementation strategy category then alphabetically by first author surname.

(Wright, 2018) was excluded from narrative synthesis as it was at critical risk, but it is included in this table.

Appendix C. Supplementary material for Chapter 4

Supplementary Box 1. Relevant studies identified by systematic literature search

We conducted a systematic literature search of MEDLINE (OVID) for articles published from 1946 to 8 August 2023 using the following subject headings and key words: ("e-cigarette$" OR "electronic nicotine delivery system$" OR "vaping" OR "vape$" OR "electronic cigarette$") AND ("electronic health$" OR "electronic medical" OR "electronic patient$" OR "medic$ info$ system$"). The search yielded 36 records of which 13 were relevant. All studies were from the United States.

D'Angelo, H., Land, S.R. and Mayne, R.G. (2021) 'Assessing Electronic Nicotine Delivery Systems Use at NCI-Designated Cancer Centers in the Cancer Moonshot-funded Cancer Center Cessation Initiative', *Cancer prevention research (Philadelphia, Pa.)*, 14(8), pp. 763–766. Available at: https://doi.org/10.1158/1940-6207.CAPR-21-0105.

Heiden, B.T. *et al.* (2022) 'Assessment of formal tobacco treatment and smoking cessation in dual users of cigarettes and e-cigarettes', *Thorax*, 78(3), pp. 267–273. Available at: https://doi.org/10.1136/THORAX-2022-218680.

Hurst, S. and Conway, M. (2018) 'Exploring Physician Attitudes Regarding Electronic Documentation of E-cigarette Use: A Qualitative Study', *Tobacco use insights*, 11, pp. 1179173X18782879-1179173X18782879. Available at: https://doi.org/10.1177/1179173X18782879.

Jose, T., Hays, J.T. and Warner, D.O. (2020) 'Improved Documentation of Electronic Cigarette Use in an Electronic Health Record', *International journal of environmental research and public health*, 17(16), p. 5908. Available at: https://doi.org/10.3390/ijerph17165908.

Khanna, N. *et al.* (2023) 'Integrating a Systematic, Comprehensive E-Cigarette and Vaping Assessment Tool into the Electronic Health Record', *The Journal of the American Board of Family Medicine*, 36(3), pp. 405–413. Available at: https://doi.org/10.3122/JABFM.2022.220410R1.

Kovach, K.A. *et al.* (2021) 'Co-creating opportunities to incorporate cessation for electronic nicotine delivery systems in family medicine - a qualitative program evaluation', *BMC family practice*, 22(1). Available at: https://doi.org/10.1186/S12875-021-01520-X.

LeLaurin, J.H. *et al.* (2020) 'Tobacco-Related Counseling and Documentation in Adolescent Primary Care Practice: Challenges and Opportunities', *Nicotine & tobacco research : official journal of the Society for Research on Nicotine and Tobacco*, 22(6), pp. 1023–1029. Available at: https://doi.org/10.1093/ntr/ntz076.

Rodriguez, Z.C. *et al.* (2021) 'Vaping: Impact of Improving Screening Questioning in Adolescent Population: A Quality Improvement Initiative', *Pediatric Quality & Safety*, 6(1), p. e370. Available at: https://doi.org/10.1097/PQ9.0000000000000370.

Sanford, B.T. *et al.* (2023) 'E-Cigarette Screening in Primary Care', *American Journal of Preventive Medicine* [Preprint]. Available at: https://doi.org/10.1016/J.AMEPRE.2023.02.030.

Winden, T.J. *et al.* (2015) 'Towards the Standardized Documentation of E-Cigarette Use in the Electronic Health Record for Population Health Surveillance and Research', *AMIA Joint Summits on Translational Science*, 2015, pp. 199–203.

Young-Wolff, K.C. *et al.* (2017) 'Do you vape? Leveraging electronic health records to assess clinician documentation of electronic nicotine delivery system use among adolescents and adults', *Preventive medicine*, 105, p. 32. Available at: https://doi.org/10.1016/J.YPMED.2017.08.009.

Young-Wolff, K.C. *et al.* (2018) 'Documentation of e-cigarette use and associations with smoking from 2012 to 2015 in an integrated healthcare delivery system', *Preventive medicine*, 109, p. 113. Available at: https://doi.org/10.1016/J.YPMED.2018.01.012.

Young-Wolff, K.C. *et al.* (2022) 'Electronic cigarette use and risk of COVID-19 among young adults without a history of cigarette smoking', *Preventive medicine*, 162. Available at: https://doi.org/10.1016/J.YPMED.2022.107151.

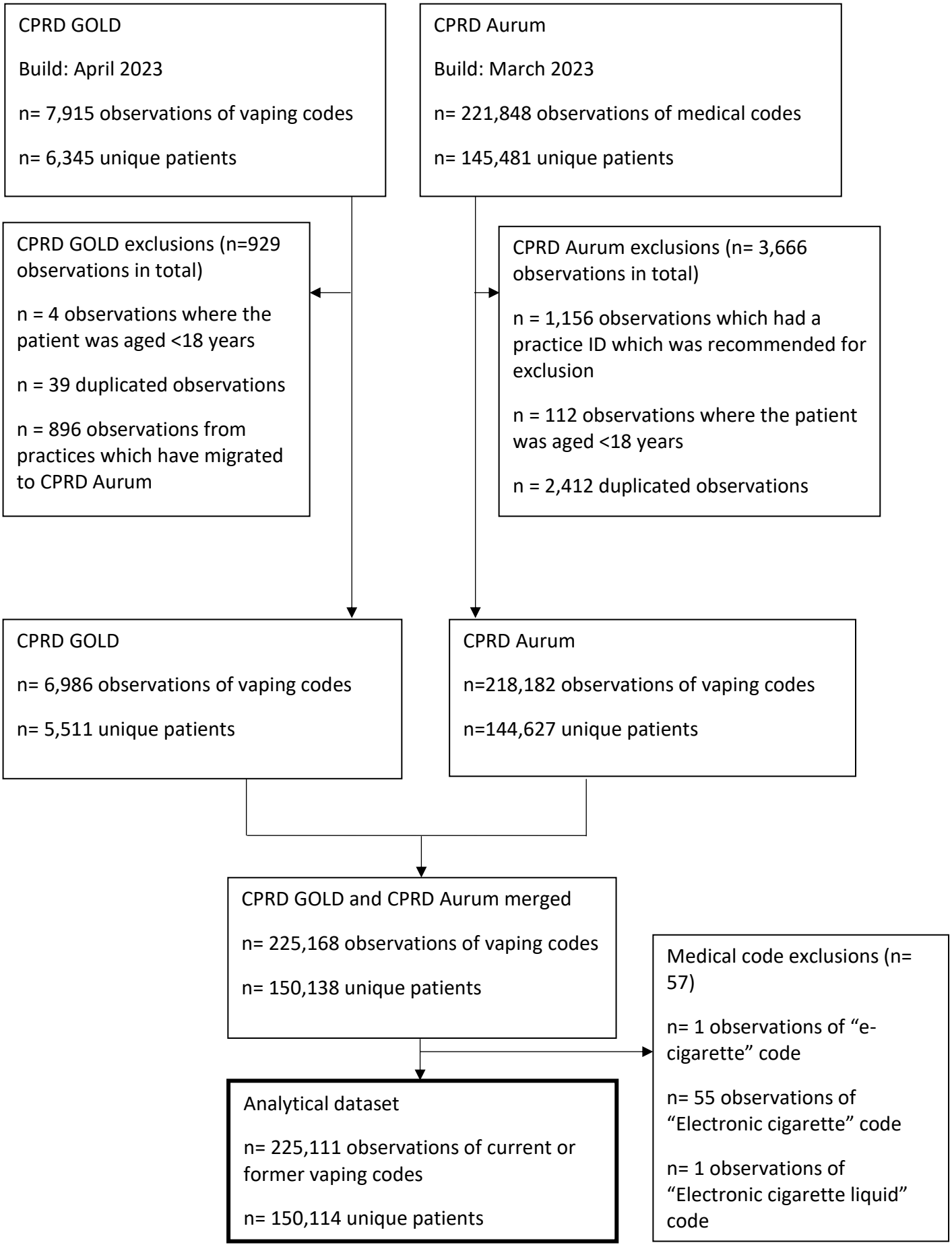
Supplementary Box 2. CPRD Denominator files

As new GP practices join and contribute their (historical and ongoing) patient data to CPRD, denominator files can be used to calculate the number of patients contributing to CPRD at specific time periods, which can be used to calculate point prevalence or incidence rate.

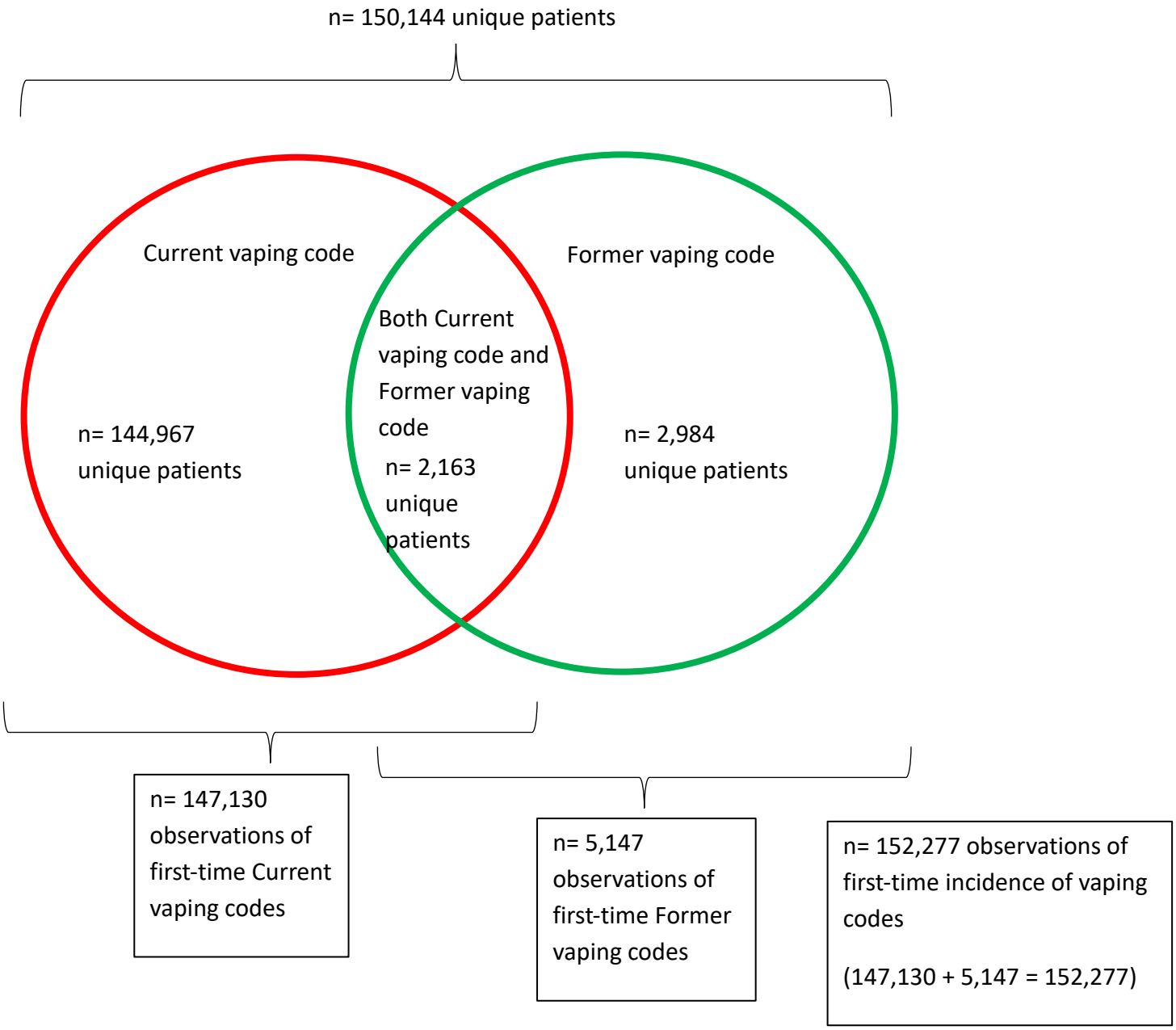
After applying the study exclusion criteria to the denominator files, the number of patients (aged ≥18 years) contributing data to CPRD in each month from September 2011 to March 2022 was calculated.

The 'start date' for each patient contributing to CPRD was the chronologically latest of 'registration start date' and 'current registration date'; the 'end date' for each patient contributing to CPRD was the chronologically earliest of the 'registration end date', 'death date', 'transfer out date', or 'last collection date' of the practice.

Supplementary Figure 1. Study inclusion – observations of vaping codes from 1 September 2006 to 31 March 2022



Supplementary Figure 2. Illustration of patient-level first-time incidence of vaping codes samples



Supplementary Table 1. Vaping medical codes in CPRD

Medical code terms	Dataset	Medical code
User of electronic cigarette	GOLD	107292
Ex user of electronic cigarette	GOLD	108503
e-cigarette user	Aurum	7832561000006114
Electronic cigarette user	Aurum	2265711000000117
User of electronic cigarette	Aurum	1879431000006110
Vaper with nicotine	Aurum	13653501000006119
Ex user of electronic cigarette	Aurum	2336091000000117
e-cigarette	Aurum	7832541000006110
Electronic cigarette	Aurum	7832521000006115
Electronic cigarette liquid	Aurum	3513803011

Using the CPRD medical code browser, medical code terms related to electronic cigarettes/e-cigarettes, vaping/vaper, electronic nicotine delivery systems (ENDS), and e-liquid were identified. Non-specific codes which only related to “nicotine user” or “nicotine dependent/dependence” were excluded.

Supplementary Table 2a. Ethnicity medical codes – CPRD GOLD

Medical code	Read Term	Ethnicity
47005	Asian and Chinese - ethnic category 2001 census	Asian
110422	Asian or Asian British: Indian - NI ethnic cat 2011 census	Asian
110590	Asian/Asian Brit: Bangladeshi- Eng+Wales eth cat 2011 census	Asian
110922	Asian/Asian Brit: Chinese - Eng+Wales ethnic cat 2011 census	Asian
110477	Asian/Asian Brit: Indian - Eng+Wales ethnic cat 2011 census	Asian
111743	Asian/Asian Brit: other Asian- Eng+Wales eth cat 2011 census	Asian
110720	Asian/Asian British: Bangladeshi - NI ethnic cat 2011 census	Asian
112363	Asian/Asian British: Chinese - NI ethnic cat 2011 census	Asian
110425	Asian/Asian British: other Asian - NI ethnic cat 2011 census	Asian
110538	Asian/Asian British: Pakistani - NI ethnic cat 2011 census	Asian
110464	Asian/Asian British:Pakistani- Eng+Wales eth cat 2011 census	Asian
111064	Asian: Chinese - Scotland ethnic category 2011 census	Asian
111368	Asian: Indian, Indian Scot/Indian Brit- Scotland 2011 census	Asian

Medical code	Read Term	Ethnicity
110855	Asian: other Asian group - Scotland ethnic cat 2011 census	Asian
110460	Asian: Pakistani/Pakistani Scot/Pakistani Brit- Scot 2011	Asian
24740	Bangladeshi	Asian
28888	Bangladeshi or British Bangladeshi - ethn categ 2001 census	Asian
112225	Bangladeshi, Bangladeshi Scot or Bangladeshi Brit- Scot 2011	Asian
12653	British Asian - ethnic category 2001 census	Asian
63872	Buddhist - ethnic category 2001 census	Asian
24272	Chinese	Asian
12718	Chinese	Asian
12468	Chinese - ethnic category 2001 census	Asian
38097	E Afric Asian/Indo-Carib (NMO)	Asian
47077	East African Asian - ethnic category 2001 census	Asian
46818	East African Asian (NMO)	Asian
12420	Filipino - ethnic category 2001 census	Asian
56127	Hindu - ethnic category 2001 census	Asian
25920	Indian	Asian
12482	Indian	Asian
12414	Indian or British Indian - ethnic category 2001 census	Asian
12473	Japanese - ethnic category 2001 census	Asian
64133	Kashmiri - ethnic category 2001 census	Asian
12730	Malaysian - ethnic category 2001 census	Asian
46056	Mixed Asian - ethnic category 2001 census	Asian
32396	Other Asian	Asian
26379	Other Asian (NMO)	Asian
12513	Other Asian background - ethnic category 2001 census	Asian
12668	Other Asian ethnic group	Asian
28935	Other Asian or Asian unspecified ethnic category 2001 census	Asian
32401	Other ethnic, Asian/White orig	Asian
24690	Pakistani	Asian
12460	Pakistani or British Pakistani - ethnic category 2001 census	Asian
26392	Punjabi - ethnic category 2001 census	Asian
49658	Sikh - ethnic category 2001 census	Asian
12887	Sinhalese - ethnic category 2001 census	Asian
46649	South East Asian	Asian
12608	Sri Lankan - ethnic category 2001 census	Asian
12760	Tamil - ethnic category 2001 census	Asian
25411	Vietnamese	Asian
12719	Vietnamese - ethnic category 2001 census	Asian
12350	African - ethnic category 2001 census	Black
111059	African: African/African Scot/African Brit - Scotland 2011	Black
110655	African: any other African - Scotland ethnic cat 2011 census	Black
35412	Black - other African country	Black
35350	Black - other Asian	Black
25676	Black - other, mixed	Black

Medical code	Read Term	Ethnicity
12778	Black African	Black
32443	Black African and White	Black
12795	Black and Asian - ethnic category 2001 census	Black
49940	Black and Chinese - ethnic category 2001 census	Black
40110	Black and White - ethnic category 2001 census	Black
57752	Black Arab	Black
26312	Black Black - other	Black
12452	Black British	Black
40097	Black British - ethnic category 2001 census	Black
47950	Black Caribbean	Black
12632	Black Caribbean	Black
32425	Black Caribbean and White	Black
57435	Black Caribbean/W.I./Guyana	Black
47965	Black E Afric Asia/Indo-Caribb	Black
57753	Black East African Asian	Black
32100	Black Guyana	Black
48005	Black Indian sub-continent	Black
57763	Black Indo-Caribbean	Black
50286	Black Iranian	Black
41329	Black N African/Arab/Iranian	Black
46812	Black North African	Black
47997	Black West Indian	Black
24339	Black, other, non-mixed origin	Black
110540	Black/Afr/Carib/Black Brit: other Black- Eng+Wales 2011 cens	Black
110630	Black/Afri/Carib/Black Brit: African- NI eth cat 2011 census	Black
110779	Black/Afri/Carib/Black Brit: Caribbean- NI eth cat 2011 cens	Black
111880	Black/Afri/Carib/Black Brit: other - NI eth cat 2011 census	Black
110437	Black/African/Carib/Black Brit: African- Eng+Wales 2011 cens	Black
110436	Black/African/Caribbn/Black Brit: Caribbean - Eng+Wales 2011	Black
112216	Carib/Black: any other Black/Caribbean grp - Scotland 2011	Black
112649	Carib/Black: Black/Black Scot/Black Brit- Scotland 2011 cens	Black
113671	Carib/Black: Caribbean/Carib Scot/Carib Brit- Scotland 2011	Black
12432	Caribbean - ethnic category 2001 census	Black
32399	Caribbean Asian - ethnic category 2001 census	Black
54593	Caribbean I./W.I./Guyana (NMO)	Black
57094	Caribbean Island (NMO)	Black
99316	Indo-Caribbean (NMO)	Black
40096	Mixed Black - ethnic category 2001 census	Black
32886	Nigerian - ethnic category 2001 census	Black
47028	North African - ethnic category 2001 census	Black
32165	Other Black - Black/Asian orig	Black
25623	Other Black - Black/White orig	Black
32389	Other Black background - ethnic category 2001 census	Black
32136	Other black ethnic group	Black

