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RESEARCH ARTICLE



Healthcare utilization and costs in chronic cough

Peter S. P. Cho^{a,b} , James Shearer^c, Anna Simpson^d, Sanchika Campbell^c, Mark Pennington^c and Surinder S. Birring^{a,b}

^aDepartment of Respiratory Medicine, King's College Hospital, London, UK; ^bCentre for Human and Applied Physiological Sciences, School of Basic and Medical Biosciences, Faculty of Life Sciences and Medicine, King's College London, London, UK; CDepartment of Psychological Medicine, Institute of Psychiatry, Psychology and Neuroscience, King's College London, London, UK; ^dMind & Body Programme, King's Health Partners, London, UK

ABSTRACT

Background: Chronic cough is a common reason for medical consultations and is associated with considerable physical and psychological morbidity. This study investigated healthcare use and cost in chronic cough and assessed its relationship with cough severity, health status, objective cough frequency (CF), and anxiety and depression.

Methods: This was a prospective study of consecutive patients with chronic cough from a specialist clinic who completed a cough severity visual analogue scale (VAS), cough-specific health status (Leicester Cough Questionnaire; LCQ) and general health status EuroQol EQ-5D-5L, Generalized Anxiety Disorder (GAD7), Patient Health Questionnaire (PHQ9), and 24-hour objective CF monitoring with Leicester Cough Monitor (LCM). Case notes were reviewed for cough-specific healthcare use 12 months before and after the first cough clinic consultation. Resource use included general practitioner and hospital clinic visits, investigations, and treatments. Unit costs for healthcare use were derived predominantly from National Health Service Reference Costs.

Results: One hundred participants with chronic cough were recruited (69% female, median duration 3 years, mean age 58 years). The diagnoses of cough were unexplained (57%), refractory (27%), and other (16%). Cough severity, health status, and CF were: median (IQR) VAS = 59.5 (30-79) mm, mean (SD) LCQ = 11.9 (4.0), mean (SD) EQ-5D-5L = 0.846 (0.178), and geometric mean (SD) CF = 15.3 (2.5) coughs/hr, respectively. The mean (SD) total cost per individual for cough-related healthcare utilization was £1,663 (747). Diagnostic investigations were the largest contributor to cost (63%), followed by cough clinic consultations (25%). In multivariate analysis, anxiety (GAD7) and cough-related health status (LCQ) were associated with increased cost ($p \le .001$ and .037).

Conclusion: Healthcare cost associated with chronic cough are largely due to diagnostic investigations and clinic consultations. The predictors of costs were health status (LCQ) and anxiety. Further studies should investigate the optimal management protocols for patients with chronic cough.

ARTICI E HISTORY

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KEYWORDS

Cough; healthcare utilization; cost

Introduction

Chronic cough is defined as a cough of over 8 weeks in duration¹ and affects up to 9.6% of the global population². Chronic cough is one of the commonest reasons for medical consultations^{3,4} and is associated with considerable physical and psychological morbidity $^{5-7}$. Guidelines for the management of chronic cough advocate the use of a wide range of investigations and therapies. There is, however, a paucity of data on healthcare utilization and its associated cost in chronic cough.

There are emerging pharmacological and pharmacological therapies in chronic cough, including gefapixant, an inhibitor of the P2X2/3 c-fibre sensory nerve receptor and physiotherapy and speech and language therapy intervention (PSALTI)^{8,9}. An increasing number of clinical trials are being carried out to assess novel therapies in chronic cough. Healthcare cost data in chronic cough would help with the assessment of cost-effectiveness of existing and future antitussive therapies. The identification of the characteristics of patients with cough that predict high healthcare costs may facilitate targeted and earlier interventions to reduce patient suffering and associated costs. We hypothesized that healthcare use in chronic cough is related to demographics, clinical characteristics of chronic cough, symptom severity, health status, and objective cough frequency.

In a preliminary observational study, we investigated the healthcare use and costs in patients referred with chronic

CONTACT Surinder S. Birring 🔯 surinder.birring@nhs.net 🔁 Department of Respiratory Medicine, Chest Unit, Cheyne Wing, King's College Hospital, Denmark Hill, London SE5 9RS, UK

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This is an Open Access article distributed under the terms of the Creative Commons Attribution-NonCommercial-NoDerivatives License (http://creativecommons.org/licenses/by-nc-nd/ 4.0/), which permits non-commercial re-use, distribution, and reproduction in any medium, provided the original work is properly cited, and is not altered, transformed, or built upon cough for 12 months prior to and after first presentation to a specialist cough clinic. We also investigated the relationship between healthcare costs in chronic cough and demographics, clinical characteristics of chronic cough, symptom severity, health status, objective cough frequency, and anxiety and depressive symptoms.

