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Drug-related deaths associated with vaping product use in the United Kingdom

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Background and Aims Between March 2019 and February 2020 there was an outbreak of acute lung injury associated with vaping tetrahydrocannabinol (THC), contaminated with vitamin E acetate, in the United States. To date, there has been no comprehensive study of drug-related deaths associated with vaping products in the United Kingdom. We aimed to identify any trends in drug-related deaths associated with vaping product use in the United Kingdom.

Methods We retrospectively identified any deaths associated with the use of vaping products reported to the UK National Programme on Substance Abuse Deaths (NPSAD). This contains voluntarily reported information from UK Coroners on more than 42 000 deaths related to psychoactive drugs, other than nicotine or caffeine, which occurred between 1997 and 2020. **Results** Two drug-related deaths were reported which were associated with vaping products, one person having died in 2017 and one in 2018. Both decedents were men currently serving prison sentences in England and were aged 26 and 42 years at the time of death. Both deaths were associated with recent use of Synthetic Cannabinoid Receptor Agonists (SCRAs), with no other substances found to be implicated in death. No details regarding the type of vaping products were available. **Conclusions** In a UK sample (1997 to 2020) of 42 000 deaths related to psychoactive drugs other than nicotine or caffeine, only two deaths were associated with vaping products, and those involved use of synthetic cannabinoid receptor agonists.

Keywords Death, EVALI, SCRA, surveillance, toxicology, vaping.

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INTRODUCTION

Between March 2019 and February 2020, there was an outbreak of acute lung injury associated with vaping tetrahydrocannabinol (THC) and other cannabinoid products contaminated with vitamin E acetate in the United States [1]. This resulted in 2807 hospitalizations and 68 deaths [2]. The US Centers for Disease Control and Prevention (CDC) described this cluster of acute lung injuries as 'e-cigarette, or vaping, product use-associated lung injury' (EVALI). While the US Food and Drug Administration (FDA) linked the aetiology of the outbreak to vaping THC in August 2020, it was only in late October that the CDC attributed vitamin E acetate-contaminated THC vaping products, mainly bought from informal sources, as the primary cause of the outbreak. However, the term 'EVALI' remained in place, leading to a great deal of confusion between the vaping of THC and vitamin E acetate and the

vaping of nicotine among academics, clinicians, media and the general public which persists to this day [3]. Subsequently, relative harm perceptions of nicotine vaping products versus tobacco cigarette smoking deteriorated after the US "EVALI" outbreak [4].

Cannabis product vaping is legal over the age of 21 years and is popular in several US states, and also common in states where cannabis products remain illegal [3], while in the United Kingdom it is illegal to possess, supply, produce, import or export cannabis (and cannabis products containing THC) without a Home Office licence except for medical cannabis, which has to be prescribed by a registered specialist doctor, and some over-the-counter (OTC) preparations of cannabidiol (CBD). A recent report estimated that 1.7% of 16–19-year-olds in England vaped cannabis products in 2018 compared to 5.1% in the United States [5], and a further study in a convenience sample of 2501 UK adults reported that 340 (13.5%) had ever vaped

and 236 (9%) currently (past 30-day use) vaped recreational drugs; the most common drug vaped was cannabis (6% ever use, 4% past 30-day use); 3% of participants had ever vaped and approximately 1.5% currently vaped synthetic cannabinoid receptor agonists [6]. As seen with other technological advancements, such as the invention of the hypodermic needle, the use of vaping products as a method of drug delivery is likely to increase as innovation in e-cigarette and vaping technology inevitably changes the way drugs are consumed [7,8].

To our knowledge, there has been no comprehensive study of drug-related deaths associated with vaping products in the United Kingdom. The Medicines and Healthcare products Regulatory Agency (MHRA) acts as the national competent authority for regulating and monitoring nicotine vaping products in the United Kingdom and operates a yellow card system, similar to that for other medicines, for monitoring adverse effects potentially attributable to nicotine vaping products. However, an adverse report is not, by itself, proof of a side effect or causal link between vaping and an adverse reaction. In January 2020, the MHRA reported that they had identified two possible cases of EVALI through the yellow card scheme, both of which had a fatal outcome [9,10]. However, the MHRA would not necessarily be advised of non-nicotine containing vaping product-related injuries or injuries relating to vaping drugs.

Although the "EVALI" outbreak was largely confined to the United States, existing literature suggests that cannabis product vaping is prevalent in the United Kingdom [5,6], and current regulatory systems would not necessarily capture deaths related to vaping non-nicotine drugs. Accurate up-to-date evidence is essential to inform consumers, retailers and clinicians of the number of deaths associated with drug consumption using vaping products. We aimed to identify any trends in drug-related deaths associated with vaping product use in the United Kingdom between 1997 and 2020.