Medical code	Read Term	Ethnicity
46047	Other Black or Black unspecified ethnic category 2001 census	Black
46752	Other Pacific ethnic group	Black
12443	Somali - ethnic category 2001 census	Black
57075	West Indian (NMO)	Black
12706	Chinese and White - ethnic category 2001 census	Mixed
110696	Mixed/multiple ethnic grps: any- Scot ethnic cat 2011 census	Mixed
110654	Mixed: other Mixed/multiple backgrd - Eng+Wales 2011 census	Mixed
110536	Mixed: other Mixed/multiple ethnic backgrd - NI 2011 census	Mixed
110471	Mixed: White and Asian - NI ethnic category 2011 census	Mixed
110651	Mixed: White and Black African - NI ethnic cat 2011 census	Mixed
110661	Mixed: White and Black Caribbean - NI ethnic cat 2011 census	Mixed
110652	Mixed: White+Asian - Eng+Wales ethnic category 2011 census	Mixed
110421	Mixed: White+Black African - Eng+Wales eth cat 2011 census	Mixed
110445	Mixed: White+Black Caribbean - Eng+Wales eth cat 2011 census	Mixed
47401	Other ethnic, Black/White orig	Mixed
12696	Other ethnic, mixed origin	Mixed
32420	Other ethnic, other mixed orig	Mixed
12873	Other Mixed background - ethnic category 2001 census	Mixed
32408	Other Mixed or Mixed unspecified ethnic category 2001 census	Mixed
12638	White and Asian - ethnic category 2001 census	Mixed
12437	White and Black African - ethnic category 2001 census	Mixed
12742	White and Black Caribbean - ethnic category 2001 census	Mixed
26455	Any other group - ethnic category 2001 census	Other
46059	Arab - ethnic category 2001 census	Other
32110	Brit. ethnic minor. spec.(NMO)	Other
57764	Brit. ethnic minor. unsp (NMO)	Other
12435	Ethnic category - 2001 census	Other
110472	Ethnic category - 2011 census	Other
110417	Ethnic category - 2011 census England and Wales	Other
112302	Ethnic category - 2011 census Northern Ireland	Other
110962	Ethnic category - 2011 census Scotland	Other
12459	Ethnic category not stated - 2001 census	Other
10196	Ethnic groups (census)	Other
45199	Ethnic groups (census) NOS	Other
23955	Ethnicity and other related nationality data	Other
64609	Fijian	Other
25937	Iranian - ethnic category 2001 census	Other
25082	Iranian (NMO)	Other
45964	Kurdish - ethnic category 2001 census	Other
26246	Latin American - ethnic category 2001 census	Other

Medical code	Read Term	Ethnicity
25451	Moroccan - ethnic category 2001 census	Other
47091	Muslim - ethnic category 2001 census	Other
24962	N African Arab/Iranian (NMO)	Other
47285	North African Arab (NMO)	Other
25969	O/E - ethnic group	Other
60284	O/E - ethnic group NOS	Other
12332	O/E - ethnic origin	Other
12434	Other - ethnic category 2001 census	Other
12757	Other ethnic group	Other
110646	Other ethnic group: any other grp- NI ethnic cat 2011 census	Other
110555	Other ethnic group: Arab - Eng+Wales ethnic cat 2011 census	Other
110780	Other ethnic group: Arab - NI ethnic category 2011 census	Other
111806	Other ethnic grp: any other ethnic grp- Scotland 2011 census	Other
112245	Other ethnic grp: Arab/Arab Scot/Arab British- Scotland 2011	Other
41214	Other ethnic NEC (NMO)	Other
30280	Other ethnic non-mixed (NMO)	Other
110742	Other ethnic: any other grp - Eng+Wales eth cat 2011 census	Other
64610	Samoan	Other
12756	South and Central American - ethnic category 2001 census	Other
94487	Yemeni	Other
25422	Albanian - ethnic category 2001 census	White
12433	Baltic Estonian/Latvian/Lithuanian - ethn categ 2001 census	White
46956	Bosnian - ethnic category 2001 census	White
12351	British or mixed British - ethnic category 2001 census	White
99788	Bulgarian	White
28887	Cornish - ethnic category 2001 census	White
28866	Croatian - ethnic category 2001 census	White
32778	Cypriot (part not stated) - ethnic category 2001 census	White
100143	Czech	White
12352	English - ethnic category 2001 census	White
12355	Greek - ethnic category 2001 census	White
45955	Greek (NMO)	White
12769	Greek Cypriot - ethnic category 2001 census	White
47949	Greek Cypriot (NMO)	White
45947	Greek/Greek Cypriot (NMO)	White
42290	Gypsy/Romany - ethnic category 2001 census	White
12532	Irish - ethnic category 2001 census	White
24270	Irish (NMO)	White
47601	Irish traveller	White
55223	Irish Traveller - ethnic category 2001 census	White
115519	Irish Traveller - Northern Ireland ethnic cat 2011 census	White
46964	Israeli - ethnic category 2001 census	White
12412	Italian - ethnic category 2001 census	White
46063	Jewish - ethnic category 2001 census	White
26341	Kosovan - ethnic category 2001 census	White

Medical code	Read Term	Ethnicity
26391	Mixed Irish and other White - ethnic category 2001 census	White
71425	New Zealand ethnic group NOS	White
45008	New Zealand ethnic groups	White
57286	New Zealand European	White
32479	New Zealand Maori	White
42294	Northern Irish - ethnic category 2001 census	White
12402	Oth White European/European unsp/Mixed European 2001 census	White
35459	Other ethnic, mixed white orig	White
12633	Other European (NMO)	White
85505	Other European in New Zealand	White
28900	Other mixed White - ethnic category 2001 census	White
96789	Other New Zealand ethnic group	White
28936	Other republics former Yugoslavia - ethnic categ 2001 census	White
12421	Other White background - ethnic category 2001 census	White
26310	Other white British ethnic group	White
12444	Other white ethnic group	White
12591	Other White or White unspecified ethnic category 2001 census	White
12467	Polish - ethnic category 2001 census	White
101219	Portuguese	White
99808	Romanian	White
12436	Scottish - ethnic category 2001 census	White
47074	Serbian - ethnic category 2001 census	White
55113	Traveller - ethnic category 2001 census	White
12746	Turkish - ethnic category 2001 census	White
32126	Turkish (NMO)	White
32413	Turkish Cypriot - ethnic category 2001 census	White
32069	Turkish Cypriot (NMO)	White
32066	Turkish/Turkish Cypriot (NMO)	White
40102	Ulster Scots - ethnic category 2001 census	White
12681	Welsh - ethnic category 2001 census	White
22467	White	White
112899	White - Northern Ireland ethnic category 2011 census	White
12446	White British	White
98111	White British - ethnic category 2001 census	White
24837	White Irish	White
98213	White Irish - ethnic category 2001 census	White
26467	White Scottish	White
111386	White: Gypsy/Irish Traveller - Eng+Wales eth cat 2011 census	White
113253	White: Gypsy/Irish Traveller - Scotland ethnic cat 2011 cens	White
110556	White: Irish - England and Wales ethnic category 2011 census	White
110687	White: Irish - Scotland ethnic category 2011 census	White
110694	White: other British - Scotland ethnic category 2011 census	White

Medical code	Read Term	Ethnicity
110407	White: other White backgrd- Eng+Wales ethnic cat 2011 census	White
110695	White: other White ethnic grp- Scotland ethnic cat 2011 cens	White
110465	White: Polish - Scotland ethnic category 2011 census	White
110432	White: Scottish - Scotland ethnic category 2011 census	White
110420	White:Eng/Welsh/Scot/NI/Brit - England and Wales 2011 census	White

Where a patient had inconsistent records for ethnicity, the most frequently occurring category for that patient was used. Ethnicity was recorded as 'unknown' if no category was most frequent or if no information was recorded.

Supplementary Table 2b. Ethnicity medical codes – CPRD Aurum

Medical code	Term	Ethnicity
141531000000112	Kashmiri - ethnic category 2001 census	Asian
1564521000006118	Chinese	Asian
1968481000006118	Asian or Asian Scottish or Asian British: Pakistani, Pakistani Scottish or Pakistani British - Scotland ethnic category 2011 census	Asian
550541000006110	Chinese	Asian
141651000000118	Malaysian - ethnic category 2001 census	Asian
1564921000006112	Indian	Asian
285977016	Other Asian (NMO)	Asian
216045018	Reads Chinese	Asian
411583012	East African Asian (NMO)	Asian
781081000006113	Indian	Asian
141361000000114	Pakistani or British Pakistani - ethnic category 2001 census	Asian
285956019	Bangladeshi	Asian
141641000000116	Filipino - ethnic category 2001 census	Asian
285955015	Pakistani	Asian
1968171000006110	Asian or Asian British: any other Asian background - England and Wales ethnic category 2011 census	Asian
1968131000006112	Asian or Asian British: Indian - England and Wales ethnic category 2011 census	Asian
285954016	Indian	Asian
136081000000111	Sri Lankan - ethnic category 2001 census	Asian
1565441000006111	Pakistani	Asian
141561000000119	British Asian - ethnic category 2001 census	Asian
1751671000006110	NHS Sickle Cell and Thalassaemia Screening Programme Pakistan family origin	Asian

Medical code	Term	Ethnicity
1968501000006111	Asian or Asian Scottish or Asian British: Bangladeshi, Bangladeshi Scottish or Bangladeshi British - Scotland ethnic category 2011 census	Asian
141521000000110	Punjabi - ethnic category 2001 census	Asian
158361000000116	Asian and Chinese - ethnic category 2001 census	Asian
286020010	Asian - ethnic group	Asian
1968521000006118	Asian or Asian Scottish or Asian British: any other Asian group - Scotland ethnic category 2011 census	Asian
141401000000117	Chinese - ethnic category 2001 census	Asian
4740361000006111	Other ethnic, Asian/White origin	Asian
1968491000006115	Asian or Asian Scottish or Asian British: Indian, Indian Scottish or Indian British - Scotland ethnic category 2011 census	Asian
142891000000115	Sikh - ethnic category 2001 census	Asian
1968341000006116	Asian or Asian British: any other Asian background - Northern Ireland ethnic category 2011 census	Asian
142881000000117	Buddhist - ethnic category 2001 census	Asian
1968151000006117	Asian or Asian British: Bangladeshi - England and Wales ethnic category 2011 census	Asian
157271000000119	Indian or British Indian - ethnic category 2001 census	Asian
141511000000116	Mixed Asian - ethnic category 2001 census	Asian
285991010	Other ethnic, Asian/White orig	Asian
196721000006111	RACE: Pakistani	Asian
286018012	South East Asian	Asian
1968321000006111	Asian or Asian British: Bangladeshi - Northern Ireland ethnic category 2011 census	Asian
4917941000006114	Bangladesh	Asian
250224013	Asian origin	Asian
1751681000006113	NHS Sickle Cell and Thalassaemia Screening Programme Bangladesh family origin	Asian
1751701000006111	NHS Sickle Cell and Thalassaemia Screening Programme Chinese family origin	Asian
1751661000006115	NHS Sickle Cell and Thalassaemia Screening Programme India or African-Indian family origin	Asian
196651000006112	RACE: Chinese	Asian
459784018	Other Asian ethnic group	Asian
1968331000006114	Asian or Asian British: Chinese - Northern Ireland ethnic category 2011 census	Asian
405069018	E Afric Asian/Indo-Carib (NMO)	Asian
141381000000117	Other Asian background - ethnic category 2001 census	Asian
1968141000006119	Asian or Asian British: Pakistani - England and Wales ethnic category 2011 census	Asian
937651000006117	Other Asian or Asian unspecified - ethnic category 2001 census	Asian
1968311000006115	Asian or Asian British: Pakistani - Northern Ireland ethnic category 2011 census	Asian
157351000000115	Hindu - ethnic category 2001 census	Asian
141541000000115	East African Asian - ethnic category 2001 census	Asian

Medical code	Term	Ethnicity
56590016	Chinese	Asian
196611000006111	Afro-Caucasian	Asian
157301000000116	Sinhalese - ethnic category 2001 census	Asian
412016016	O/E - Asian origin	Asian
1751651000006117	NHS Sickle Cell and Thalassaemia Screening Programme family origin South Asia (Asian)	Asian
141621000000111	Vietnamese - ethnic category 2001 census	Asian
1968301000006118	Asian or Asian British: Indian - Northern Ireland ethnic category 2011 census	Asian
250228011	Indian origin	Asian
141631000000113	Japanese - ethnic category 2001 census	Asian
937541000006115	Bangladeshi or British Bangladeshi - ethnic category 2001 census	Asian
141551000000117	Tamil - ethnic category 2001 census	Asian
1968161000006115	Asian or Asian British: Chinese - England and Wales ethnic category 2011 census	Asian
1968511000006114	Asian or Asian Scottish or Asian British: Chinese - Scotland ethnic category 2011 census	Asian
1564291000006119	Bangladeshi	Asian
937941000006111	Multi-ethnic islands: Mauritian or Seychellois or Maldivian or St Helena - ethnic category 2001 census	Asian
196631000006117	RACE: Bangladeshi	Asian
142811000000112	North African - ethnic category 2001 census	Black
1968191000006111	Black or African or Caribbean or Black British: Caribbean - England and Wales ethnic category 2011 census	Black
250223019	African origin	Black
285931013	Black, other, non-mixed origin	Black
30683015	Black African	Black
285951012	Black - other, mixed	Black
285930014	Black Caribbean	Black
1751621000006114	NHS Sickle Cell and Thalassaemia Screening Programme family origin African or African-Caribbean (black)	Black
285943014	Black - other African country	Black
285950013	Black Black - other	Black
459782019	Other black ethnic group	Black
411584018	Indo-Caribbean (NMO)	Black
141601000000119	Nigerian - ethnic category 2001 census	Black
158351000000119	Other Black background - ethnic category 2001 census	Black
1968551000006110	Caribbean or Black: Caribbean, Caribbean Scottish or Caribbean British - Scotland ethnic category 2011 census	Black
285932018	Black British	Black
1968361000006117	Black or African or Caribbean or Black British: Caribbean - Northern Ireland ethnic category 2011 census	Black
405064011	Black Caribbean/W.I./Guyana	Black
453110019	Black Guyana	Black
411574019	Black Arab	Black

Medical code	Term	Ethnicity
1968371000006112	Black or African or Caribbean or Black British: other Black or African or Caribbean background - Northern Ireland ethnic category 2011 census	Black
141391000000115	African - ethnic category 2001 census	Black
411576017	Black East African Asian	Black
250231012	West Indian origin	Black
285949013	Black - other Asian	Black
1968561000006112	Caribbean or Black: Black, Black Scottish or Black British - Scotland ethnic category 2011 census	Black
141571000000114	Caribbean Asian - ethnic category 2001 census	Black
1968351000006119	Black or African or Caribbean or Black British: African - Northern Ireland ethnic category 2011 census	Black
411579012	West Indian (NMO)	Black
1564491000006115	Central African	Black
1968571000006117	Caribbean or Black: any other Black or Caribbean group - Scotland ethnic category 2011 census	Black
286017019	Other Pacific ethnic group	Black
1968201000006114	Black or African or Caribbean or Black British: other Black or African or Caribbean background - England and Wales ethnic category 2011 census	Black
459730016	Black - ethnic group	Black
514611000006111	Black Caribbean	Black
157311000000119	Black British - ethnic category 2001 census	Black
1751641000006119	NHS Sickle Cell and Thalassaemia Screening Programme African family origin	Black
459731017	Black	Black
1968531000006115	African: African, African Scottish or African British - Scotland ethnic category 2011 census	Black
158371000000111	Mixed Black - ethnic category 2001 census	Black
154401000000118	Caribbean - ethnic category 2001 census	Black
514651000006112	Black East African Asian/Indo-Caribbean	Black
1968181000006113	Black or African or Caribbean or Black British: African - England and Wales ethnic category 2011 census	Black
411577014	Black Indo-Caribbean	Black
141591000000113	Somali - ethnic category 2001 census	Black
285948017	Black Indian sub-continent	Black
411573013	Black North African	Black
405065012	Black N African/Arab/Iranian	Black
405067016	Caribbean I./W.I./Guyana (NMO)	Black
285952017	Other Black - Black/White orig	Black
411575018	Black Iranian	Black
1968541000006113	African: any other African - Scotland ethnic category 2011 census	Black
937731000006115	Other Black or Black unspecified - ethnic category 2001 census	Black
285953010	Other Black - Black/Asian orig	Black
453109012	Black West Indian	Black

Medical code	Term	Ethnicity
250243013	Race: West indian	Black
196601000006113	Afro-Caribbean	Black
141331000000116	White and Black African - ethnic category 2001 census	Mixed
141321000000118	White and Black Caribbean - ethnic category 2001 census	Mixed
285990011	Other ethnic, Black/White orig	Mixed
1968271000006115	Mixed multiple ethnic groups: White and Black African - Northern Ireland ethnic category 2011 census	Mixed
1968281000006117	Mixed multiple ethnic groups: White and Asian - Northern Ireland ethnic category 2011 census	Mixed
460153018	Black Caribbean and White	Mixed
141471000000113	Black and Asian - ethnic category 2001 census	Mixed
157291000000115	Black and White - ethnic category 2001 census	Mixed
1968291000006119	Mixed multiple ethnic groups: any other Mixed or multiple ethnic background - Northern Ireland ethnic category 2011 census	Mixed
460154012	Black African and White	Mixed
141341000000113	White and Asian - ethnic category 2001 census	Mixed
1968101000006116	Mixed multiple ethnic groups: White and Black African - England and Wales ethnic category 2011 census	Mixed
141481000000110	Black and Chinese - ethnic category 2001 census	Mixed
1968121000006114	Mixed multiple ethnic groups: any other Mixed or multiple ethnic background - England and Wales ethnic category 2011 census	Mixed
141491000000112	Chinese and White - ethnic category 2001 census	Mixed
141351000000111	Other Mixed background - ethnic category 2001 census	Mixed
285989019	Other ethnic, mixed origin	Mixed
1968111000006118	Mixed multiple ethnic groups: White and Asian - England and Wales ethnic category 2011 census	Mixed
1968261000006110	Mixed multiple ethnic groups: White and Black Caribbean - Northern Ireland ethnic category 2011 census	Mixed
1968091000006110	Mixed multiple ethnic groups: White and Black Caribbean - England and Wales ethnic category 2011 census	Mixed
459729014	Mixed ethnic census group	Mixed
937511000006119	Other Mixed or Mixed unspecified - ethnic category 2001 census	Mixed
4740401000006118	Other ethnic, other mixed origin	Mixed
1968471000006116	Mixed or multiple ethnic groups: any Mixed or multiple ethnic group - Scotland ethnic category 2011 census	Mixed
285993013	Other ethnic, other mixed orig	Mixed
4740341000006112	Other ethnic, Black/White origin	Mixed
138271000000119	South and Central American - ethnic category 2001 census	Other
138261000000114	Iranian - ethnic category 2001 census	Other
459785017	Ethnic group	Other
2484511000000112	Ethnic category - 2011 census England and Wales	Other
142901000000119	Any other group - ethnic category 2001 census	Other
649261000006110	Ethnic group finding	Other
4740241000006117	British ethnic minority specified (NMO)	Other