Methods

Participants

Consecutive patients with chronic cough (>8 weeks in duration) from a tertiary care specialist cough clinic (King's College Hospital, London, UK) were evaluated between 2016 and 2018. The investigation, diagnosis, and management of chronic cough was assessed by clinicians according to the British Thoracic Society guidelines for the management of chronic cough in adults 10. Inclusion criteria were a diagnosis of chronic cough, first attendance to a specialist cough clinic, and able to read and understand English. Exclusion criterion was respiratory tract infections within the preceding 4 weeks. The study was granted ethical approval as part of the IMPARTS programme¹¹, which has NHS REC approval (Health Research Authority South Central - Oxford C, 18/SC/0039) for a research database, which can be interrogated to analyse patient reported outcomes collected via an online platform used for routine clinical care, and all elements of the study were conducted in accordance with the Declaration of Helsinki. All participants provided informed consent for participation in the study.

Protocol

At the first cough clinic consultation, demographic and anthropometric data were collected. Participants were invited to complete subjective assessments of cough severity, health status, anxiety, and depression *via* the IMPARTS platform on tablets while waiting for their appointment. Participants underwent objective cough frequency monitoring as part of their routine clinical assessment. Case notes were reviewed to record the clinical characteristics of chronic cough and cough-related healthcare service utilization for the 12 months prior to and 12 months following the first cough clinic consultation. Participants underwent objective cough frequency monitoring as part of their routine clinical assessment.

Resource use and costing

Health resource use relating to cough was recorded after patients had been assessed in the specialist cough clinic. Cough-related healthcare utilized between 12 months prior to and 12 months following the first cough clinic consultation was recorded. Case notes were reviewed for previous specialist referrals (e.g. ear, nose and throat, and gastroenterology), investigations, and treatments. Investigations and treatments for asthma, gastro-oesophageal reflux, and rhinitis were recorded, whether occurring in primary or secondary care.

Unit costs for diagnostic investigations and clinic consultations were derived from National Health Service (NHS) Reference Costs (https://improvement.nhs.uk/resources/national-tariff-1719/) with the exception of cough clinic consultations and physiotherapy/speech therapy interventions which were derived from King's College Hospital tariffs. Medication costs (excluding dispensing fees) were calculated using daily dose information, and the cost of the generic drug according to the NHS Business Services Authority (http://www.nhsbsa.nhs.uk/PrescriptionServices/1821.aspx). All unit costs are for the financial year 2017/18, and are reported in Supplementary Table E1.

Patient reported outcome measures

Generic health status, anxiety, and depression

The EuroQol EQ-5D-5L is a non-disease-specific measure for describing and valuing health-related quality-of-life¹². The measure includes a rating of own health in five domains; mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. Responses can be converted to a numeric score ranging from 1 for full health to values below zero, with zero representing death and values below zero attached to health states considered worse than death. EQ-5D-5L responses were assigned a utility score using a published algorithm derived from survey data from England¹³.

The self-administered Patient Health Questionnaire (PHQ 9 items) and Generalized Anxiety Disorder Assessment (GAD7) (range 0-21; higher score indicate more severe anxiety) were used to assess depression and anxiety status, respectively^{14,15}. All participants completed the initial section of the questionnaire and only those with a score greater than the threshold for "some symptoms" completed the remaining items 11,16,17. There are three possible PHQ responses: (1) Probable major depression [at least 5 items (including items 1 and/or 2) occurring \geq half the days; item 9 \geq several days], (2) Some depressive symptoms [item 1 or 2 occurring > half the days, but not meeting criteria for major depression], and (3) Negative depression screen (not met the criteria for some depressive symptoms)¹¹. The criteria for anxiety screening with the GAD7 score was: Probable generalized anxiety disorder (total score \geq 10) and some symptoms of anxiety (total score = 5–9)¹¹.