METHODS

The National Programme on Substance Abuse Deaths (NPSAD) receives information on a voluntary basis from Coroners for any deaths related to psychoactive drugs other than nicotine or caffeine, and has been previously described [11]. In total, NPSAD holds records on more than 42 000 deaths with reports received from England, Wales, the Channel Islands and the Isle of Man since 1997. Additional reports were received from the Scottish Crime and Drug Enforcement Agency between 2004 and 2011 and from the General Register Office for Northern Ireland since 2004. Deaths are referred to a Coroner if a death is of an unknown cause, is violent or unnatural, sudden and unexplained, occurred during or following a period of

anaesthesia or may have been caused by an industrial disease or poisoning. Toxicology is discretionally requested, dependent upon individual circumstances, and Coroners voluntarily report a death to NPSAD if: (1) psychoactive substance(s) are directly implicated in death, (2) an individual has a history of dependence or misuse of drugs or (3) if controlled drugs are identified at post-mortem. Coronial inquest files typically include statements from witnesses, family and friends, first responders (e.g. police, emergency services), general practitioner (GP), psychiatric and hospital records, as well as post-mortem and toxicology results.

The King's College London (KCL) Biomedical and Health Sciences, Dentistry, Medicine and Natural and Mathematical Sciences Research Ethics Subcommittee (BDM RESC) confirmed in November 2020 that NPSAD does not require REC review, as all subjects are deceased [12].

We retrospectively identified relevant cases associated with the use of vaping products by searching NPSAD for the following terms: 'vape*', 'vapo*', 'vaping*' 'electronic*' and 'e-cig*'. The analysis was not pre-registered and the results should be considered exploratory.

RESULTS

Two drug-related deaths were associated with vaping products, one person having died in 2017 and one in 2018. Both decedents were men currently serving prison sentences in England and were aged 26 and 42 years at the time of their death. Both deaths were associated with recent use of synthetic cannabinoid receptor agonists (SCRAs), with no other substances found to be implicated in death. 5F-ADB metabolites were detectable in post-mortem blood samples in both cases, in addition to AB-FUBINACA metabolites in one case.

Official causes of death were reported as sudden cardiac death precipitated by SCRA use, and SCRA toxicity and Coronial documentation did not mention acute lung injury as a cause in either death. Vaping products were reported as the presumptive SCRA route of administration for both deaths in associated documentation submitted to the Coroner, but no details regarding the type of vaping products were available.

DISCUSSION

Between 1997 and 2020 no non-nicotine non-caffeine drug-related deaths involving vaping products were reported in the United Kingdom besides men currently serving prison sentences and using SCRAs. While cannabis was not implicated in either of the vaping product-associated deaths, perhaps suggesting that manufacture or supply of vitamin E acetate-contaminated THC and other

cannabinoid oils linked to the US outbreak does not appear to have had the same devastating impact in the United Kingdom [10], this highlights the potential harms of vaping SCRAAs. Additionally, this study indicates the utility of NSPAD for contemporaneous monitoring of drug-related deaths involving vaping products (as well as other delivery systems).

This study has a number of limitations. Only a small subset of deaths in the United Kingdom undergo Coronal investigations, and comprehensive toxicology testing is not carried out for all investigated deaths. Additionally, even when toxicological assays are performed, they may fail to detect the presence of a substance due to a lack of sensitivity or the concentration of the ingested substance being beyond the limit of test detection. Cases are also voluntarily referred to NPSAD, and vaping may not have been reported in Coronal documentation due to lack of knowledge of decedents' preferred route of substance administration or a lack of perceived relevance on the part of documenters.

Our findings indicate, however, in the largest sample in United Kingdom studied to date, that the only psychoactive non-nicotine non-caffeine drug-related deaths associated with vaping products occurred using SCRAAs. Users, clinicians, retailers and prison staff should be aware of these cases, be alert to vaping as a potential method of SCRA administration [6,8] and be prepared to make people aware that deaths have been linked to SCRA consumption. Given the deaths caused by vaping contaminated drug products in the United States [2], and as vaping becomes better understood as a means of ingesting drugs [7,10], it is important to monitor the risks of doing so, and NSPAD is a low-cost means of monitoring vaping product drug-related deaths in the United Kingdom. As such, we recommend that the NSPAD be used to monitor vaping product-associated drug-related deaths and the circumstances pertaining to the use of any vaping products appropriately explored. Given that any associated harms are more likely to result in hospitalization than death, further research into drug-related harms associated with vaping product use should also focus upon data sources which include inpatient hospitalization and accident and emergency department records.

The misnomer 'EVALI' outbreak in the United States has caused long-standing confusion in relation to nicotine vaping products in the United Kingdom and, moving forward, it is vitally important that there is a clear distinction between any harms associated with nicotine or non-nicotine drug vaping in any communications.

Declaration of interests

None.

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Author contributions

Emmert Roberts: Conceptualization; formal analysis; funding acquisition; investigation; methodology; project administration; writing-original draft; writing-review & editing. **Caroline Copeland:** Data curation; methodology; project administration; writing-review & editing. **Deborah Robson:** Conceptualization; investigation; supervision; validation; writing-review & editing. **Ann McNeill:** Conceptualization; investigation; resources; supervision; validation; writing-review & editing.

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