Medical code	Term	Ethnicity
142851000000111	Moroccan - ethnic category 2001 census	Other
285988010	Other ethnic NEC (NMO)	Other
405068014	N African Arab/Iranian (NMO)	Other
4740261000006118	British ethnic minority unspecified (NMO)	Other
253628018	O/E - ethnic origin	Other
250229015	Middle Eastern origin	Other
4740421000006111	Ethnicity / related nationality data	Other
285960016	Brit. ethnic minor. unsp (NMO)	Other
141291000000111	Ethnic category - 2001 census	Other
411581014	North African Arab (NMO)	Other
141411000000115	Other - ethnic category 2001 census	Other
142841000000113	Kurdish - ethnic category 2001 census	Other
6270381000006117	Ethnic groups (1991 census) (UK)	Other
141421000000114	Ethnic category not stated - 2001 census	Other
1968211000006112	Other ethnic group: Arab - England and Wales ethnic category 2011 census	Other
6260901000006118	Ethnic group	Other
2484591000000115	Ethnic category - 2011 census Scotland	Other
253627011	O/E - ethnic group	Other
286005016	Ethnicity and other related nationality data	Other
8224821000006111	Ethnicity	Other
1968221000006116	Other ethnic group: any other ethnic group - England and Wales ethnic category 2011 census	Other
1968581000006119	Other ethnic group: Arab, Arab Scottish or Arab British - Scotland ethnic category 2011 census	Other
6270401000006117	Ethnicity / related nationality data - finding	Other
142861000000114	Latin American - ethnic category 2001 census	Other
285959014	Brit. ethnic minor. spec.(NMO)	Other
285958018	Other ethnic non-mixed (NMO)	Other
6270391000006119	Ethnic groups (1991 census) (United Kingdom)	Other
6591901000006115	Ethnicity	Other
1968381000006110	Other ethnic group: Arab - Northern Ireland ethnic category 2011 census	Other
1968591000006116	Other ethnic group: any other ethnic group - Scotland ethnic category 2011 census	Other
6597601000006118	Ethnic background	Other
2484551000000111	Ethnic category - 2011 census Northern Ireland	Other
138281000000117	Muslim - ethnic category 2001 census	Other
286003011	Ethnic groups (census) NOS	Other
2484471000000115	Ethnic category - 2011 census	Other
138251000000111	Arab - ethnic category 2001 census	Other
253635014	O/E - ethnic group NOS	Other
1968391000006113	Other ethnic group: any other ethnic group - Northern Ireland ethnic category 2011 census	Other
937871000006114	Middle Eastern (excluding Israeli, Iranian and Arab) - ethnic category 2001 census	Other

Medical code	Term	Ethnicity
2484671000000118	White: Irish - England and Wales ethnic category 2011 census	White
2487361000000112	White: Irish - Scotland ethnic category 2011 census	White
937371000006116	Other republics which made up the former Yugoslavia - ethnic category 2001 census	White
142701000000116	Greek - ethnic category 2001 census	White
158481000000115	Italian - ethnic category 2001 census	White
141311000000112	Other White background - ethnic category 2001 census	White
286021014	Other New Zealand ethnic group	White
138201000000110	Polish - ethnic category 2001 census	White
142721000000113	Turkish Cypriot - ethnic category 2001 census	White
2486161000000112	White - Northern Ireland ethnic category 2011 census	White
1564391000006113	British	White
286009010	Other European in New Zealand	White
937301000006110	Baltic States (Estonian or Latvian or Lithuanian) - ethnic category 2001 census	White
141431000000111	Scottish - ethnic category 2001 census	White
1063981000000117	White British - ethnic category 2001 census	White
142781000000114	Mixed Irish and other White - ethnic category 2001 census	White
142831000000116	Israeli - ethnic category 2001 census	White
142691000000116	Ulster Scots - ethnic category 2001 census	White
1968051000006116	White: English or Welsh or Scottish or Northern Irish or British - England and Wales ethnic category 2011 census	White
459726019	White British	White
285925010	White	White
937311000006113	Commonwealth of (Russian) Independent States - ethnic category 2001 census	White
142761000000117	Croatian - ethnic category 2001 census	White
459728018	White - ethnic group	White
157991000000110	Serbian - ethnic category 2001 census	White
937411000006115	Other White or White unspecified - ethnic category 2001 census	White
1968081000006112	White: any other White background - England and Wales ethnic category 2011 census	White
285987017	Other European (NMO)	White
411595012	Greek Cypriot (NMO)	White
138191000000113	Gypsy/Romany - ethnic category 2001 census	White
405070017	Greek/Greek Cypriot (NMO)	White
4740381000006118	Other ethnic, mixed white origin	White
156921000000110	Turkish - ethnic category 2001 census	White
196641000006110	Caucasian race	White
937391000006115	Other White European or European unspecified or Mixed European - ethnic category 2001 census	White
286022019	New Zealand ethnic group NOS	White
2645811000000115	Roma ethnic group	White
1780407014	White Scottish	White

Medical code	Term	Ethnicity
1968251000006113	Irish Traveller - Northern Ireland ethnic category 2011 census	White
138231000000116	Albanian - ethnic category 2001 census	White
286007012	New Zealand European	White
142751000000115	Bosnian - ethnic category 2001 census	White
286006015	New Zealand ethnic groups	White
2487281000000112	White: Scottish - Scotland ethnic category 2011 census	White
138171000000114	Irish Traveller - ethnic category 2001 census	White
142711000000119	Greek Cypriot - ethnic category 2001 census	White
1968441000006112	White: Gypsy or Irish Traveller - Scotland ethnic category 2011 census	White
141441000000119	Welsh - ethnic category 2001 census	White
1751821000006113	NHS Sickle Cell and Thalassaemia Screening Programme family origin Northern European (white)	White
141301000000110	Irish - ethnic category 2001 census	White
157281000000117	English - ethnic category 2001 census	White
141661000000115	Cypriot (part not stated) - ethnic category 2001 census	White
142741000000118	Kosovan - ethnic category 2001 census	White
141451000000116	Northern Irish - ethnic category 2001 census	White
285992015	Other ethnic, mixed white orig	White
1968071000006114	White: Gypsy or Irish Traveller - England and Wales ethnic category 2011 census	White
158341000000117	British or mixed British - ethnic category 2001 census	White
1780408016	Other white British ethnic group	White
2537217015	Race: White	White
2487481000000113	White: Polish - Scotland ethnic category 2011 census	White
405071018	Turkish/Turkish Cypriot (NMO)	White
411597016	Turkish Cypriot (NMO)	White
142791000000111	Other mixed White - ethnic category 2001 census	White
6846371000006111	Caucasian	White
2487321000000116	White: other British - Scotland ethnic category 2011 census	White
1968461000006111	White: any other White ethnic group - Scotland ethnic category 2011 census	White
138181000000111	Traveller - ethnic category 2001 census	White
141461000000118	Cornish - ethnic category 2001 census	White
1064041000000111	White Irish - ethnic category 2001 census	White
138241000000113	Jewish - ethnic category 2001 census	White
459727011	White Irish	White

Where a patient had inconsistent records for ethnicity, the most frequently occurring category for that patient was used. Ethnicity was recorded as ‘unknown’ if no category was most frequent or if no information was recorded.

Supplementary Table 3a. Smoking status medical codes – CPRD GOLD

Medical code	Read term	Smoking status
32973	Chews tobacco	currently smoke
12963	Cigar consumption	currently smoke
12943	Cigar smoker	currently smoke
12965	Cigarette consumption	currently smoke
46300	Cigarette pack-years	currently smoke
93	Cigarette smoker	currently smoke
10558	Current smoker	currently smoke
101338	Failed attempt to stop smoking	currently smoke
3568	Heavy smoker - 20-39 cigs/day	currently smoke
12964	Keeps trying to stop smoking	currently smoke
12944	Light smoker - 1-9 cigs/day	currently smoke
62686	Minutes from waking to first tobacco consumption	currently smoke
1878	Moderate smoker - 10-19 cigs/d	currently smoke
30762	Not interested in stopping smoking	currently smoke
12941	Occasional smoker	currently smoke
12947	Pipe smoker	currently smoke
12967	Pipe tobacco consumption	currently smoke
31114	Ready to stop smoking	currently smoke
46321	Reason for restarting smoking	currently smoke
12945	Rolls own cigarettes	currently smoke
1823	Smoker	currently smoke
12942	Smoker - amount smoked	currently smoke
12966	Smoking reduced	currently smoke
12951	Smoking restarted	currently smoke
41979	Smoking restarted	currently smoke
12952	Smoking started	currently smoke
30423	Thinking about stopping smoking	currently smoke
12960	Tobacco consumption NOS	currently smoke
12958	Trivial smoker - < 1 cig/day	currently smoke
12240	Trying to give up smoking	currently smoke
1822	Very heavy smoker - 40+cigs/d	currently smoke
105501	Waterpipe tobacco consumption	currently smoke
12878	Date ceased smoking	formerly smoked
19488	Ex cigar smoker	formerly smoked
26470	Ex pipe smoker	formerly smoked
100495	Ex roll-up cigarette smoker	formerly smoked
90	Ex smoker	formerly smoked
97210	Ex-cigarette smoker	formerly smoked
12956	Ex-heavy smoker (20-39/day)	formerly smoked
12957	Ex-light smoker (1-9/day)	formerly smoked
12955	Ex-moderate smoker (10-19/day)	formerly smoked
12946	Ex-smoker - amount unknown	formerly smoked

Medical code	Read term	Smoking status
106891	Ex-tobacco chewer	formerly smoked
12961	Ex-trivial smoker (<1/day)	formerly smoked
12959	Ex-very heavy smoker (40+/day)	formerly smoked
99838	Recently stopped smoking	formerly smoked
776	Stopped smoking	formerly smoked
60	Current non-smoker	never smoked
33	Never smoked tobacco	never smoked
11788	Non-smoker	never smoked

Supplementary Table 3b. Smoking status medical codes – CPRD Aurum

Medical code	Term	Smoking status
482771000000118	Smoking cessation drug therapy	currently smoke
492511000000117	Smoking cessation therapy	currently smoke
3959111000006111	Tobacco dependence syndrome	currently smoke
250372012	Trying to give up smoking	currently smoke
102951000006115	Tobacco dependence	currently smoke
3419101000006116	Moderate smoker (20 or less per day)	currently smoke
5003151000006116	Light cigarette smoker	currently smoke
854961000006110	Grade B light smoker (1-10/day)	currently smoke
4980831000006112	Finding relating to tobacco chewing	currently smoke
854981000006117	Grade C moderate smoker (11-20/day)	currently smoke
504769011	Chews tobacco	currently smoke
604961000006114	Current Smoker NOS	currently smoke
7832511000006111	Cigar	currently smoke
108938018	Cigarette smoker	currently smoke
4074561000006112	Tobacco smoke	currently smoke
5003161000006119	Moderate cigarette smoker	currently smoke
5003171000006114	Heavy cigarette smoker	currently smoke
295256013	Tobacco dependence, unspecified	currently smoke
7832501000006113	Cigarette	currently smoke
88471000006112	Trivial cigarette smoker (less than one cigarette/day)	currently smoke
2669652019	Smoking started	currently smoke
5003141000006118	Trivial cigarette smoker	currently smoke
3430571000006116	Tobacco	currently smoke
5495901000006112	Amount and type of tobacco smoked	currently smoke
1538681000006118	Smoke	currently smoke
4948531000006116	Smokes in bed	currently smoke
250375014	Rolls own cigarettes	currently smoke
344793011	Cigarette consumption	currently smoke
13619901000006116	Number of calculated smoking pack years	currently smoke
852981000006111	Rolls own cigarettes	currently smoke
298701000000114	History of tobacco use	currently smoke

Medical code	Term	Smoking status
2670126018	Smoking restarted	currently smoke
8063181000006116	Wants to stop smoking	currently smoke
136515019	Pipe smoker	currently smoke
137791000006118	Smoking restarted	currently smoke
342574011	Total time smoked	currently smoke
854021000006115	Cigarette smoker	currently smoke
3142921000006110	Tobacco	currently smoke
3874641000006110	Pipe smoking tobacco	currently smoke
503483019	Current smoker	currently smoke
295258014	Tobacco dependence, episodic	currently smoke
128130017	Smoker	currently smoke
1484936019	Smoking status at 52 weeks	currently smoke
102921000006112	Tobacco smoking consumption	currently smoke
4980581000006110	Age at starting smoking	currently smoke
1780396011	Cigarette pack-years	currently smoke
6282331000006114	Tobacco smoking behaviour - finding	currently smoke
700121000006118	Moderate cigarette smoker (10-19 cigs/day)	currently smoke
1714541000006110	Current smoker annual review - enhanced services admin	currently smoke
961581000006114	Smokes/uses tobacco products	currently smoke
2170961000000116	Waterpipe tobacco consumption	currently smoke
4980741000006114	Moist tobacco consumption	currently smoke
6282371000006112	Tobacco smoking consumption - finding	currently smoke
4980781000006115	User of moist powdered tobacco	currently smoke
460828018	Tobacco user	currently smoke
295260011	Tobacco dependence NOS	currently smoke
397733018	Occasional smoker	currently smoke
295259018	Tobacco dependence in remission	currently smoke
4074571000006117	Cigarette smoke	currently smoke
3422221000006116	Heavy smoker (over 20 per day)	currently smoke
1484935015	Smoking status between 4 and 52 weeks	currently smoke
342445017	Smokes drugs through a pipe	currently smoke
2474719011	Minutes from waking to first tobacco consumption	currently smoke
3544141000006118	Smoke	currently smoke
819331000006110	Heavy cigarette smoker (20-39 cigs/day)	currently smoke
344794017	Cigar consumption	currently smoke
8153371000006117	Occasional tobacco smoker	currently smoke
1484934016	Smoking status at 4 weeks	currently smoke
99639019	Cigar smoker	currently smoke
344795016	Pipe tobacco consumption	currently smoke
743331000006116	Light cigarette smoker (1-9 cigs/day)	currently smoke
855001000006114	Grade D heavy smoker (>20 Day)	currently smoke
854071000006119	Current smoker	currently smoke
7375991000006118	Smokes tobacco daily	currently smoke
5003191000006110	Chain smoker	currently smoke

Medical code	Term	Smoking status
295257016	Tobacco dependence, continuous	currently smoke
904041000006113	Waking time to first cigarette	currently smoke
5003181000006112	Very heavy cigarette smoker	currently smoke
137771000006119	Smoking Age Started	currently smoke
5495951000006111	Occasional cigarette smoker (less than one cigarette/day)	currently smoke
250387019	Tobacco consumption NOS	currently smoke
1809121000006113	Waterpipe tobacco consumption	currently smoke
137711000006111	Smoker (Read codes)	currently smoke
1152111000000118	Current smoker annual review	currently smoke
11904991000006116	Occasional cigarette smoker	currently smoke
137721000006115	Smoker - amount smoked	currently smoke
6282351000006119	Smoking	currently smoke
67621000006112	Very heavy cigarette smoker (40+ cigs/day)	currently smoke
1819411000006114	Smoking increased	currently smoke
216212011	Smoking reduced	currently smoke
649821000006115	Ex-cigar smoker	formerly smoked
854051000006112	Ex-pipe smoker	formerly smoked
5496021000006114	Tobacco smoking consumption unknown	formerly smoked
418914010	Ex-cigarette smoker	formerly smoked
250363016	Ex-trivial cigarette smoker (<1/day)	formerly smoked
7368971000006117	Stopped smoking before pregnancy	formerly smoked
4980561000006117	Time since stopped smoking	formerly smoked
2636041000006110	Cessation of smoking	formerly smoked
2735201000000112	Ex-very heavy smoker (40+/day)	formerly smoked
649841000006110	Ex-smoker	formerly smoked
1817431000006112	Tobacco use and exposure	formerly smoked
903041000006110	EX-Smoker NOS	formerly smoked
7368961000006112	Stopped smoking during pregnancy	formerly smoked
250364010	Ex-light cigarette smoker (1-9/day)	formerly smoked
854151000006111	Date stopped smoking	formerly smoked
1123951000000110	Ex-smoker annual review - enhanced services administration	formerly smoked
649861000006114	Ex-Cigarette Smoker	formerly smoked
649851000006112	Ex- Rolled Tobacco Smoker	formerly smoked
137761000006114	Smoking Age Ceased	formerly smoked
250366012	Ex-heavy cigarette smoker (20-39/day)	formerly smoked
5495941000006114	Occasional smoker	formerly smoked
250373019	Stopped smoking	formerly smoked
1154471000000114	Ex-smoker annual review	formerly smoked
7368651000006119	Smoked before confirmation of pregnancy	formerly smoked
250371017	Ex-smoker - amount unknown	formerly smoked
250367015	Ex-very heavy cigarette smoker (40+/day)	formerly smoked
2735421000000119	Ex-trivial smoker (<1/day)	formerly smoked
2735281000000119	Ex-heavy smoker (20-39/day)	formerly smoked
2735331000000112	Ex-moderate smoker (10-19/day)	formerly smoked

Medical code	Term	Smoking status
137811000006119	Smoking Status	formerly smoked
1059701000000119	Ex roll-up cigarette smoker	formerly smoked
854111000006110	Past smoker	formerly smoked
1809131000006111	Total time smoked	formerly smoked
2735381000000111	Ex-light smoker (1-9/day)	formerly smoked
250365011	Ex-moderate cigarette smoker (10-19/day)	formerly smoked
2735181000000113	Ex-smoker amount unknown	formerly smoked
1151791000000117	Recently stopped smoking	formerly smoked
5496031000006112	Ex-cigarette smoker amount unknown	formerly smoked
8017571000006117	Ex-smoker for more than 1 year	formerly smoked
342602019	Ex-tobacco chewer	formerly smoked
6217151000006116	Intolerant ex-smoker	formerly smoked
6217281000006116	Aggressive ex-smoker	formerly smoked
649831000006117	Ex-pipe smoker	formerly smoked
1488873010	Smoking free weeks	formerly smoked
3513199018	Ex-smoker for less than 1 year	formerly smoked
853001000006110	Ex-smoker NOS	formerly smoked
250374013	Current non-smoker	never smoked
4980871000006110	Never chewed tobacco	never smoked
903051000006112	Tobacco Consumption Nil	never smoked
1123751000000113	Non-smoker annual review - enhanced services administration	never smoked
6718071000006115	Current non smoker but past smoking history unknown	never smoked
7965041000006111	Never smoked any substance	never smoked
5495921000006119	Never smoked	never smoked
14866014	Non-smoker	never smoked
1009271000006118	Non Smoker - Nos	never smoked
4980861000006115	Does not chew tobacco	never smoked
1154431000000112	Non-smoker annual review	never smoked
854951000006113	Grade A non-smoker	never smoked
397732011	Never smoked tobacco	never smoked
7569061000006118	Never used tobacco	never smoked
4980751000006111	Does not use moist powdered tobacco	never smoked

Supplementary Table 4. Frequency of vaping codes per unique patient

Number of vaping codes per unique patient	Freq (n)
1	107,901
2	25,480
3	9,195
4	3,877
5	1,804
>5	1,857
TOTAL unique patients	**150,114**