Cough severity and cough-specific health status

Cough severity was recorded on a visual analogue scale (VAS) (range $= 0-100 \, \text{mm}$; higher scores indicate higher severity)¹⁸. Cough-specific health status was recorded with the validated self-administered 19-item Leicester Cough Questionnaire (LCQ) (range = 3-21; higher scores indicate better health status)¹⁹.

Cough frequency monitoring

Cough frequency was recorded for 24 h with the Leicester Cough Monitor (LCM). The LCM is a validated ambulatory cough monitoring system which comprises a MP3 audio recorder (ICD-PX333, Sony Corporation, Tokyo,



Table 1. Demographics, anthropometrics, and clinical characteristics of participants with chronic cough.

	Participants with chronic cough ($n = 100$)
Age (years)	57.9 (14.6)
Gender (female)	69
BMI (kg/m ²)	27.9 (25.3–31.2)
Smoking status	
Current	0
Ex	26
Never	74
Spirometry	
FEV ₁ % predicted	92.8 (23.3)
FVC % predicted	104.6 (21.5)
Source of referral	
Primary care	34
Secondary care	66
Duration of cough (years)*	3.0 (1.9–10.0)
Diagnoses	
Refractory chronic cough	27
Unexplained chronic cough	57
Other	16
EQ-5Q-5L [†]	0.846 (0.178)
GAD7	
Probable generalized anxiety disorder (n%)	12
Some symptoms of anxiety (n%)	7
No anxiety symptom (n%)	81
PHQ9	
Probable major depression (n%)	11
Some depressive symptoms (n%)	13
No depressive symptom (n%)	76
Cough severity VAS (mm) [‡]	59.5 (30.0–79.0)
LCQ [‡]	
Physical	4.3 (1.2)
Psychological	3.9 (1.5)
Social	3.8 (1.6)
Total	11.9 (4.0)
24-hour cough monitoring $(n = 57)^{\#}$	
Total cough counts (coughs)	363.0 (2.6)
Total cough frequency (coughs/hr)	15.3 (2.5)

Data presented as mean (SD), median (IQR), or absolute number unless otherwise stated. Abbreviations. BMI, body mass index; FEV1, forced expiratory volume in 1s; FVC, forced vital capacity; GAD7, Generalized Anxiety Disorder Assessment; PHQ9, Patient Health Questionnaire; VAS, visual analogue scale; LCQ, Leicester Cough Questionnaire. *n = 98, $^{\dagger}n = 27$, $^{\dagger}n = 96$, $^{\S}n = 57$. $^{\#}Geometric mean (SD).$

a free-field microphone (LFH9173, Amsterdam, Netherlands), and custom-built semi-automated cough detection software²⁰. A cough was detected as a single event whether they occurred as part of a bout or in isolation²⁰. Total 24-hour and awake cough counts and frequencies were reported.

Statistical analysis

Statistical analyses were performed using Stata version 15 (Timberlake Consultants Ltd, Richmond Upon Thames, UK) and Prism version 8.4.1 (GraphPad Software, San Diego, CA). Patient response data were summarized as the mean and standard deviation (SD) unless the D'Agostino-Pearson test indicated departures from normality, in which case median and interquartile range (IQR) were reported. Resource use is reported as the mean (SD) and the percentage of the group who had at least one contact or course of treatment. Costs are reported as the mean (SD). Resource use and cost data for the 12 months prior to cough clinic admission and presented separately 12 months post-admission are (Supplementary Tables E2 and E3).

The distribution of cost data is typically skewed and may exhibit a large mass at zero. Accordingly, the study used robust statistical methods for inference testing around mean values, including bootstrapped confidence intervals and generalized linear modelling using the gamma distribution recommended for cost data and the identity link function²¹. Variables that could potentially impact cost (age, gender, smoking status, referral source, diagnosis of chronic cough, cough severity VAS, LCQ, EQ-5D-5L, PHQ9, GAD7, and objective cough frequency) were investigated as predictors of cost in univariate analysis. PHQ9 and GAD7 scores were dichotomized as probable major disease or some symptoms/no symptoms (defined as above). Variables at the 0.05 level of significance in univariate analysis, together with age and gender, were then entered into multivariate regression analyses. Variables with a strong collinear relationship or high level of missing data were excluded from multi-variate analysis. The stronger or more valid variable was kept for analysis in the case of collinearity.