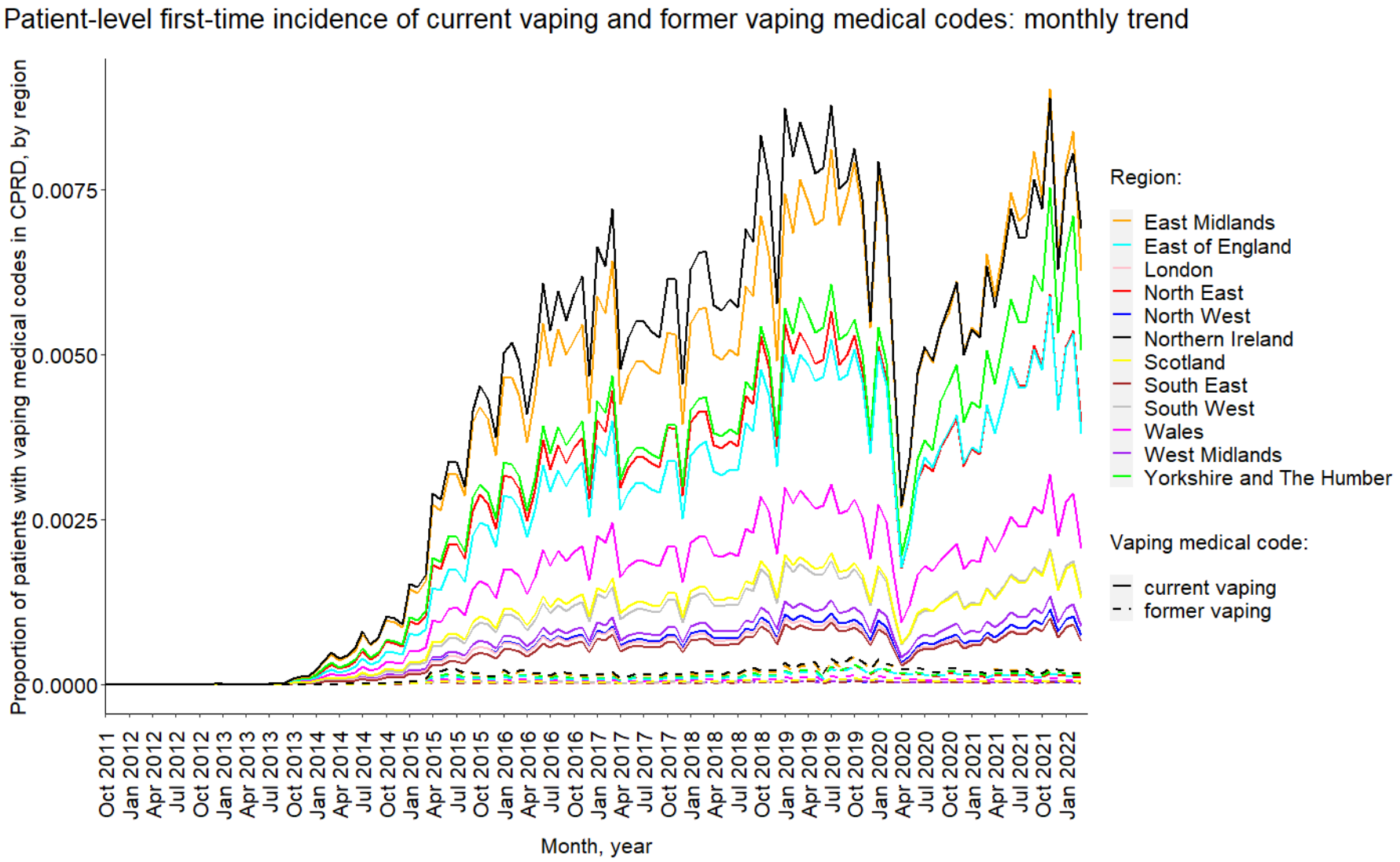
Supplementary Table 5a. Previous and subsequent smoking status of patients who received a current vaping code

Previous smoking status	**Subsequent (>12 months) smoking status**	**Current vaping code frequency, n (%) 147,130 (100.0)**	Proportion where 100% is the previous smoking status, Currently smoke: 80,986, 100% Formerly smoked: 56,300, 100% Never smoked: 8,211, 100% Unknown: 1,633, 100%
Currently smoke	Currently smoke	27,703 (18.8)	34.2
Currently smoke	Formerly smoked	19,209 (13.1)	23.7
Currently smoke	Never smoked	1,384 (0.9)	1.7
Currently smoke	Unknown	32,690 (22.2)	40.4
Formerly smoked	Currently smoke	6,705 (4.6)	11.9
Formerly smoked	Formerly smoked	21,017 (14.3)	37.3
Formerly smoked	Never smoked	1,532 (1.0)	2.7
Formerly smoked	Unknown	27,046 (18.4)	48.0
Never smoked	Currently smoke	628 (0.4)	7.7
Never smoked	Formerly smoked	1,547 (1.1)	18.8
Never smoked	Never smoked	693 (0.5)	8.4
Never smoked	Unknown	5,343 (3.6)	65.1
Unknown	Currently smoke	186 (0.1)	11.4
Unknown	Formerly smoked	294 (0.2)	18.0
Unknown	Never smoked	39 (0.0)	2.4
Unknown	Unknown	1,114 (0.8)	68.2

Supplementary Table 5b. Previous and subsequent smoking status of patients who received a former vaping code

Previous smoking status	**Subsequent (>12 months) smoking status**	**Former vaping code frequency, n (%)** **5,147 (100.0)**	Proportion where 100% is the previous smoking status, Currently smoke: 3,127, 100% Formerly smoked: 1,779, 100% Never smoked: 204, 100% Unknown: 37, 100%
Currently smoke	Currently smoke	1,357 (26.4)	43.4
Currently smoke	Formerly smoked	606 (11.8)	19.4
Currently smoke	Never smoked	56 (1.1)	1.8
Currently smoke	Unknown	1,108 (21.5)	35.4
Formerly smoked	Currently smoke	229 (4.5)	12.9
Formerly smoked	Formerly smoked	708 (13.8)	39.8
Formerly smoked	Never smoked	49 (1.0)	2.8
Formerly smoked	Unknown	793 (15.4)	44.6
Never smoked	Currently smoke	27 (0.5)	13.2
Never smoked	Formerly smoked	39 (0.8)	19.1
Never smoked	Never smoked	28 (0.5)	13.7
Never smoked	Unknown	110 (2.1)	53.9
Unknown	Currently smoke	8 (0.2)	21.6
Unknown	Formerly smoked	12 (0.2)	32.4
Unknown	Never smoked	2 (0.0)	5.4
Unknown	Unknown	15 (0.3)	40.5

Supplementary Graph 1: Patient-level first-time incidence of current vaping and former medical codes, by region

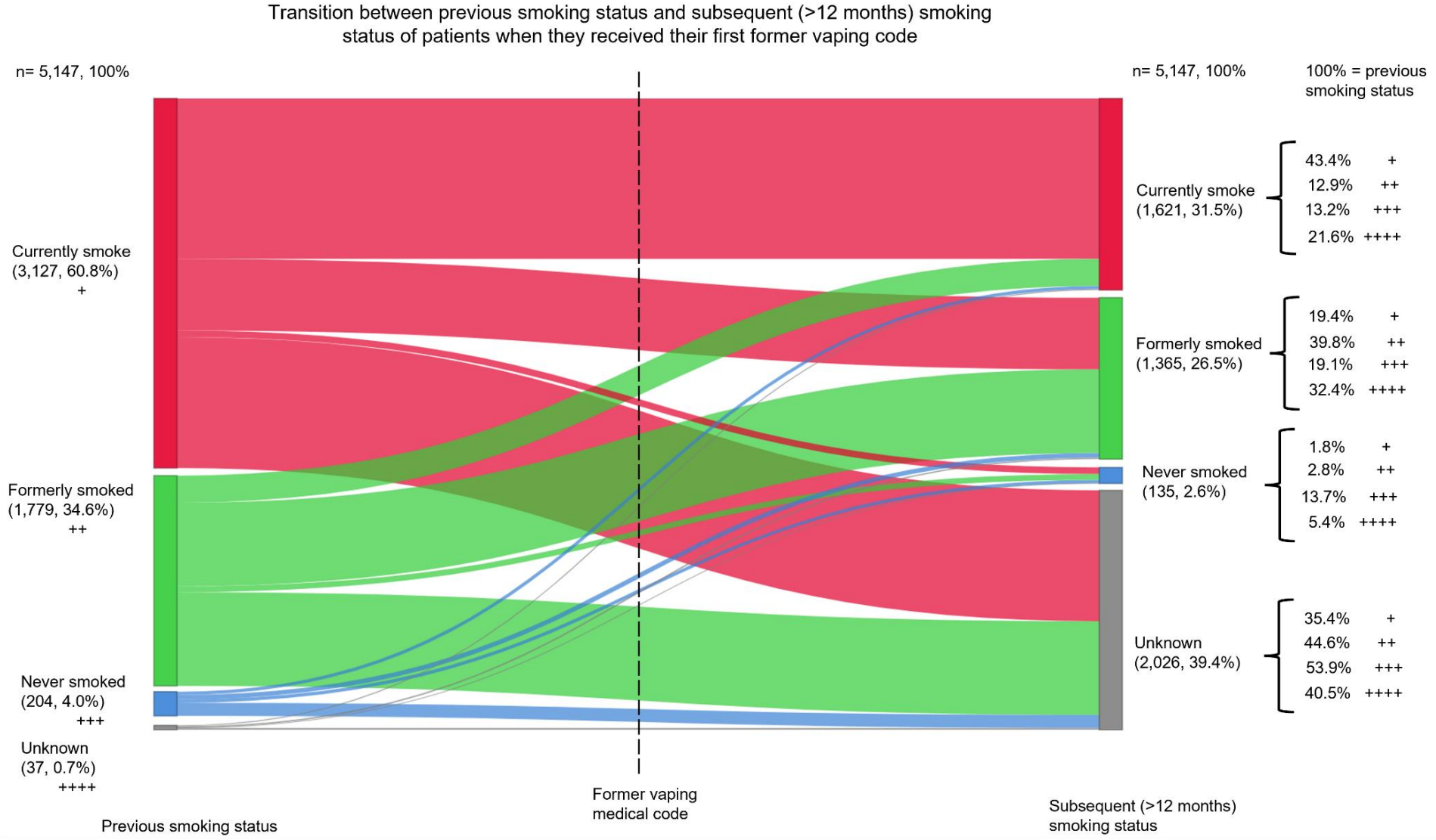


Supplementary Graph 2: Transition between previous smoking status and subsequent (>12 months) smoking status of patients when they received their first former vaping code

The 'nodes' (vertical bars) are coloured to represent the smoking status record obtained in the consultation (red: currently smoke, green: formerly smoked, blue: never smoked, unknown: grey). The 'connections' (transitions from left to right) are coloured to represent the previous smoking status (red: currently smoke, green: formerly smoked, blue: never smoked, unknown: grey).

The + signs on the right side (subsequent smoking status) indicate the proportion breakdown of previous smoking status categories. For example: Those who 'currently smoke' before receiving the former vaping code, >12 months after they received the former vaping code: 43.4% of them were currently smoking, 19.4% of them had quit smoking, 1.8% received a 'never smoked' code, and 35.4% had no smoking status recorded. (43.4% + 19.4% + 1.8% + 35.4 = 100%)

The mean time difference between the previous smoking status record and the former vaping code record was 430.6 days (SD: 535.7, range: 1.0 to 9,276.0, median: 313.5). The mean time difference between the subsequent smoking status record and the former vaping code record was 1,101.3 days (SD: 557.4, range: 366.0 to 2,761.0, median: 970.0).

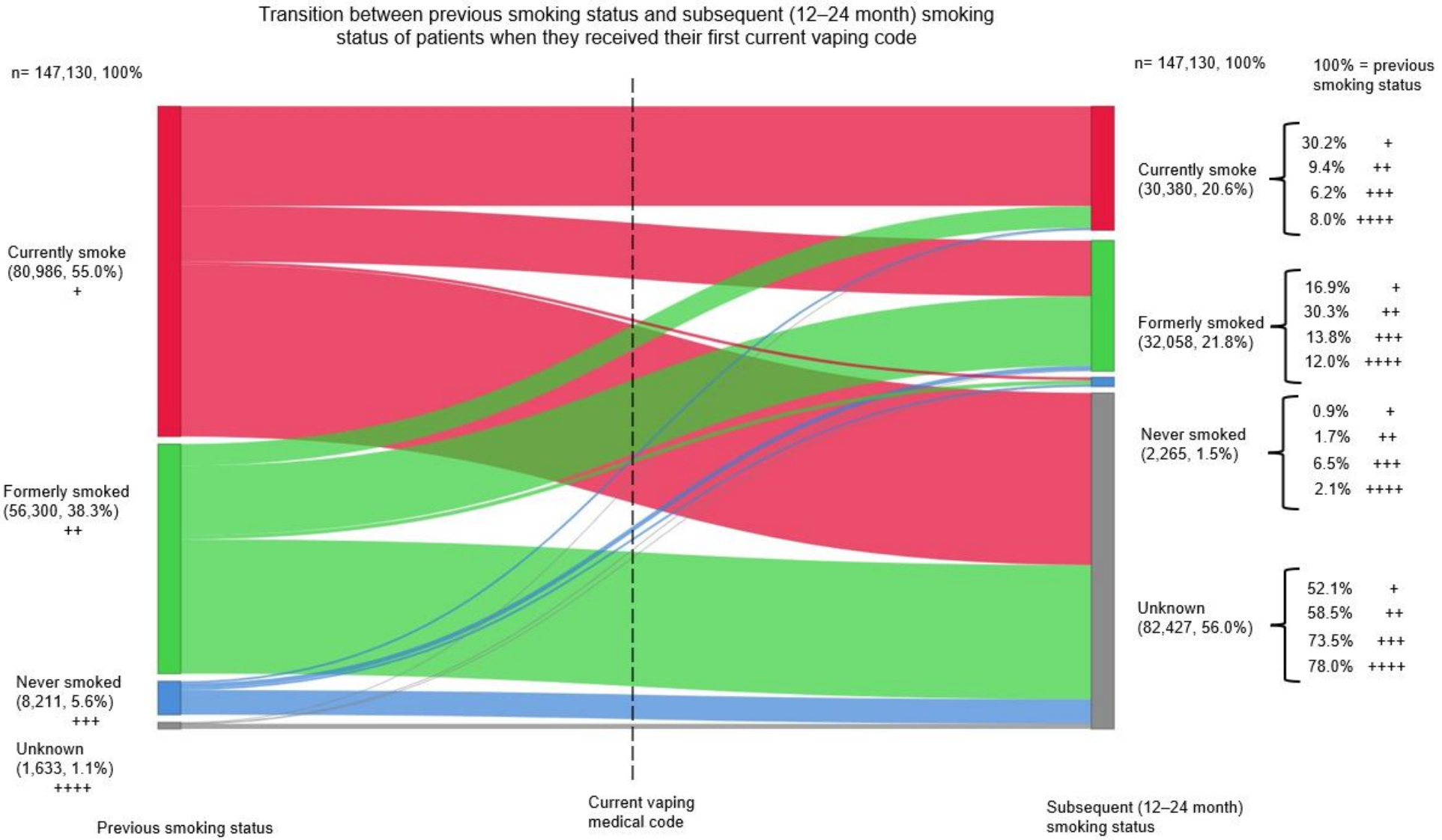

Transition between previous smoking status and subsequent (>12 months) smoking status of patients when they received their first former vaping code
n= 5,147, 100%
Currently smoke (3,127, 60.8%) +
Formerly smoked (1,779, 34.6%) ++
Never smoked (204, 4.0%) +++
Unknown (37, 0.7%) ++++
Previous smoking status
Former vaping medical code
n= 5,147, 100%
Currently smoke (1,621, 31.5%)
Formerly smoked (1,365, 26.5%)
Never smoked (135, 2.6%)
Unknown (2,026, 39.4%)
Subsequent (>12 months) smoking status
100% = previous smoking status
43.4% +
12.9% ++
13.2% +++
21.6% ++++
19.4% +
39.8% ++
19.1% +++
32.4% ++++
1.8% +
2.8% ++
13.7% +++
5.4% ++++
35.4% +
44.6% ++
53.9% +++
40.5% ++++

Supplementary Graph 3: Transition between previous smoking status and subsequent (>12–≤24 months) smoking status of patients when they received their first current vaping code

The 'nodes' (vertical bars) are coloured to represent the smoking status record obtained in the consultation (red: currently smoke, green: formerly smoked, blue: never smoked, unknown: grey). The 'connections' (transitions from left to right) are coloured to represent the previous smoking status (red: currently smoke, green: formerly smoked, blue: never smoked, unknown: grey).

The + signs on the right side (subsequent smoking status) indicate the proportion breakdown of previous smoking status categories. For example: Those who 'currently smoke' before receiving the current vaping code, >12–≤24 months after they received the current vaping code: 30.2% of them were currently smoking, 16.9% of them had quit smoking, 0.9% received a 'never smoked' code, and 52.1% had no smoking status recorded. (30.2% + 16.9% + 0.9% + 52.1% = 100%)

The mean time difference between the previous smoking status record and the current vaping medical code record was 542.6 days (SD: 668.1 days, range: 1.0 to 14,729.0, median: 344.0). The mean time difference between the subsequent smoking status record and the current vaping medical code record was 564.1 days (SD: 111.8, range: 366.0 to 730.0, median: 574.0).


Transition between previous smoking status and subsequent (12–24 month) smoking status of patients when they received their first current vaping code
n= 147,130, 100%
Currently smoke (80,986, 55.0%) +
Formerly smoked (56,300, 38.3%) ++
Never smoked (8,211, 5.6%) +++
Unknown (1,633, 1.1%) ++++
Previous smoking status
Current vaping medical code
n= 147,130, 100%
100% = previous smoking status
Currently smoke (30,380, 20.6%)
30.2% +
9.4% ++
6.2% +++
8.0% ++++
Formerly smoked (32,058, 21.8%)
16.9% +
30.3% ++
13.8% +++
12.0% ++++
Never smoked (2,265, 1.5%)
0.9% +
1.7% ++
6.5% +++
2.1% ++++
Unknown (82,427, 56.0%)
52.1% +
58.5% ++
73.5% +++
78.0% ++++
Subsequent (12–24 month) smoking status

Appendix D. Supplementary material for Chapter 5

Supplementary table 1. Mental health condition and covariates by healthcare professional interactions regarding smoking cessation and nicotine vaping. Cross-sectional International Tobacco Control Four Country Smoking and Vaping (ITC 4CV) Survey, 2018.

Variable	Categories	Visiting a health professional (n*= 11040)			Advice to quit smoking from health professional (n*= 8319)			Discussion about nicotine vaping products (n*= 8280)			Positive recommendation to use nicotine vaping products (n*= 859)		
		No	**Yes**	**Refused/don't know**	**No**	**Yes**	**Refused/don't know**	**No**	**Yes**	**Refused/don't know**	**No**	**Yes**	**Refused/don't know**
TOTAL		2599[+] (25.2[++])	8319 (74)	122 (0.7)	4087 (51.2)	4101 (47)	131 (1.7)	7341 (93.1)	859 (6.1)	80 (0.8)	562 (65.1)	288 (32.7)	9 (2.1)
Gender	**Male**	1523 (30.6)	3777 (68.5)	72 (0.9)	1775 (49.5)	1940 (48.5)	62 (2)	3232 (92.3)	488 (6.7)	41 (1)	313 (60.1)	170 (36.9)	5 (2.9)
	Female	1076 (18.9)	4542 (80.5)	50 (0.6)	2312 (53)	2161 (45.5)	69 (1.5)	4109 (93.9)	371 (5.5)	39 (0.6)	249 (71.4)	118 (27.6)	4 (1.1)
Age group (years)	**18-24**	683 (33.2)	1427 (65)	57 (1.8)	794 (62.6)	610 (35.8)	23 (1.6)	1135 (90.2)	262 (8.5)	21 (1.2)	168 (65.4)	93 (34.6)	1 (0.1)
	25-39	757 (32.7)	1617 (66.5)	32 (0.8)	881 (56.1)	708 (41.5)	28 (2.3)	1373 (92.3)	215 (6.6)	22 (1.1)	129 (53.9)	83 (43.3)	3 (2.8)
	40-54	650 (23.3)	2198 (75.9)	24 (0.8)	1077 (51.2)	1088 (47.4)	33 (1.4)	1979 (93.4)	187 (5.8)	21 (0.8)	128 (72.3)	58 (26.8)	1 (0.9)
	55 and up	509 (15.4)	3077 (84.4)	9 (0.2)	1335 (43.6)	1695 (54.9)	47 (1.5)	2854 (94.4)	195 (5.3)	16 (0.4)	137 (71.1)	54 (25.4)	4 (3.5)
Ethnicity	**Minority group**	438 (27)	1168 (71.7)	30 (1.3)	547 (48.2)	603 (50)	18 (1.8)	952 (89.9)	190 (8.1)	20 (2)	124 (66.5)	66 (33.5)	0 (0)
	Majority group	2161 (25)	7151 (74.4)	92 (0.6)	3540 (51.7)	3498 (46.6)	113 (1.7)	6389 (93.6)	669 (5.8)	60 (0.6)	438 (64.9)	222 (32.6)	9 (2.5)
Education	**Low**	861 (25.3)	2616 (74)	42 (0.7)	1283 (47)	1283 (50.6)	50 (2.4)	2351 (93.9)	224 (5.2)	26 (0.9)	151 (74)	72 (26)	1 (0)
	Moderate	1034 (25.3)	3543 (73.8)	50 (0.8)	1723 (51.7)	1771 (46.9)	49 (1.4)	3148 (92.9)	346 (6.4)	35 (0.7)	244 (64.1)	97 (32.1)	5 (3.8)
	High	704 (24.9)	2160 (74.6)	30 (0.5)	1081 (56.3)	1047 (42)	32 (1.7)	1842 (92.3)	289 (6.8)	19 (0.9)	167 (57.5)	119 (41.6)	3 (1)

Variable	Categories	Visiting a health professional (n*= 11040)			Advice to quit smoking from health professional (n*= 8319)			Discussion about nicotine vaping products (n*= 8280)			Positive recommendation to use nicotine vaping products (n*= 859)		
Income	**Low**	767 (23.3)	2725 (76)	41 (0.7)	1330 (50)	1347 (48.4)	48 (1.6)	2435 (93.6)	242 (5.4)	32 (1.1)	170 (67.8)	67 (28.4)	5 (3.8)
	Moderate	982 (27.1)	2673 (72)	51 (0.9)	1296 (50.8)	1331 (46.7)	46 (2.5)	2360 (93)	278 (6.1)	24 (0.9)	183 (66.7)	94 (32.5)	1 (0.8)
	High	728 (24.5)	2499 (74.8)	22 (0.7)	1229 (52.7)	1239 (46.1)	31 (1.2)	2161 (92.6)	308 (6.9)	21 (0.5)	187 (59.8)	118 (38)	3 (2.3)
	No answer	122 (28.7)	422 (70.5)	8 (0.8)	232 (53.7)	184 (45.4)	6 (0.8)	385 (93.5)	31 (6)	3 (0.5)	22 (77.4)	9 (22.6)	0 (0)
Cigarette smoking status	**Daily**	1895 (25.1)	6142 (74.3)	77 (0.5)	2797 (47.5)	3252 (51)	93 (1.6)	5451 (93.5)	611 (5.9)	49 (0.6)	380 (64.5)	227 (34.1)	4 (1.4)
	Non-daily	488 (29.5)	1143 (68.3)	37 (2.2)	671 (66.4)	455 (31.3)	17 (2.3)	939 (90.2)	181 (8)	19 (1.7)	132 (68.4)	48 (31.5)	1 (0.2)
	Former	216 (21.2)	1034 (78.2)	8 (0.6)	619 (63.1)	394 (34.7)	21 (2.3)	951 (93.3)	67 (5.4)	12 (1.2)	50 (65.2)	13 (24.1)	4 (10.7)
Problematic alcohol use	**No**	1458 (23)	5451 (76.5)	42 (0.5)	2633 (50.3)	2735 (48.1)	83 (1.7)	4865 (93.3)	501 (5.7)	58 (1)	336 (70.2)	160 (28.4)	5 (1.4)
	Yes	1009 (28.5)	2599 (70.6)	61 (0.9)	1298 (52.8)	1263 (45.3)	38 (1.8)	2229 (92.4)	340 (7.2)	19 (0.4)	216 (57)	120 (39.6)	4 (3.4)
	No answer	132 (34)	269 (63.3)	19 (2.8)	156 (55.2)	103 (42.2)	10 (2.7)	247 (95.3)	18 (4.3)	3 (0.4)	10 (66.7)	8 (33.3)	0 (0)
Mental health status	**No depression or anxiety**	2049 (30)	5279 (69.3)	65 (0.7)	2650 (51.9)	2550 (46.4)	79 (1.7)	4738 (93.7)	459 (5.3)	56 (1)	302 (67.2)	150 (30.6)	7 (2.2)
	Depression only	137 (15.2)	763 (84.2)	18 (0.6)	312 (42)	437 (55.6)	14 (2.4)	643 (92.2)	110 (7.3)	7 (0.5)	68 (61.2)	42 (38.8)	0 (0)
	Anxiety only	162 (17.6)	662 (80.8)	20 (1.6)	333 (55)	317 (43.4)	12 (1.7)	564 (92.9)	89 (6.9)	6 (0.3)	61 (62.9)	28 (37.1)	0 (0)
	Depression and anxiety	251 (12.3)	1615 (87)	19 (0.7)	792 (51.9)	797 (46.6)	26 (1.5)	1396 (91.5)	201 (7.9)	11 (0.5)	131 (62.8)	68 (33.8)	2 (3.5)
Country	**Australia**	145 (14.2)	1222 (85.4)	5 (0.4)	553 (45.3)	650 (52.2)	19 (2.4)	1155 (96.7)	52 (3)	7 (0.3)	40 (83.4)	12 (16.6)	0 (0)

Variable	**Categories**	**Visiting a health professional** (n*= 11040)			**Advice to quit smoking from health professional** (n*= 8319)			**Discussion about nicotine vaping products** (n*= 8280)			**Positive recommendation to use nicotine vaping products** (n*= 859)		
	Canada	659 (20.6)	2473 (78.9)	25 (0.5)	1285 (54)	1159 (45)	29 (1)	2217 (94.1)	228 (5.1)	22 (0.8)	162 (63.8)	64 (34.6)	2 (1.6)
	England	1325 (32.6)	2822 (66.4)	70 (1)	1539 (57.1)	1242 (41.6)	41 (1.3)	2385 (90.9)	389 (8.4)	31 (0.7)	216 (58.7)	166 (37.6)	7 (3.6)
	US	470 (24.5)	1802 (74.8)	22 (0.8)	710 (41.9)	1050 (55.1)	42 (3)	1584 (92.7)	190 (5.9)	20 (1.4)	144 (75.2)	46 (24.8)	0 (0)

* n is unweighted frequency, total number of respondents who were asked this survey question

+ Unweighted frequency of respondents who responded to the outcome

++ Weighted proportion of respondents who responded to the outcome. Denominator is frequency of respondents who responded ‘Yes’ and ‘No’ to the outcome, including refused and don’t know responses

Supplementary Table 2. Odds ratios, with 95% CI for all independent variables and covariates for all of the logistic regression models, for each outcome measure.

- Model 1: unadjusted model with mental health condition as the only independent variable
- Model 2: model adjusted for country, sex, age, education, ethnicity, and income
- Model 3 (fully adjusted): adjusted for country, sex, age, education, ethnicity, and income, cigarette smoking status and problematic alcohol use
- Model 4 (country-differences): adjusted for country, gender, age, education, income, ethnicity, cigarette smoking status, problematic alcohol use, and mental health*country interaction term

RQ1: Visiting a health professional

Supplementary Table 2a

Model 1

Variable	Category	beta	OR	Lower 95% CI	Upper 95% CI	p-value
	(Intercept)	0.84	2.31	2.20	2.42	0.000
Mental health	No depression/anxiety (ref)		1.00			
	Depression only	0.88	2.40	1.98	2.93	0.000
	Anxiety only	0.69	2.00	1.64	2.44	0.000
	Depression and anxiety	1.12	3.08	2.65	3.58	0.000

Supplementary Table 2b

Model 2

Variable	Category	beta	OR	Lower 95% CI	Upper 95% CI	p-value
	(Intercept)	-0.63	0.53	0.42	0.67	0.000

Mental health	No depression/anxiety (ref)		1.00			
	Depression only	0.96	2.62	2.15	3.23	0.000
	Anxiety only	0.73	2.08	1.70	2.57	0.000
	Depression and anxiety	1.31	3.71	3.17	4.36	0.000
Gender	Male (ref)		1.00			
	Female	0.68	1.98	1.79	2.18	0.000
Age	18-24 (ref)		1.00			
	25-39	0.09	1.09	0.93	1.28	0.287
	40-54	0.67	1.96	1.66	2.31	0.000
	55 and up	1.35	3.84	3.22	4.58	0.000
Ethnicity	Minority group		1.00			
	Majority group	-0.07	0.94	0.81	1.07	0.339
Education	Low (ref)		1.00			
	Moderate	0.24	1.27	1.14	1.42	0.000
	High	0.29	1.33	1.16	1.53	0.000
Income	Low (ref)		1.00			
	Moderate	0.11	1.11	0.99	1.25	0.083
	High	0.23	1.26	1.11	1.43	0.000
	No answer	-0.09	0.91	0.73	1.14	0.418
Country	England (ref)		1.00			
	Australia	1.19	3.30	2.77	3.95	0.000
	Canada	0.65	1.91	1.69	2.15	0.000
	US	0.43	1.54	1.35	1.75	0.000

Supplementary Table 2c

Model 3 (fully adjusted)

Variable	**Category**	**beta**	**OR**	**Lower 95% CI**	**Upper 95% CI**	**p-value**
	(Intercept)	-0.57	0.57	0.45	0.72	0.000

Mental health	No depression/anxiety (ref)		1.00			
	Depression only	0.98	2.65	2.17	3.27	0.000
	Anxiety only	0.73	2.08	1.70	2.57	0.000
	Depression and anxiety	1.32	3.74	3.19	4.40	0.000
Gender	Male (ref)		1.00			
	Female	0.67	1.95	1.77	2.15	0.000
Age	18-24 (ref)		1.00			
	25-39	0.06	1.06	0.90	1.24	0.468
	40-54	0.66	1.93	1.63	2.29	0.000
	55 and up	1.32	3.75	3.14	4.49	0.000
Ethnicity	Minority group		1.00			
	Majority group	-0.07	0.93	0.81	1.07	0.305
Education	Low (ref)		1.00			
	Moderate	0.24	1.27	1.13	1.42	0.000
	High	0.27	1.31	1.14	1.50	0.000
Income	Low (ref)		1.00			
	Moderate	0.10	1.10	0.98	1.24	0.109
	High	0.22	1.25	1.10	1.42	0.001
	No answer	-0.08	0.92	0.74	1.15	0.471
Country	England (ref)		1.00			
	Australia	1.19	3.27	2.75	3.91	0.000
	Canada	0.63	1.88	1.67	2.12	0.000
	US	0.40	1.49	1.31	1.70	0.000
Problematic alcohol use (Y/N)	No		1.00			
	Yes	-0.08	0.93	0.84	1.02	0.133
	No answer	-0.37	0.69	0.55	0.87	0.002
Cigarette smoking status	Daily (ref)		1.00			
	Non-daily	-0.08	0.92	0.80	1.06	0.257
	Former	0.35	1.42	1.21	1.67	0.000

Supplementary Table 2d

Model 4 (country-differences)

Variable	Category	beta	OR	Lower 95% CI	Upper 95% CI	p-value
	(Intercept)	-0.61	0.54	0.43	0.69	0.000
Mental health	No depression/anxiety (ref)		1.00			
	Depression only	1.27	3.58	2.70	4.81	0.000
	Anxiety only	0.77	2.17	1.55	3.08	0.000
	Depression and anxiety	1.56	4.76	3.77	6.06	0.000
Country	England (ref)		1.00			
	Australia	1.26	3.53	2.90	4.32	0.000
	Canada	0.73	2.08	1.82	2.38	0.000
	US	0.47	1.60	1.38	1.85	0.000
Gender	Male (ref)		1.00			
	Female	0.67	1.96	1.78	2.16	0.000
Age	18-24 (ref)		1.00			
	25-39	0.06	1.06	0.90	1.24	0.484
	40-54	0.65	1.92	1.62	2.28	0.000
	55 and up	1.32	3.75	3.13	4.49	0.000
Ethnicity	Minority group		1.00			
	Majority group	-0.07	0.93	0.81	1.07	0.296
Education	Low (ref)		1.00			
	Moderate	0.23	1.26	1.13	1.41	0.000
	High	0.27	1.31	1.14	1.51	0.000
Income	Low (ref)		1.00			
	Moderate	0.10	1.11	0.98	1.25	0.100
	High	0.23	1.25	1.10	1.43	0.001
	No answer	-0.07	0.93	0.75	1.16	0.518
Problematic alcohol use (Y/N)	No		1.00			

	Yes	-0.08	0.92	0.84	1.02	0.123
	No answer	-0.38	0.68	0.54	0.86	0.001
Cigarette smoking status	Daily (ref)		1.00			
	Non-daily	-0.09	0.91	0.79	1.05	0.209
	Former	0.34	1.41	1.20	1.66	0.000
Mental health*country interaction term	No depression/anxiety*England (ref)		1.00			
	Depression only*Australia	-0.59	0.55	0.28	1.18	0.103
	Anxiety only*Australia	-0.65	0.52	0.27	1.05	0.060
	Depression and anxiety*Australia	0.08	1.09	0.58	2.21	0.802
	Depression only*Canada	-0.62	0.54	0.32	0.92	0.021
	Anxiety only*Canada	-0.11	0.89	0.54	1.49	0.659
	Depression and anxiety*Canada	-0.64	0.53	0.36	0.78	0.001
	Depression only*US	-0.63	0.53	0.31	0.91	0.020
	Anxiety only*US	0.24	1.27	0.72	2.27	0.412
	Depression and anxiety*US	-0.44	0.64	0.44	0.95	0.027

Likelihood-ratio test between Model 3 (fully adjusted) and Model 4 (country-differences): p=0.002

RQ2: Advice to quit smoking from health professional

Supplementary Table 2e

Model 1

Variable	**Category**	**beta**	**OR**	**Lower 95% CI**	**Upper 95% CI**	**p-value**
	(Intercept)	-0.11	0.89	0.85	0.94	0.000
Mental health	No depression/anxiety (ref)		1.00			

	Depression only	0.39	1.48	1.27	1.74	0.000
	Anxiety only	-0.13	0.88	0.74	1.05	0.152
	Depression and anxiety	0.00	1.00	0.90	1.12	0.951

Supplementary Table 2f

Model 2

Variable	**Category**	**beta**	**OR**	**Lower 95% CI**	**Upper 95% CI**	**p-value**
	(Intercept)	-0.57	0.57	0.45	0.72	0.000
Mental health	No depression/anxiety (ref)		1.00			
	Depression only	0.46	1.58	1.34	1.86	0.000
	Anxiety only	-0.05	0.95	0.80	1.14	0.601
	Depression and anxiety	0.14	1.15	1.02	1.30	0.022
Gender	Male (ref)		1.00			
	Female	-0.09	0.91	0.83	1.00	0.043
Age	18-24 (ref)		1.00			
	25-39	0.25	1.29	1.08	1.54	0.005
	40-54	0.49	1.63	1.37	1.96	0.000
	55 and up	0.80	2.23	1.87	2.68	0.000
Ethnicity	Minority group		1.00			
	Majority group	-0.22	0.81	0.70	0.92	0.002
Education	Low (ref)		1.00			
	Moderate	-0.02	0.98	0.88	1.09	0.737
	High	-0.25	0.78	0.69	0.89	0.000
Income	Low (ref)		1.00			
	Moderate	0.05	1.05	0.94	1.18	0.365
	High	0.00	1.00	0.89	1.13	0.986
	No answer	0.02	1.02	0.82	1.26	0.876
Country	England (ref)		1.00			

	Australia	0.46	1.58	1.37	1.83	0.000
	Canada	0.12	1.13	1.01	1.26	0.040
	US	0.55	1.73	1.52	1.96	0.000

Supplementary Table 2g

Model 3 (fully adjusted)

Variable	**Category**	**beta**	**OR**	**Lower 95% CI**	**Upper 95% CI**	**p-value**
	(Intercept)	-0.35	0.71	0.55	0.90	0.006
Mental health	No depression/anxiety (ref)		1.00			
	Depression only	0.45	1.58	1.34	1.86	0.000
	Anxiety only	-0.06	0.94	0.79	1.12	0.493
	Depression and anxiety	0.14	1.14	1.01	1.29	0.031
Gender	Male (ref)		1.00			
	Female	-0.11	0.89	0.81	0.98	0.016
Age	18-24 (ref)		1.00			
	25-39	0.16	1.17	0.98	1.41	0.090
	40-54	0.34	1.40	1.17	1.69	0.000
	55 and up	0.65	1.92	1.60	2.31	0.000
Ethnicity	Minority group		1.00			
	Majority group	-0.23	0.79	0.69	0.91	0.001
Education	Low (ref)		1.00			
	Moderate	0.03	1.03	0.92	1.14	0.627
	High	-0.14	0.87	0.76	0.99	0.039
Income	Low (ref)		1.00			
	Moderate	0.05	1.05	0.94	1.18	0.367
	High	0.04	1.04	0.92	1.18	0.515
	No answer	0.06	1.07	0.86	1.33	0.570
Country	England (ref)		1.00			

	Australia	0.46	1.58	1.36	1.82	0.000
	Canada	0.16	1.17	1.05	1.32	0.007
	US	0.60	1.82	1.60	2.08	0.000
Problematic alcohol use (Y/N)	No		1.00			
	Yes	0.00	1.00	0.90	1.10	0.939
	No answer	-0.20	0.82	0.63	1.06	0.129
Cigarette smoking status	Daily (ref)		1.00			
	Non-daily	-0.72	0.49	0.42	0.57	0.000
	Former	-0.67	0.51	0.44	0.60	0.000

Supplementary Table 2h

Model 4 (country-differences)

Variable	**Category**	**beta**	**OR**	**Lower 95% CI**	**Upper 95% CI**	**p-value**
	(Intercept)	-0.32	0.73	0.56	0.93	0.013
Mental health	No depression/anxiety (ref)		1.00			
	Depression only	0.59	1.81	1.41	2.32	0.000
	Anxiety only	-0.18	0.84	0.58	1.19	0.330
	Depression and anxiety	0.01	1.01	0.82	1.23	0.954
Country	England (ref)		1.00			
	Australia	0.31	1.37	1.14	1.64	0.001
	Canada	0.14	1.15	1.00	1.32	0.047
	US	0.64	1.90	1.62	2.23	0.000
Gender	Male (ref)		1.00			
	Female	-0.11	0.89	0.81	0.98	0.017
Age	18-24 (ref)		1.00			
	25-39	0.14	1.15	0.96	1.38	0.130
	40-54	0.33	1.39	1.16	1.67	0.000
	55 and up	0.64	1.90	1.58	2.29	0.000

Ethnicity	Minority group		1.00			
	Majority group	-0.22	0.80	0.70	0.92	0.002
Education	Low (ref)		1.00			
	Moderate	0.02	1.02	0.92	1.14	0.689
	High	-0.14	0.87	0.76	1.00	0.048
Income	Low (ref)		1.00			
	Moderate	0.05	1.05	0.94	1.18	0.408
	High	0.04	1.04	0.92	1.17	0.566
	No answer	0.05	1.05	0.84	1.31	0.667
Problematic alcohol use (Y/N)	No		1.00			
	Yes	0.00	1.00	0.91	1.11	0.968
	No answer	-0.20	0.82	0.63	1.06	0.131
Cigarette smoking status	Daily (ref)		1.00			
	Non-daily	-0.72	0.49	0.42	0.57	0.000
	Former	-0.67	0.51	0.44	0.60	0.000
Mental health*country interaction term	No depression/anxiety*England (ref)		1.00			
	Depression only*Australia	0.17	1.19	0.73	1.94	0.490
	Anxiety only*Australia	0.76	2.15	1.20	3.89	0.011
	Depression and anxiety*Australia	0.36	1.44	1.01	2.04	0.044
	Depression only*Canada	-0.30	0.74	0.49	1.12	0.150
	Anxiety only*Canada	0.16	1.17	0.74	1.87	0.508
	Depression and anxiety*Canada	0.18	1.20	0.89	1.62	0.235
	Depression only*US	-0.56	0.57	0.36	0.92	0.020
	Anxiety only*US	-0.21	0.81	0.49	1.35	0.420
	Depression and anxiety*US	0.12	1.13	0.82	1.55	0.468