Results

Participant characteristics

The demographics, anthropometrics, spirometry, and clinical characteristics of 100 participants are summarized in Table 1. The median (IQR) duration of chronic cough was

Table 2. Cough-related healthcare utility and cost for 12 months prior to and 12 months following first specialist clinic consultation.

Items	Utilization by participants (n)	Utilization per participant	Cost per participant (GBP)	
Cough clinic consultations	100	2.55 (1.08)	436.25 (123.81)	
Imaging				
Chest radiograph	99	1.33 (0.55)	41.23 (17.10)	
CT chest	71	0.75 (0.52)	67.50 (46.78)	
CT sinus	18	0.20 (0.45)	18.00 (40.45)	
Subtotal imaging			126.73 (68.57)	
Pulmonary function test				
Spirometry	99	1.55 (0.59)	263.50 (100.72)	
Body plethysmography	9	0.09 (0.29)	16.02 (51.20)	
Diffusion capacity of CO	22	0.21 (0.41)	37.59 (73.78)	
Reversibility	22	0.22 (0.42)	26.45 (51.31)	
Methacholine challenge	1	0.01 (0.10)	1.97 (19.70)	
Subtotal pulmonary function test			345.53 (155.30)	
Other respiratory investigations				
Skin prick test	20	0.20 (0.40)	34.80 (60.19)	
Overnight pulse oximetry	20	0.20 (0.40)	38.80 (77.99)	
Sputum culture	2	0.02 (0.14)	0.16 (1.13)	
Bronchoscopy	14	0.14 (0.35)	39.06 (97.29)	
Subtotal other respiratory investigations			112.82 (125.57)	
Gastrointestinal investigations				
Gastroscopy	11	0.11 (0.35)	38.72 (121.47)	
Barium swallow	3	0.03 (0.17)	4.41 (25.20)	
Video fluoroscopy	1	0.01 (0.10)	1.43 (14.30)	
24-hour oesophageal manometry	23	0.24 (0.45)	137.76 (259.54)	
Subtotal gastrointestinal investigations		(******)	182.32 (350.65)	
Other investigations			(51500)	
Nasoendoscopy	13	0.13 (0.34)	16.25 (42.45)	
Nerve conduction study	1	0.01 (0.10)	1.87 (18.70)	
Ultrasound thyroid	1	0.01 (0.10)	0.54 (5.40)	
Electrocardiogram	1	0.01 (0.10)	1.20 (12.00)	
Subtotal other investigations			19.86 (55.13)	
Other out-patient consultations			19100 (331.3)	
Ear, nose and throat	62	0.68 (0.58)	81.60 (70.08)	
Gastroenterology	28	0.32 (0.55)	60.16 (103.08)	
Immunology and allergy	4	0.04 (0.19)	8.84 (43.43)	
Rheumatology	1	0.01 (0.10)	3.13 (31.30)	
Subtotal other out-patient consultations	•	0.01 (0.10)	153.73 (134.36)	
Medications			133.73 (131.30)	
Antibiotics (unspecified)	15	0.17 (0.45)	0.19 (0.51)	
Inhaled corticosteroid	61	0.75 (0.69)	9.04 (12.73)	
Inhaled long-acting β -agonist	27	0.29 (0.50)	29.85 (86.99)	
Prednisolone	77	0.83 (0.51)	2.22 (2.05)	
Montelukast	3	0.03 (0.17)	0.70 (5.49)	
Omeprazole	93	1.11 (0.49)	8.29 (14.43)	
Nasal steroid	45	0.49 (0.58)	2.69 (3.44)	
Gabapentin trial	43	0.49 (0.58)	2.54 (3.26)	
•	8		0.34 (1.66)	
Amitriptyline trial		0.29 (1.38)		
Long-term gabapentin	25	0.27 (0.49)	9.11 (16.51)	
Long-term amitriptyline Subtotal medications	2	1.04 (7.31)	0.23 (1.63) 65.20 (97.28)	
Other treatments			05.20 (97.28)	
	61	0.62 (0.53)	152.72 (120.15)	
Physiotherapy/Speech (PSALTI)	61	0.63 (0.53)	153.72 (128.15)	
Nissen fundoplication	2	0.02 (0.14)	51.76 (364.14)	
Antral washout	1	0.01 (0.10)	14.93 (149.30)	
Subtotal other treatments			220.41 (412.75)	
Total costs over 2 years			1,662.85 (747.29)	

Data presented as mean (SD) or absolute.