Likelihood-ratio test between Model 3 (fully adjusted) and Model 4 (country-differences): p=0.009

RQ3: Discussion about nicotine vaping products

Supplementary Table 2i

Model 1

Variable	Category	beta	OR	Lower 95% CI	Upper 95% CI	p-value
	(Intercept)	-2.87	0.06	0.05	0.06	0.000
Mental health	No depression/anxiety (ref)		1.00			
	Depression only	0.33	1.40	1.02	1.88	0.032
	Anxiety only	0.27	1.30	0.92	1.81	0.126
	Depression and anxiety	0.42	1.52	1.22	1.89	0.000

Supplementary Table 2j

Model 2

Variable	Category	beta	OR	Lower 95% CI	Upper 95% CI	p-value
	(Intercept)	-1.99	0.14	0.09	0.21	0.000
Mental health	No depression/anxiety (ref)		1.00			
	Depression only	0.36	1.44	1.04	1.95	0.023
	Anxiety only	0.37	1.45	1.01	2.03	0.036
	Depression and anxiety	0.50	1.65	1.30	2.09	0.000
Gender	Male (ref)		1.00			
	Female	-0.31	0.73	0.61	0.88	0.001
Age	18-24 (ref)		1.00			
	25-39	-0.14	0.87	0.64	1.21	0.399
	40-54	-0.28	0.76	0.55	1.05	0.093
	55 and up	-0.29	0.75	0.54	1.05	0.092
Ethnicity	Minority group		1.00			
	Majority group	-0.39	0.68	0.53	0.87	0.002

Education	Low (ref)		1.00			
	Moderate	0.00	1.00	0.80	1.26	0.988
	High	0.09	1.09	0.83	1.44	0.531
Income	Low (ref)		1.00			
	Moderate	0.06	1.06	0.83	1.35	0.654
	High	0.32	1.38	1.07	1.77	0.012
	No answer	0.10	1.11	0.68	1.71	0.668
Country	England (ref)		1.00			
	Australia	-1.13	0.32	0.22	0.46	0.000
	Canada	-0.53	0.59	0.46	0.74	0.000
	US	-0.43	0.65	0.50	0.84	0.001

Supplementary Table 2k

Model 3 (fully adjusted)

Variable	**Category**	**beta**	**OR**	**Lower 95% CI**	**Upper 95% CI**	**p-value**
	(Intercept)	-2.06	0.13	0.08	0.20	0.000
Mental health	No depression/anxiety (ref)		1.00			
	Depression only	0.36	1.44	1.04	1.95	0.023
	Anxiety only	0.37	1.45	1.01	2.03	0.037
	Depression and anxiety	0.49	1.63	1.29	2.06	0.000
Gender	Male (ref)		1.00			
	Female	-0.29	0.75	0.62	0.91	0.004
Age	18-24 (ref)		1.00			
	25-39	-0.11	0.89	0.65	1.24	0.501
	40-54	-0.25	0.78	0.56	1.10	0.149
	55 and up	-0.24	0.78	0.56	1.11	0.163
Ethnicity	Minority group		1.00			
	Majority group	-0.41	0.67	0.52	0.86	0.002

Education	Low (ref)		1.00			
	Moderate	-0.01	0.99	0.79	1.25	0.938
	High	0.08	1.09	0.82	1.43	0.556
Income	Low (ref)		1.00			
	Moderate	0.05	1.05	0.82	1.34	0.698
	High	0.31	1.36	1.06	1.75	0.016
	No answer	0.12	1.12	0.70	1.75	0.615
Country	England (ref)		1.00			
	Australia	-1.11	0.33	0.22	0.47	0.000
	Canada	-0.54	0.58	0.46	0.74	0.000
	US	-0.41	0.67	0.51	0.86	0.002
Problematic alcohol use (Y/N)	No		1.00			
	Yes	0.14	1.15	0.94	1.39	0.180
	No answer	-0.40	0.67	0.34	1.19	0.210
Cigarette smoking status	Daily (ref)		1.00			
	Non-daily	0.16	1.18	0.89	1.54	0.240
	Former	-0.12	0.89	0.64	1.20	0.462

Supplementary Table 2l

Model 4 (country-differences)

Variable	**Category**	**beta**	**OR**	**Lower 95% CI**	**Upper 95% CI**	**p-value**
	(Intercept)	-2.10	0.12	0.08	0.19	0.000
Mental health	No depression/anxiety (ref)		1.00			
	Depression only	0.45	1.57	1.02	2.34	0.033
	Anxiety only	0.73	2.07	1.21	3.39	0.005
	Depression and anxiety	0.40	1.50	1.06	2.09	0.019
Country	England (ref)		1.00			
	Australia	-1.04	0.35	0.21	0.56	0.000

	Canada	-0.49	0.61	0.46	0.82	0.001
	US	-0.42	0.66	0.47	0.92	0.015
Gender	Male (ref)		1.00			
	Female	-0.29	0.75	0.62	0.91	0.004
Age	18-24 (ref)		1.00			
	25-39	-0.10	0.91	0.66	1.26	0.562
	40-54	-0.23	0.80	0.57	1.12	0.178
	55 and up	-0.22	0.80	0.57	1.14	0.207
Ethnicity	Minority group		1.00			
	Majority group	-0.40	0.67	0.52	0.87	0.002
Education	Low (ref)		1.00			
	Moderate	0.00	1.00	0.79	1.26	0.990
	High	0.10	1.11	0.84	1.46	0.481
Income	Low (ref)		1.00			
	Moderate	0.04	1.04	0.81	1.32	0.768
	High	0.30	1.34	1.05	1.73	0.021
	No answer	0.13	1.14	0.70	1.76	0.585
Problematic alcohol use (Y/N)	No		1.00			
	Yes	0.15	1.16	0.95	1.41	0.150
	No answer	-0.41	0.67	0.34	1.18	0.200
Cigarette smoking status	Daily (ref)		1.00			
	Non-daily	0.17	1.18	0.89	1.55	0.227
	Former	-0.12	0.88	0.64	1.19	0.434
Mental health*country interaction term	No depression/anxiety*England (ref)		1.00			
	Depression only*Australia	0.33	1.39	0.47	3.67	0.519
	Anxiety only*Australia	-1.47	0.23	0.01	1.22	0.159
	Depression and anxiety*Australia	-0.14	0.87	0.34	2.06	0.758
	Depression only*Canada	-0.36	0.70	0.27	1.59	0.417
	Anxiety only*Canada	-0.49	0.61	0.26	1.37	0.240

	Depression and anxiety*Canada	0.07	1.07	0.60	1.88	0.806
	Depression only*US	-0.40	0.67	0.24	1.63	0.404
	Anxiety only*US	-0.57	0.57	0.22	1.37	0.222
	Depression and anxiety*US	0.37	1.44	0.82	2.53	0.202

Likelihood-ratio test between Model 3 (fully adjusted) and Model 4 (country-differences): p=0.415

RQ4: Positive recommendation to use nicotine vaping products

Supplementary Table 2m

Model 1

Variable	Category	beta	OR	Lower 95% CI	Upper 95% CI	p-value
	(Intercept)	-0.78697	0.46	0.37	0.55	0.000
Mental health	No depression/anxiety (ref)		1.00			
	Depression only	0.329851	1.39	0.87	2.21	0.166
	Anxiety only	0.259387	1.30	0.76	2.17	0.331
	Depression and anxiety	0.167331	1.18	0.83	1.67	0.343

Supplementary Table 2n

Model 2

Variable	Category	beta	OR	Lower 95% CI	Upper 95% CI	p-value
	(Intercept)	-0.78584	0.46	0.22	0.92	0.029
Mental health	No depression/anxiety (ref)		1.00			

	Depression only	0.328175	1.39	0.83	2.30	0.204
	Anxiety only	0.06195	1.06	0.60	1.86	0.831
	Depression and anxiety	0.247724	1.28	0.86	1.90	0.218
Gender	Male (ref)		1.00			
	Female	-0.4939	0.61	0.45	0.83	0.002
Age	18-24 (ref)		1.00			
	25-39	0.354833	1.43	0.87	2.37	0.164
	40-54	-0.49003	0.61	0.36	1.05	0.073
	55 and up	-0.32982	0.72	0.42	1.24	0.233
Ethnicity	Minority group		1.00			
	Majority group	0.252891	1.29	0.83	2.01	0.259
Education	Low (ref)		1.00			
	Moderate	0.196878	1.22	0.82	1.82	0.334
	High	0.556871	1.75	1.10	2.78	0.019
Income	Low (ref)		1.00			
	Moderate	0.023276	1.02	0.68	1.54	0.911
	High	0.17508	1.19	0.78	1.82	0.417
	No answer	-0.31529	0.73	0.30	1.62	0.457
Country	England (ref)		1.00			
	Australia	-1.28757	0.28	0.12	0.56	0.001
	Canada	-0.04017	0.96	0.65	1.42	0.841
	US	-0.5582	0.57	0.37	0.89	0.013

Supplementary Table 2o

Model 3 (fully adjusted)

Variable	**Category**	**beta**	**OR**	**Lower 95% CI**	**Upper 95% CI**	**p-value**
	(Intercept)	-0.76783	0.46	0.22	0.98	0.045
Mental health	No depression/anxiety (ref)		1.00			

	Depression only	0.307861	1.36	0.81	2.26	0.240
	Anxiety only	0.020313	1.02	0.57	1.81	0.945
	Depression and anxiety	0.238358	1.27	0.85	1.89	0.240
Gender	Male (ref)		1.00			
	Female	-0.4655	0.63	0.45	0.87	0.005
Age	18-24 (ref)		1.00			
	25-39	0.250262	1.28	0.77	2.15	0.338
	40-54	-0.63619	0.53	0.30	0.92	0.024
	55 and up	-0.40505	0.67	0.38	1.17	0.159
Ethnicity	Minority group		1.00			
	Majority group	0.19366	1.21	0.78	1.90	0.393
Education	Low (ref)		1.00			
	Moderate	0.264145	1.30	0.87	1.96	0.201
	High	0.726933	2.07	1.28	3.36	0.003
Income	Low (ref)		1.00			
	Moderate	0.008834	1.01	0.67	1.53	0.966
	High	0.092974	1.10	0.71	1.69	0.674
	No answer	-0.41987	0.66	0.27	1.49	0.333
Country	England (ref)		1.00			
	Australia	-1.20143	0.30	0.13	0.62	0.002
	Canada	0.095251	1.10	0.73	1.65	0.645
	US	-0.45725	0.63	0.40	0.99	0.048
Problematic alcohol use (Y/N)	No		1.00			
	Yes	0.332198	1.39	0.98	1.97	0.061
	No answer	0.23702	1.27	0.41	3.55	0.661
Cigarette smoking status	Daily (ref)		1.00			
	Non-daily	-0.49388	0.61	0.38	0.96	0.038
	Former	-0.45376	0.64	0.34	1.13	0.133

Supplementary Table 2p

Model 4 (country-differences)

Variable	Category	beta	OR	Lower 95% CI	Upper 95% CI	p-value
	(Intercept)	-0.68906	0.50	0.23	1.08	0.081
Mental health	No depression/anxiety (ref)		1.00			
	Depression only	-0.12952	0.88	0.44	1.72	0.709
	Anxiety only	0.358144	1.43	0.63	3.28	0.392
	Depression and anxiety	0.288494	1.33	0.76	2.34	0.316
Country	England (ref)		1.00			
	Australia	-2.09746	0.12	0.03	0.40	0.002
	Canada	0.207044	1.23	0.73	2.05	0.430
	US	-0.5784	0.56	0.30	1.02	0.064
Gender	Male (ref)		1.00			
	Female	-0.54273	0.58	0.41	0.81	0.002
Age	18-24 (ref)		1.00			
	25-39	0.229897	1.26	0.75	2.14	0.392
	40-54	-0.58543	0.56	0.32	0.99	0.044
	55 and up	-0.40161	0.67	0.38	1.20	0.173
Ethnicity	Minority group		1.00			
	Majority group	0.151895	1.16	0.74	1.85	0.514
Education	Low (ref)		1.00			
	Moderate	0.256897	1.29	0.85	1.98	0.232
	High	0.70506	2.02	1.23	3.35	0.006
Income	Low (ref)		1.00			
	Moderate	0.038565	1.04	0.68	1.60	0.859
	High	0.085482	1.09	0.70	1.71	0.708
	No answer	-0.47473	0.62	0.25	1.44	0.285
Problematic alcohol use (Y/N)	No		1.00			

	Yes	0.360392	1.43	1.00	2.06	0.050
	No answer	0.26229	1.30	0.41	3.77	0.638
Cigarette smoking status	Daily (ref)		1.00			
	Non-daily	-0.55277	0.58	0.35	0.92	0.025
	Former	-0.45563	0.63	0.34	1.16	0.149
Mental health*country interaction term	No depression/anxiety*England (ref)		1.00			
	Depression only*Australia	2.801618	16.47	2.47	136.18	0.005
	Anxiety only*Australia	-10.774	0.00	NA	22769453165899200000000000	0.979
	Depression and anxiety*Australia	0.719362	2.05	0.15	19.32	0.538
	Depression only*Canada	0.933002	2.54	0.61	10.56	0.196
	Anxiety only*Canada	-1.54585	0.21	0.04	0.93	0.052
	Depression and anxiety*Canada	-0.34615	0.71	0.27	1.80	0.471
	Depression only*US	0.381836	1.46	0.22	7.51	0.663
	Anxiety only*US	0.195571	1.22	0.24	5.52	0.804
	Depression and anxiety*US	0.118814	1.13	0.41	3.09	0.818

Likelihood-ratio test between Model 3 (fully adjusted) and Model 4 (country-differences): p=0.064

Appendix E. Supplementary material for Chapter 6

Supplementary Table 1. Mental health condition and sample characteristics by cessation aid used during last attempt to quit smoking.
Unweighted frequencies and weighted proportions

Variable	Categories	Used any cessation aid (n*= 5177)			Used vaping products (n*= 5177)			Used NRT (n*= 5177)			Used varenicline or bupropion (n*= 5177)			Used behavioural support (n*= 5177)		
		No	Yes	R/D	No	Yes	R/D	No	Yes	R/D	No	Yes	R/D	No	Yes	R/D
	TOTAL	1592 (39.9)	3550 (59.2)	35 (0.9)	2820 (68.7)	2333 (30.9)	24 (0.4)	3562 (70.1)	1563 (28.6)	52 (1.2)	4399 (86.8)	726 (12.0)	52 (1.2)	4411 (87.9)	714 (10.9)	52 (1.2)
Gender	**Male**	699 (38.7)	1721 (60.4)	14 (0.9)	1260 (67.5)	1159 (32.0)	15 (0.5)	1680 (69.9)	730 (28.7)	24 (1.4)	2042 (86.3)	368 (12.3)	24 (1.4)	2040 (87.5)	370 (11.1)	24 (1.4)
	Female	893 (41.1)	1829 (57.9)	21 (0.9)	1560 (70.0)	1174 (29.8)	9 (0.2)	1882 (70.4)	833 (28.6)	28 (1.1)	2357 (87.3)	358 (11.6)	28 (1.1)	2371 (88.2)	344 (10.7)	28 (1.1)
Age group (years)	**18-24**	389 (45.4)	770 (52.9)	14 (1.7)	566 (63.2)	599 (36.3)	8 (0.5)	818 (73.2)	336 (24.9)	19 (2.0)	1047 (93.8)	107 (4.2)	19 (2.0)	985 (88.6)	169 (9.4)	19 (2.0)
	25-39	410 (42.7)	890 (56.2)	9 (1.1)	631 (64.7)	671 (34.8)	7 (0.5)	946 (74.2)	342 (23.9)	21 (1.9)	1112 (89.3)	176 (8.9)	21 (1.9)	1106 (87.7)	182 (10.4)	21 (1.9)
	40-54	343 (34.6)	911 (64.4)	9 (1.0)	694 (69.4)	563 (30.3)	6 (0.3)	847 (66.9)	409 (32.3)	7 (0.8)	1051 (83.0)	205 (16.1)	7 (0.8)	1082 (88.0)	174 (11.1)	7 (0.8)
	55 and up	450 (37.9)	979 (61.8)	3 (0.3)	929 (77.4)	500 (22.3)	3 (0.3)	951 (65.3)	476 (34.4)	5 (0.3)	1189 (83.0)	238 (16.8)	5 (0.3)	1238 (87.5)	189 (12.2)	5 (0.3)
Ethnicity	**Minority group**	256 (41.4)	563 (57.0)	8 (1.5)	445 (70.1)	374 (29.1)	8 (0.8)	551 (70.6)	268 (26.9)	8 (2.4)	697 (88.2)	122 (9.4)	8 (2.4)	665 (82.2)	154 (15.4)	8 (2.4)
	Majority group	1336 (39.6)	2987 (59.6)	27 (0.8)	2375 (68.4)	1959 (31.2)	16 (0.3)	3011 (70.1)	1295 (28.9)	44 (1.0)	3702 (86.5)	604 (12.4)	44 (1.0)	3746 (88.8)	560 (10.1)	44 (1.0)
Education	**Low**	478 (38.9)	1053 (59.9)	13 (1.2)	896 (73.4)	640 (26.3)	8 (0.3)	1059 (66.7)	472 (32.1)	13 (1.2)	1317 (85.3)	214 (13.5)	13 (1.2)	1352 (89.6)	179 (9.3)	13 (1.2)
	Moderate	686 (39.0)	1536 (60.1)	14 (0.9)	1187 (65.0)	1040 (34.5)	9 (0.5)	1536 (70.3)	672 (28.1)	28 (1.6)	1921 (88.1)	287 (10.3)	28 (1.6)	1909 (87.6)	299 (10.8)	28 (1.6)
	High	428 (42.8)	961 (56.6)	8 (0.6)	737 (70.3)	653 (29.4)	7 (0.3)	967 (74.1)	419 (25.3)	11 (0.6)	1161 (86.0)	225 (13.4)	11 (0.6)	1150 (86.4)	236 (13.0)	11 (0.6)

Income	**Low**	521 (38.6)	1063 (60.3)	12 (1.1)	946 (72.7)	644 (27.0)	6 (0.3)	1081 (68.3)	500 (30.6)	15 (1.1)	1362 (85.6)	219 (13.3)	15 (1.1)	1360 (87.1)	221 (11.8)	15 (1.1)
	Moderate	466 (38.2)	1223 (60.6)	14 (1.3)	835 (63.9)	857 (35.6)	11 (0.5)	1189 (70.1)	490 (27.8)	24 (2.0)	1457 (88.5)	222 (9.5)	24 (2.0)	1434 (88.2)	245 (9.7)	24 (2.0)
	High	515 (42.2)	1109 (57.5)	7 (0.4)	881 (69.6)	744 (30.2)	6 (0.2)	1128 (71.7)	493 (27.8)	10 (0.5)	1358 (85.9)	263 (13.6)	10 (0.5)	1398 (88.0)	223 (11.5)	10 (0.5)
	No answer	90 (43.0)	155 (55.0)	2 (1.9)	158 (70.8)	88 (27.9)	1 (1.3)	164 (70.3)	80 (27.6)	3 (2.1)	222 (88.5)	22 (9.4)	3 (2.1)	219 (89.1)	25 (8.7)	3 (2.1)
Cigarette smoking status	**Daily**	867 (35.8)	2205 (63.5)	20 (0.7)	1697 (68.9)	1382 (30.9)	13 (0.2)	1977 (64.7)	1086 (34.2)	29 (1.1)	2561 (85.4)	502 (13.5)	29 (1.1)	2601 (86.7)	462 (12.2)	29 (1.1)
	Non-daily	259 (49.6)	561 (48.9)	7 (1.5)	388 (68.6)	434 (31.0)	5 (0.4)	579 (74.5)	235 (23.2)	13 (2.3)	728 (90.7)	86 (7.1)	13 (2.3)	692 (87.9)	122 (9.8)	13 (2.3)
	Quit	466 (45.5)	784 (53.3)	8 (1.2)	735 (68.3)	517 (30.9)	6 (0.8)	1006 (81.9)	242 (16.9)	10 (1.2)	1110 (88.4)	138 (10.5)	10 (1.2)	1118 (90.8)	130 (8.0)	10 (1.2)
Problematic alcohol use	**No**	1036 (39.3)	2302 (59.9)	19 (0.8)	1865 (69.1)	1478 (30.6)	14 (0.3)	2286 (70.1)	1041 (28.8)	30 (1.1)	2870 (86.3)	457 (12.5)	30 (1.1)	2867 (87.2)	460 (11.7)	30 (1.1)
	Yes	506 (41.6)	1144 (57.8)	9 (0.6)	863 (68.3)	791 (31.3)	5 (0.3)	1165 (71.3)	478 (27.8)	16 (0.8)	1391 (87.9)	252 (11.2)	16 (0.8)	1407 (90.0)	236 (9.2)	16 (0.8)
	No answer	50 (32.1)	104 (58.6)	7 (9.2)	92 (63.7)	64 (32.6)	5 (3.7)	111 (57.7)	44 (33.3)	6 (9.0)	138 (83.6)	17 (7.4)	6 (9.0)	137 (79.1)	18 (11.9)	6 (9.0)
Mental health	**No depression or anxiety**	1076 (41.4)	2206 (57.7)	24 (0.9)	1863 (69.2)	1430 (30.5)	13 (0.3)	2319 (71.8)	954 (27.1)	33 (1.1)	2865 (87.7)	408 (11.2)	33 (1.1)	2868 (89.3)	405 (9.6)	33 (1.1)
	Depression only	115 (38.4)	335 (61.3)	3 (0.3)	243 (69.4)	207 (30.1)	3 (0.5)	296 (69.3)	152 (30.3)	5 (0.4)	345 (84.5)	103 (15.1)	5 (0.4)	370 (85.3)	78 (14.3)	5 (0.4)
	Anxiety only	120 (34.3)	319 (63.4)	2 (2.3)	217 (64.8)	221 (34.1)	3 (1.1)	294 (64.9)	141 (32.4)	6 (2.7)	353 (82.8)	82 (14.5)	6 (2.7)	362 (84.2)	73 (13.2)	6 (2.7)
	Depression and anxiety	281 (36.9)	690 (62.1)	6 (1.0)	497 (68.1)	475 (31.6)	5 (0.3)	653 (66.3)	316 (32.2)	8 (1.4)	836 (86.0)	133 (12.5)	8 (1.4)	811 (85.1)	158 (13.5)	8 (1.4)
Country	**Australia**	221 (39.7)	429 (60.3)	0 (0.0)	485 (79.9)	165 (20.1)	0 (0.0)	428 (69.1)	222 (30.9)	0 (0.0)	522 (82.8)	128 (17.2)	0 (0.0)	580 (89.4)	70 (10.6)	0 (0.0)

	Canada	570 (38.7)	1121 (60.6)	9 (0.7)	1008 (73.2)	686 (26.3)	6 (0.5)	1098 (64.0)	589 (35.0)	13 (1.0)	1479 (86.3)	208 (12.7)	13 (1.0)	1456 (87.4)	231 (11.6)	13 (1.0)
	England	444 (37.9)	1322 (60.9)	16 (1.2)	723 (56.1)	1045 (43.3)	14 (0.5)	1272 (73.5)	487 (24.8)	23 (1.7)	1535 (90.8)	224 (7.4)	23 (1.7)	1465 (86.9)	294 (11.3)	23 (1.7)
	US	357 (45.2)	678 (53.2)	10 (1.5)	604 (75.0)	437 (24.7)	4 (0.3)	764 (74.7)	265 (23.6)	16 (1.7)	863 (83.5)	166 (14.8)	16 (1.7)	910 (89.0)	119 (9.3)	16 (1.7)

*n is unweighted frequency, total number of respondents who were asked this survey question.

+ Unweighted frequency of respondents who responded to the outcome.

++ Weighted proportion of respondents who responded to the outcome. Denominator is frequency of respondents who responded ‘Yes’ and ‘No’ to the outcome, including refused and don’t know responses.

R/D: Refused/ don’t know

Supplementary Table 2a. Mental health condition and number of cessation aids used during last attempt to quit smoking

		Total number of aids used in last quit attempt						
		0	**1**	**2**	**3**	**4**	**5**	**6**
	TOTAL (n*=5102)	1592[+] (40.5[++])	2110[+] (40.4[++])	999[+] (14.0[++])	309[+] (4.1[++])	69[+] (0.8[++])	18[+] (0.2[++])	5[+] (0.0[++])
Mental health	**No depression or anxiety**	1076 (42.0)	1386 (40.5)	592 (13.5)	163 (3.4)	31 (0.5)	11 (0.2)	2 (0.0)
	Depression only	115 (38.7)	176 (39.7)	103 (14.2)	38 (6.2)	9 (1.0)	3 (0.1)	1 (0.1)
	Anxiety only	120 (35.7)	157 (39.2)	110 (17.9)	37 (4.6)	7 (2.6)	1 (0.1)	0 (0.0)
	Depression and anxiety	281 (37.6)	391 (41.2)	194 (14.1)	71 (5.5)	22 (1.1)	3 (0.4)	2 (0.0)

* Unweighted frequency, excludes respondents who refused to answer or answered don't know to any of the individual cessation aid survey questions [n=75]
+ Unweighted frequency of respondents
++ Weighted proportion of respondents

Supplementary Table 2b. Mental health condition and nicotine vaping product used during last attempt to quit smoking

		Exclusive NVP use	**Non-exclusive NVP use**	**No NVP use**
	TOTAL (n*=5102)	1158[+] (17.0[++])	1148[+] (14.0[++])	2796[+] (69.0[++])
Mental health	**No depression or anxiety**	772 (17.8)	641 (12.7)	1848 (69.5)
	Depression only	73 (12.6)	132 (17.6)	240 (69.7)
	Anxiety only	84 (14.1)	133 (21.0)	215 (65.0)
	Depression and anxiety	229 (17.3)	242 (14.4)	493 (68.3)

* Unweighted frequency, excludes respondents who refused to answer or answered don't know to any of the individual cessation aid survey questions [n=75]

+ Unweighted frequency of respondents
++ Weighted proportion of respondents

Supplementary Table 3a to t. Odds ratios, with 95% confidence intervals for all covariates for all of the logistic regression models, for each outcome measure.

- Model A: unadjusted model with mental health condition as the only independent variable
- Model B: model adjusted for country, sex, age, education, ethnicity, and income
- Model C (fully adjusted): adjusted for country, sex, age, education, ethnicity, and income, cigarette smoking status and problematic alcohol use
- Model D (country-differences): adjusted for country, gender, age, education, income, ethnicity, cigarette smoking status, problematic alcohol use, and mental health*country interaction term

Used any cessation aid

Supplementary Table 3a

Model A

Variable	Category	beta	OR	Lower 95% CI	Upper 95% CI	p-value
	(Intercept)	0.33	1.40	1.30	1.49	0.000
Mental health	No depression/anxiety (ref)		1.00			
	Depression only	0.14	1.15	0.93	1.42	0.210
	Anxiety only	0.28	1.32	1.06	1.66	0.014
	Depression and anxiety	0.19	1.20	1.04	1.40	0.016

Supplementary Table 3b

Model B

Variable	Category	beta	OR	Lower 95% CI	Upper 95% CI	p-value
	(Intercept)	0.31	1.36	1.04	1.79	0.027
Mental health	No depression/anxiety (ref)		1.00			
	Depression only	0.13	1.14	0.92	1.41	0.241
	Anxiety only	0.38	1.46	1.16	1.84	0.001
	Depression and anxiety	0.27	1.31	1.12	1.54	0.001
Gender	Male (ref)		1.00			
	Female	-0.13	0.88	0.78	0.98	0.024
Age	18-24 (ref)		1.00			
	25-39	0.18	1.19	0.99	1.44	0.063
	40-54	0.55	1.73	1.42	2.11	0.000
	55 and up	0.42	1.52	1.24	1.86	0.000
Ethnicity	Minority group		1.00			
	Majority group	-0.03	0.97	0.83	1.15	0.754
Education	Low (ref)		1.00			
	Moderate	-0.03	0.97	0.84	1.12	0.679
	High	-0.17	0.85	0.72	1.00	0.052
Income	Low (ref)		1.00			
	Moderate	0.02	1.02	0.88	1.19	0.754
	High	-0.10	0.90	0.77	1.05	0.177
	No answer	-0.22	0.81	0.61	1.07	0.135
Country	England (ref)		1.00			
	Australia	-0.10	0.91	0.76	1.09	0.292
	Canada	-0.08	0.92	0.79	1.07	0.266
	US	-0.40	0.67	0.57	0.80	0.000

Supplementary Table 3c

Model C (fully adjusted)

Variable	Category	beta	OR	Lower 95% CI	Upper 95% CI	p-value
	(Intercept)	0.51	1.66	1.25	2.20	0.000
Mental health	No depression/anxiety (ref)		1.00			
	Depression only	0.12	1.13	0.91	1.40	0.277
	Anxiety only	0.36	1.43	1.14	1.81	0.002
	Depression and anxiety	0.27	1.31	1.12	1.54	0.001
Gender	Male (ref)		1.00			
	Female	-0.16	0.85	0.75	0.96	0.007
Age	18-24 (ref)		1.00			
	25-39	0.13	1.14	0.94	1.37	0.183
	40-54	0.47	1.60	1.31	1.96	0.000
	55 and up	0.34	1.40	1.14	1.72	0.001
Ethnicity	Minority group		1.00			
	Majority group	-0.02	0.98	0.83	1.15	0.794
Education	Low (ref)		1.00			
	Moderate	0.01	1.01	0.88	1.17	0.883
	High	-0.09	0.92	0.77	1.09	0.312
Income	Low (ref)		1.00			
	Moderate	0.03	1.03	0.89	1.20	0.690
	High	-0.07	0.93	0.80	1.09	0.379
	No answer	-0.19	0.83	0.62	1.10	0.190
Country	England (ref)		1.00			
	Australia	-0.12	0.89	0.74	1.06	0.191
	Canada	-0.07	0.93	0.80	1.08	0.339
	US	-0.37	0.69	0.58	0.82	0.000
Problematic alcohol use	No		1.00			
	Yes	-0.11	0.90	0.79	1.02	0.088
	No answer	0.25	1.29	0.89	1.89	0.190

Cigarette smoking status	Daily (ref)		1.00			
	Non-daily	-0.54	0.58	0.49	0.69	0.000
	Quit	-0.36	0.70	0.61	0.80	0.000

Supplementary Table 3d

Model D (country-differences)

Variable	**Category**	**beta**	**OR**	**Lower 95% CI**	**Upper 95% CI**	**p-value**
	(Intercept)	0.51	1.67	1.25	2.23	0.001
Mental health	No depression/anxiety (ref)		1.00			
	Depression only	0.20	1.22	0.86	1.77	0.276
	Anxiety only	0.54	1.71	1.08	2.77	0.024
	Depression and anxiety	0.13	1.14	0.87	1.49	0.350
Country	England (ref)		1.00			
	Australia	-0.08	0.93	0.74	1.16	0.502
	Canada	-0.09	0.91	0.77	1.08	0.284
	US	-0.41	0.66	0.54	0.81	0.000
Gender	Male (ref)		1.00			
	Female	-0.16	0.85	0.75	0.96	0.007
Age	18-24 (ref)		1.00			
	25-39	0.13	1.14	0.94	1.38	0.171
	40-54	0.48	1.61	1.31	1.97	0.000
	55 and up	0.35	1.41	1.15	1.74	0.001
Ethnicity	Minority group		1.00			
	Majority group	-0.02	0.98	0.83	1.16	0.807
Education	Low (ref)		1.00			
	Moderate	0.01	1.01	0.88	1.17	0.850
	High	-0.08	0.92	0.77	1.09	0.329
Income	Low (ref)		1.00			

	Moderate	0.03	1.03	0.88	1.19	0.729
	High	-0.08	0.92	0.79	1.08	0.315
	No answer	-0.21	0.81	0.61	1.09	0.159
Problematic alcohol use	No		1.00			
	Yes	-0.11	0.90	0.79	1.02	0.093
	No answer	0.25	1.28	0.88	1.89	0.197
Cigarette smoking status	Daily (ref)		1.00			
	Non-daily	-0.54	0.59	0.49	0.70	0.000
	Quit	-0.36	0.70	0.61	0.80	0.000
Mental health*country interaction term	No depression/anxiety*England (ref)		1.00			
	Depression only*Australia	-0.44	0.64	0.34	1.20	0.163
	Anxiety only*Australia	-0.21	0.81	0.40	1.67	0.570
	Depression and anxiety*Australia	0.05	1.05	0.65	1.70	0.849
	Depression only*Canada	0.02	1.02	0.58	1.80	0.945
	Anxiety only*Canada	-0.36	0.70	0.38	1.28	0.248
	Depression and anxiety*Canada	0.29	1.33	0.89	1.98	0.159
	Depression only*US	-0.04	0.97	0.53	1.76	0.909
	Anxiety only*US	-0.07	0.93	0.47	1.82	0.834
	Depression and anxiety*US	0.24	1.27	0.84	1.91	0.261

Likelihood-ratio test between Model C (fully adjusted) and Model D (country-differences): p=0.6595

Used vaping products

Supplementary Table 3e

Model A

Variable	Category	beta	OR	Lower 95% CI	Upper 95% CI	p-value
	(Intercept)	-0.82	0.44	0.41	0.47	0.000
Mental health	No depression/anxiety (ref)		1.00			
	Depression only	-0.02	0.98	0.78	1.23	0.875
	Anxiety only	0.18	1.20	0.95	1.50	0.121
	Depression and anxiety	0.05	1.05	0.90	1.23	0.515

Supplementary Table 3f

Model B

Variable	Category	beta	OR	Lower 95% CI	Upper 95% CI	p-value
	(Intercept)	-0.29	0.75	0.56	1.00	0.051
Mental health	No depression/anxiety (ref)		1.00			
	Depression only	0.02	1.02	0.80	1.28	0.899
	Anxiety only	0.30	1.35	1.06	1.70	0.013
	Depression and anxiety	0.05	1.05	0.89	1.25	0.538
Gender	Male (ref)		1.00			
	Female	-0.17	0.84	0.74	0.95	0.007
Age	18-24 (ref)		1.00			
	25-39	0.03	1.03	0.85	1.25	0.769
	40-54	-0.15	0.86	0.70	1.07	0.174
	55 and up	-0.57	0.57	0.45	0.71	0.000
Ethnicity	Minority group		1.00			
	Majority group	0.07	1.07	0.90	1.29	0.429
Education	Low (ref)		1.00			
	Moderate	0.09	1.09	0.94	1.27	0.271
	High	-0.07	0.93	0.77	1.12	0.444
Income	Low (ref)		1.00			
	Moderate	0.20	1.22	1.04	1.43	0.016

	High	0.10	1.10	0.93	1.31	0.253
	No answer	-0.13	0.88	0.64	1.21	0.439
Country	England (ref)		1.00			
	Australia	-1.10	0.33	0.27	0.41	0.000
	Canada	-0.67	0.51	0.44	0.60	0.000
	US	-0.78	0.46	0.38	0.55	0.000

Supplementary Table 3g

Model C (fully adjusted)

Variable	**Category**	**beta**	**OR**	**Lower 95% CI**	**Upper 95% CI**	**p-value**
	(Intercept)	-0.23	0.79	0.59	1.07	0.135
Mental health	No depression/anxiety (ref)		1.00			
	Depression only	0.02	1.02	0.80	1.29	0.861
	Anxiety only	0.30	1.34	1.06	1.70	0.013
	Depression and anxiety	0.06	1.06	0.89	1.25	0.501
Gender	Male (ref)		1.00			
	Female	-0.19	0.83	0.73	0.94	0.003
Age	18-24 (ref)		1.00			
	25-39	0.01	1.01	0.83	1.23	0.907
	40-54	-0.17	0.84	0.68	1.04	0.116
	55 and up	-0.60	0.55	0.44	0.69	0.000
Ethnicity	Minority group		1.00			
	Majority group	0.08	1.08	0.91	1.30	0.379
Education	Low (ref)		1.00			
	Moderate	0.09	1.10	0.94	1.28	0.235
	High	-0.07	0.94	0.78	1.13	0.483
Income	Low (ref)		1.00			
	Moderate	0.20	1.22	1.04	1.43	0.016

	High	0.11	1.11	0.94	1.32	0.216
	No answer	-0.13	0.88	0.64	1.20	0.426
Country	England (ref)		1.00			
	Australia	-1.10	0.33	0.27	0.41	0.000
	Canada	-0.67	0.51	0.44	0.60	0.000
	US	-0.80	0.45	0.37	0.54	0.000
Problematic alcohol use	No		1.00			
	Yes	-0.11	0.89	0.78	1.02	0.100
	No answer	-0.01	0.99	0.67	1.43	0.941
Cigarette smoking status	Daily (ref)		1.00			
	Non-daily	-0.08	0.92	0.76	1.11	0.390
	Quit	0.02	1.02	0.88	1.18	0.805

Supplementary Table 3h

Model D (country-differences)

Variable	**Category**	**beta**	**OR**	**Lower 95% CI**	**Upper 95% CI**	**p-value**
	(Intercept)	-0.22	0.81	0.59	1.09	0.166
Mental health	No depression/anxiety (ref)		1.00			
	Depression only	-0.02	0.98	0.69	1.38	0.906
	Anxiety only	0.48	1.62	1.04	2.54	0.032
	Depression and anxiety	-0.17	0.84	0.65	1.10	0.212
Country	England (ref)		1.00			
	Australia	-1.04	0.35	0.27	0.45	0.000
	Canada	-0.77	0.46	0.38	0.56	0.000
	US	-0.85	0.43	0.34	0.54	0.000
Gender	Male (ref)		1.00			
	Female	-0.19	0.82	0.72	0.94	0.003
Age	18-24 (ref)		1.00			

	25-39	0.02	1.02	0.84	1.25	0.833
	40-54	-0.16	0.85	0.69	1.05	0.132
	55 and up	-0.59	0.56	0.44	0.70	0.000
Ethnicity	Minority group		1.00			
	Majority group	0.09	1.09	0.91	1.31	0.347
Education	Low (ref)		1.00			
	Moderate	0.11	1.12	0.96	1.31	0.162
	High	-0.06	0.95	0.78	1.14	0.559
Income	Low (ref)		1.00			
	Moderate	0.19	1.21	1.03	1.42	0.021
	High	0.10	1.10	0.93	1.30	0.270
	No answer	-0.14	0.87	0.63	1.19	0.395
Problematic alcohol use	No		1.00			
	Yes	-0.11	0.90	0.78	1.03	0.112
	No answer	0.00	1.00	0.68	1.45	0.985
Cigarette smoking status	Daily (ref)		1.00			
	Non-daily	-0.08	0.93	0.76	1.12	0.438
	Quit	0.02	1.02	0.88	1.18	0.830
Mental health*country interaction term	No depression/anxiety*England (ref)		1.00			
	Depression only*Australia	-0.70	0.50	0.19	1.12	0.113
	Anxiety only*Australia	-0.47	0.63	0.28	1.33	0.232
	Depression and anxiety*Australia	0.17	1.19	0.68	2.02	0.533
	Depression only*Canada	0.48	1.61	0.90	2.85	0.103
	Anxiety only*Canada	-0.15	0.86	0.47	1.56	0.619
	Depression and anxiety*Canada	0.46	1.58	1.06	2.36	0.025
	Depression only*US	-0.02	0.98	0.49	1.88	0.944
	Anxiety only*US	-0.26	0.77	0.39	1.50	0.455
	Depression and anxiety*US	0.36	1.43	0.92	2.20	0.109

Likelihood-ratio test between Model C (fully adjusted) and Model D (country-differences): p=0.1165

Used NRT

Supplementary Table 3i

Model A

Variable	Category	beta	OR	Lower 95% CI	Upper 95% CI	p-value
	(Intercept)	-0.98	0.38	0.35	0.41	0.000
Mental health	No depression/anxiety (ref)		1.00			
	Depression only	0.15	1.16	0.92	1.45	0.201
	Anxiety only	0.28	1.32	1.05	1.66	0.017
	Depression and anxiety	0.25	1.29	1.10	1.51	0.002

Supplementary Table 3j

Model B

Variable	Category	beta	OR	Lower 95% CI	Upper 95% CI	p-value
	(Intercept)	-1.14	0.32	0.24	0.43	0.000
Mental health	No depression/anxiety (ref)		1.00			
	Depression only	0.16	1.17	0.93	1.47	0.181
	Anxiety only	0.34	1.40	1.11	1.77	0.005
	Depression and anxiety	0.36	1.43	1.21	1.69	0.000
Gender	Male (ref)		1.00			
	Female	-0.03	0.97	0.86	1.10	0.655
Age	18-24 (ref)		1.00			

	25-39	-0.03	0.97	0.78	1.20	0.774
	40-54	0.35	1.42	1.14	1.78	0.002
	55 and up	0.45	1.57	1.26	1.97	0.000
Ethnicity	Minority group		1.00			
	Majority group	-0.04	0.96	0.80	1.15	0.657
Education	Low (ref)		1.00			
	Moderate	-0.16	0.86	0.74	0.99	0.041
	High	-0.35	0.71	0.59	0.85	0.000
Income	Low (ref)		1.00			
	Moderate	0.04	1.04	0.88	1.22	0.650
	High	0.02	1.02	0.86	1.20	0.822
	No answer	-0.09	0.91	0.66	1.24	0.566
Country	England (ref)		1.00			
	Australia	0.23	1.26	1.03	1.53	0.023
	Canada	0.42	1.52	1.30	1.78	0.000
	US	-0.20	0.82	0.67	0.99	0.042

Supplementary Table 3k

Model C (fully adjusted)

Variable	**Category**	**beta**	**OR**	**Lower 95% CI**	**Upper 95% CI**	**p-value**
	(Intercept)	-0.95	0.39	0.28	0.53	0.000
Mental health	No depression/anxiety (ref)		1.00			
	Depression only	0.12	1.13	0.89	1.42	0.318
	Anxiety only	0.31	1.36	1.07	1.73	0.011
	Depression and anxiety	0.34	1.41	1.19	1.67	0.000
Gender	Male (ref)		1.00			
	Female	-0.06	0.94	0.82	1.07	0.327
Age	18-24 (ref)		1.00			

	25-39	-0.05	0.95	0.76	1.18	0.623
	40-54	0.29	1.34	1.07	1.68	0.011
	55 and up	0.42	1.52	1.21	1.92	0.000
Ethnicity	Minority group		1.00			
	Majority group	-0.04	0.96	0.80	1.16	0.679
Education	Low (ref)		1.00			
	Moderate	-0.11	0.90	0.77	1.04	0.156
	High	-0.24	0.79	0.65	0.95	0.012
Income	Low (ref)		1.00			
	Moderate	0.05	1.06	0.90	1.24	0.513
	High	0.08	1.08	0.92	1.28	0.340
	No answer	-0.05	0.95	0.69	1.30	0.757
Country	England (ref)		1.00			
	Australia	0.23	1.26	1.03	1.54	0.023
	Canada	0.44	1.55	1.33	1.82	0.000
	US	-0.12	0.89	0.73	1.08	0.242
Problematic alcohol use	No		1.00			
	Yes	-0.02	0.98	0.85	1.12	0.764
	No answer	0.52	1.68	1.14	2.46	0.008
Cigarette smoking status	Daily (ref)		1.00			
	Non-daily	-0.48	0.62	0.50	0.76	0.000
	Quit	-0.88	0.41	0.35	0.49	0.000

Supplementary Table 3l

Model D (country-differences)

Variable	**Category**	**beta**	**OR**	**Lower 95% CI**	**Upper 95% CI**	**p-value**
	(Intercept)	-0.99	0.37	0.27	0.51	0.000
Mental health	No depression/anxiety (ref)		1.00			

	Depression only	0.12	1.13	0.76	1.66	0.544
	Anxiety only	0.56	1.74	1.08	2.77	0.021
	Depression and anxiety	0.39	1.47	1.09	1.97	0.010
Country	England (ref)		1.00			
	Australia	0.35	1.42	1.11	1.81	0.005
	Canada	0.47	1.60	1.32	1.93	0.000
	US	-0.15	0.86	0.67	1.10	0.224
Gender	Male (ref)		1.00			
	Female	-0.06	0.94	0.82	1.07	0.344
Age	18-24 (ref)		1.00			
	25-39	-0.04	0.96	0.78	1.20	0.741
	40-54	0.31	1.36	1.09	1.71	0.008
	55 and up	0.44	1.55	1.23	1.95	0.000
Ethnicity	Minority group		1.00			
	Majority group	-0.04	0.96	0.80	1.15	0.651
Education	Low (ref)		1.00			
	Moderate	-0.10	0.90	0.77	1.05	0.183
	High	-0.23	0.79	0.66	0.95	0.015
Income	Low (ref)		1.00			
	Moderate	0.06	1.06	0.90	1.25	0.489
	High	0.08	1.08	0.91	1.28	0.360
	No answer	-0.04	0.96	0.69	1.32	0.805
Problematic alcohol use	No		1.00			
	Yes	-0.03	0.97	0.85	1.12	0.710
	No answer	0.51	1.67	1.13	2.44	0.009
Cigarette smoking status	Daily (ref)		1.00			
	Non-daily	-0.48	0.62	0.50	0.76	0.000
	Quit	-0.89	0.41	0.35	0.49	0.000
Mental health*country interaction term	No depression/anxiety*England (ref)		1.00			

	Depression only*Australia	-0.30	0.74	0.37	1.46	0.393
	Anxiety only*Australia	-0.61	0.54	0.26	1.13	0.105
	Depression and anxiety*Australia	-0.24	0.79	0.47	1.31	0.358
	Depression only*Canada	0.12	1.13	0.63	2.03	0.688
	Anxiety only*Canada	-0.33	0.72	0.39	1.33	0.285
	Depression and anxiety*Canada	-0.08	0.92	0.61	1.39	0.705
	Depression only*US	0.10	1.11	0.56	2.16	0.770
	Anxiety only*US	-0.05	0.95	0.46	1.94	0.894
	Depression and anxiety*US	0.09	1.10	0.70	1.73	0.688

Likelihood-ratio test between Model C (fully adjusted) and Model D (country-differences): p=0.7993

Used varenicline or bupropion

Supplementary Table 3m

Model A

Variable	Category	beta	OR	Lower 95% CI	Upper 95% CI	p-value
	(Intercept)	-2.06	0.13	0.11	0.14	0.000
Mental health	No depression/anxiety (ref)		1.00			
	Depression only	0.33	1.40	1.03	1.86	0.026
	Anxiety only	0.32	1.37	1.00	1.85	0.042
	Depression and anxiety	0.13	1.14	0.91	1.42	0.253

Supplementary Table 3n

Model B

Variable	Category	beta	OR	Lower 95% CI	Upper 95% CI	p-value

	(Intercept)	-3.71	0.02	0.01	0.04	0.000
Mental health	No depression/anxiety (ref)		1.00			
	Depression only	0.29	1.34	0.98	1.80	0.056
	Anxiety only	0.37	1.45	1.05	1.98	0.021
	Depression and anxiety	0.28	1.33	1.04	1.68	0.020
Gender	Male (ref)		1.00			
	Female	-0.05	0.95	0.79	1.13	0.542
Age	18-24 (ref)		1.00			
	25-39	0.68	1.98	1.32	3.08	0.001
	40-54	1.38	3.97	2.66	6.15	0.000
	55 and up	1.42	4.12	2.75	6.42	0.000
Ethnicity	Minority group		1.00			
	Majority group	0.26	1.30	1.00	1.71	0.059
Education	Low (ref)		1.00			
	Moderate	-0.02	0.98	0.79	1.21	0.824
	High	0.18	1.20	0.94	1.53	0.147
Income	Low (ref)		1.00			
	Moderate	-0.20	0.82	0.65	1.03	0.084
	High	0.02	1.02	0.82	1.27	0.860
	No answer	-0.17	0.84	0.51	1.32	0.470
Country	England (ref)		1.00			
	Australia	0.81	2.25	1.72	2.94	0.000
	Canada	0.40	1.49	1.18	1.90	0.001
	US	0.67	1.95	1.50	2.53	0.000

Supplementary Table 3o

Model C (fully adjusted)

Variable	**Category**	**beta**	**OR**	**Lower 95% CI**	**Upper 95% CI**	**p-value**

	(Intercept)	-3.55	0.03	0.02	0.05	0.000
Mental health	No depression/anxiety (ref)		1.00			
	Depression only	0.29	1.34	0.98	1.80	0.060
	Anxiety only	0.36	1.43	1.03	1.95	0.028
	Depression and anxiety	0.26	1.30	1.02	1.65	0.031
Gender	Male (ref)		1.00			
	Female	-0.06	0.94	0.78	1.12	0.491
Age	18-24 (ref)		1.00			
	25-39	0.64	1.89	1.26	2.95	0.003
	40-54	1.32	3.73	2.49	5.81	0.000
	55 and up	1.35	3.87	2.57	6.05	0.000
Ethnicity	Minority group		1.00			
	Majority group	0.25	1.28	0.98	1.69	0.077
Education	Low (ref)		1.00			
	Moderate	0.00	1.00	0.81	1.24	0.969
	High	0.24	1.27	0.99	1.62	0.062
Income	Low (ref)		1.00			
	Moderate	-0.20	0.82	0.65	1.04	0.096
	High	0.05	1.05	0.84	1.31	0.674
	No answer	-0.14	0.87	0.53	1.38	0.578
Country	England (ref)		1.00			
	Australia	0.79	2.21	1.68	2.90	0.000
	Canada	0.41	1.50	1.18	1.92	0.001
	US	0.69	2.00	1.53	2.61	0.000
Problematic alcohol use	No		1.00			
	Yes	-0.01	0.99	0.81	1.20	0.905
	No answer	-0.30	0.74	0.36	1.37	0.376
Cigarette smoking status	Daily (ref)		1.00			
	Non-daily	-0.56	0.57	0.40	0.78	0.001

	Quit	-0.29	0.74	0.60	0.92	0.007

Supplementary Table 3p

Model D (country-differences)

Variable	**Category**	**beta**	**OR**	**Lower 95% CI**	**Upper 95% CI**	**p-value**
	(Intercept)	-3.54	0.03	0.02	0.05	0.000
Mental health	No depression/anxiety (ref)		1.00			
	Depression only	0.34	1.41	0.76	2.45	0.251
	Anxiety only	0.75	2.12	1.00	4.08	0.034
	Depression and anxiety	0.00	1.00	0.57	1.68	0.998
Country	England (ref)		1.00			
	Australia	0.87	2.39	1.71	3.34	0.000
	Canada	0.38	1.46	1.09	1.96	0.012
	US	0.62	1.87	1.34	2.60	0.000
Gender	Male (ref)		1.00			
	Female	-0.07	0.94	0.78	1.12	0.477
Age	18-24 (ref)		1.00			
	25-39	0.65	1.91	1.27	2.99	0.003
	40-54	1.34	3.81	2.54	5.95	0.000
	55 and up	1.38	3.96	2.62	6.20	0.000
Ethnicity	Minority group		1.00			
	Majority group	0.25	1.28	0.98	1.70	0.078
Education	Low (ref)		1.00			
	Moderate	0.00	1.00	0.81	1.24	0.998
	High	0.23	1.25	0.98	1.61	0.076
Income	Low (ref)		1.00			
	Moderate	-0.20	0.82	0.65	1.04	0.096
	High	0.03	1.03	0.82	1.29	0.794

	No answer	-0.19	0.83	0.50	1.32	0.448
Problematic alcohol use	No		1.00			
	Yes	-0.02	0.98	0.81	1.20	0.870
	No answer	-0.31	0.73	0.35	1.36	0.361
Cigarette smoking status	Daily (ref)		1.00			
	Non-daily	-0.56	0.57	0.41	0.79	0.001
	Quit	-0.29	0.75	0.60	0.93	0.008
Mental health*country interaction term	No depression/anxiety*England (ref)		1.00			
	Depression only*Australia	-0.47	0.63	0.25	1.53	0.307
	Anxiety only*Australia	-0.16	0.86	0.34	2.21	0.742
	Depression and anxiety*Australia	-0.16	0.85	0.39	1.85	0.676
	Depression only*Canada	-0.04	0.96	0.42	2.21	0.932
	Anxiety only*Canada	-0.96	0.38	0.15	1.00	0.046
	Depression and anxiety*Canada	0.62	1.86	0.97	3.66	0.068
	Depression only*US	0.23	1.26	0.55	2.94	0.584
	Anxiety only*US	-0.27	0.76	0.30	1.98	0.568
	Depression and anxiety*US	0.34	1.41	0.71	2.86	0.332

Likelihood-ratio test between Model C (fully adjusted) and Model D (country-differences): p=0.07356

Used behavioural support

Supplementary Table 3q

Model A

Variable	Category	beta	OR	Lower 95% CI	Upper 95% CI	p-value

	(Intercept)	-2.23	0.11	0.10	0.12	0.000
Mental health	No depression/anxiety (ref)		1.00			
	Depression only	0.45	1.57	1.15	2.10	0.003
	Anxiety only	0.38	1.46	1.05	1.99	0.021
	Depression and anxiety	0.39	1.47	1.18	1.83	0.001

Supplementary Table 3r

Model B

Variable	**Category**	**beta**	**OR**	**Lower 95% CI**	**Upper 95% CI**	**p-value**
	(Intercept)	-1.92	0.15	0.10	0.22	0.000
Mental health	No depression/anxiety (ref)		1.00			
	Depression only	0.47	1.59	1.17	2.15	0.003
	Anxiety only	0.44	1.55	1.11	2.13	0.008
	Depression and anxiety	0.51	1.66	1.31	2.09	0.000
Gender	Male (ref)		1.00			
	Female	-0.06	0.94	0.79	1.13	0.521
Age	18-24 (ref)		1.00			
	25-39	0.16	1.17	0.86	1.61	0.322
	40-54	0.28	1.32	0.96	1.84	0.095
	55 and up	0.50	1.66	1.20	2.32	0.003
Ethnicity	Minority group		1.00			
	Majority group	-0.60	0.55	0.44	0.69	0.000
Education	Low (ref)		1.00			
	Moderate	0.16	1.17	0.93	1.48	0.173
	High	0.32	1.38	1.06	1.79	0.016
Income	Low (ref)		1.00			
	Moderate	-0.22	0.80	0.64	1.02	0.068

	High	-0.03	0.97	0.77	1.22	0.791
	No answer	-0.38	0.69	0.41	1.09	0.127
Country	England (ref)		1.00			
	Australia	-0.18	0.84	0.63	1.11	0.221
	Canada	-0.13	0.88	0.70	1.10	0.262
	US	-0.39	0.68	0.51	0.89	0.006

Supplementary Table 3s

Model C (fully adjusted)

Variable	**Category**	**beta**	**OR**	**Lower 95% CI**	**Upper 95% CI**	**p-value**
	(Intercept)	-1.69	0.18	0.12	0.28	0.000
Mental health	No depression/anxiety (ref)		1.00			
	Depression only	0.44	1.56	1.14	2.11	0.005
	Anxiety only	0.43	1.53	1.09	2.10	0.010
	Depression and anxiety	0.50	1.65	1.30	2.08	0.000
Gender	Male (ref)		1.00			
	Female	-0.12	0.89	0.74	1.07	0.209
Age	18-24 (ref)		1.00			
	25-39	0.14	1.14	0.84	1.58	0.397
	40-54	0.21	1.23	0.89	1.72	0.215
	55 and up	0.43	1.54	1.10	2.16	0.012
Ethnicity	Minority group		1.00			
	Majority group	-0.58	0.56	0.45	0.71	0.000
Education	Low (ref)		1.00			
	Moderate	0.20	1.22	0.97	1.53	0.093
	High	0.39	1.48	1.14	1.93	0.004
Income	Low (ref)		1.00			
	Moderate	-0.21	0.81	0.64	1.02	0.078

	High	0.01	1.01	0.80	1.28	0.903
	No answer	-0.36	0.70	0.42	1.11	0.142
Country	England (ref)		1.00			
	Australia	-0.19	0.83	0.62	1.10	0.200
	Canada	-0.14	0.87	0.70	1.09	0.230
	US	-0.38	0.69	0.52	0.90	0.008
Problematic alcohol use	No		1.00			
	Yes	-0.29	0.75	0.61	0.92	0.005
	No answer	0.17	1.19	0.67	1.98	0.523
Cigarette smoking status	Daily (ref)		1.00			
	Non-daily	-0.28	0.76	0.56	1.00	0.058
	Quit	-0.49	0.62	0.49	0.77	0.000

Supplementary Table 3t

Model D (country-differences)

Variable	**Category**	**beta**	**OR**	**Lower 95% CI**	**Upper 95% CI**	**p-value**
	(Intercept)	-1.67	0.19	0.12	0.29	0.000
Mental health	No depression/anxiety (ref)		1.00			
	Depression only	0.81	2.25	1.42	3.49	0.000
	Anxiety only	0.81	2.25	1.23	3.89	0.005
	Depression and anxiety	0.14	1.15	0.74	1.75	0.513
Country	England (ref)		1.00			
	Australia	-0.38	0.68	0.46	1.01	0.060
	Canada	-0.05	0.95	0.72	1.25	0.730
	US	-0.39	0.68	0.47	0.97	0.037
Gender	Male (ref)		1.00			

	Female	-0.13	0.88	0.73	1.05	0.161
Age	18-24 (ref)		1.00			
	25-39	0.12	1.12	0.82	1.55	0.472
	40-54	0.19	1.21	0.87	1.70	0.253
	55 and up	0.42	1.52	1.09	2.14	0.015
Ethnicity	Minority group		1.00			
	Majority group	-0.56	0.57	0.45	0.72	0.000
Education	Low (ref)		1.00			
	Moderate	0.19	1.21	0.96	1.53	0.104
	High	0.41	1.50	1.15	1.96	0.003
Income	Low (ref)		1.00			
	Moderate	-0.23	0.79	0.63	1.01	0.056
	High	-0.02	0.98	0.78	1.25	0.891
	No answer	-0.43	0.65	0.39	1.04	0.088
Problematic alcohol use	No		1.00			
	Yes	-0.29	0.75	0.61	0.92	0.006
	No answer	0.18	1.19	0.67	1.99	0.525
Cigarette smoking status	Daily (ref)		1.00			
	Non-daily	-0.24	0.78	0.58	1.04	0.099
	Quit	-0.50	0.61	0.48	0.77	0.000
Mental health*country interaction term	No depression/anxiety*England (ref)		1.00			
	Depression only*Australia	-0.41	0.66	0.25	1.63	0.389
	Anxiety only*Australia	0.31	1.36	0.55	3.33	0.504
	Depression and anxiety*Australia	0.83	2.29	1.12	4.67	0.023
	Depression only*Canada	-0.69	0.50	0.22	1.07	0.081
	Anxiety only*Canada	-1.12	0.33	0.13	0.77	0.012
	Depression and anxiety*Canada	0.33	1.39	0.78	2.49	0.270
	Depression only*US	-0.79	0.46	0.16	1.14	0.109
	Anxiety only*US	-0.52	0.60	0.22	1.55	0.299

	Depression and anxiety*US	0.57	1.78	0.94	3.38	0.079

Likelihood-ratio test between Model C (fully adjusted) and Model D (country-differences): p=0.007253

END OF THESIS