Abbreviations. CT, computer tomography; CO, carbon monoxide; PSALTI, physiotherapy and speech and language therapy intervention; GBP, British Pound Sterling.

3.0 (1.9–10.0) years. The median (IQR) cough severity VAS was 59.5 (30.0–79.0) mm, and the mean (SD) LCQ was 11.9 (4.0). Primary care was the source of referral to the specialist cough clinic in 34 participants, whilst the remaining participants were referred by secondary care physicians. The diagnoses of cough were unexplained (57%), refractory (27%), and other (16%) (Table 1). The diagnoses in the refractory group were asthma/eosinophilic bronchitis (55%), reflux (30%), and postnasal drip/upper airway cough syndrome (15%). The prevalence of depressive and anxiety cases were: probable major

depression (11%), some depressive symptoms (13%), and negative depression screen (76%), probable generalized anxiety disorder (12%), some symptoms of anxiety (7%), and negative anxiety screen (81%).

Healthcare resource use and costs

Healthcare resource use and associated costs are summarized in Table 2. Participants' accrued mean (SD) total cough-related healthcare costs of £1,663 (747) each. The mean cost

Table 3. Multivariate analysis of potential predictors of cough-related healthcare costs following removal of co-linear variables.

Variables	Correlation coefficients	Bootstrap SE	<i>p</i> -values	95% CI
Age	1.049412	5.581534	.851	-9.890193 to 11.98902
Gender	143.4239	186.8128	.443	-222.7224 to 509.5702
Duration of cough	12.41278	9.750369	.203	-6.697588 to 31.52316
Diagnosis of unexplained chronic cough	280.3927	177.7009	.115	-67.89472 to 628.6802
LCQ total	-41.00865	19.63903	.037	-79.50044 to -2.516848
Anxiety case	-652.6497	167.3116	<.001	-980.5744 to -324.7251

Abbreviations. VAS, visual analogue scale; LCQ, Leicester Cough Questionnaire. Bold values represent p < .05.

of healthcare per participant prior to cough clinic was £645, and cough clinic-related healthcare costs were £1,017 (Supplementary Tables E2 and E3, respectively). The largest contributor to costs was investigations and procedures (57% of total cost), of which lung function and oesophageal pH/ impedance/manometry accounted for over half of the diagnostic procedure costs. The next highest costs were cough clinic consultations and other specialist clinic consultations; mean (SD) cost per participant: £436 (124) and £154 (134), respectively. Investigation of the relationship between participant characteristics (sex, smoking status, duration of cough, LCQ, and cough frequency) and the number of clinic consultations did not identify any significant associations. Costs associated with treatments were modest, reflecting the low unit costs of most drug treatments. The most expensive therapy was physiotherapy/speech therapy, which 61 participants received.

The total costs for patients according to diagnosis were £1,267.53 for patients with refractory cough, £1,781.66 for patients with unexplained cough, and £1,646.34 for the remaining patients. Supplementary Table E4 in supplementary material provides a breakdown of costs by category and according to diagnosis. Regression analysis using GLM indicated that total costs for patients with refractory cough were significantly lower than costs for unexplained patients (p = .02). The total costs for patients referred by a GP were £1,582.75; total costs for the remaining patients were £1,704.13. Supplementary Table E5 provides a breakdown of costs by category and according to mode of referral. Regression analysis using GLM indicated no significant difference in total costs according to mode of referral.

Predictors of cost

The results of the univariate analyses are presented in Supplementary Table E6. The duration of cough and a diagnosis of unexplained cough were associated with cost (p=.024 and .017, respectively). Cough severity VAS and LCQ were significantly related to costs (both p < .001) but generic quality-of-life (EQ-5D-5L) was not (p = .542). Cough frequency (24-hours) was also associated with cost (p = .044). Neither age, sex, or smoking status were related to costs (p = .310, .199 and .547, respectively).

In a multivariate analysis, the variable 24-hour total cough frequency was excluded as responses were missing for 46 patients. Cough severity VAS was also excluded after postestimation variance inflation factors indicated a high correlation between the LCQ and cough severity VAS (LCQ was considered a better validated tool and one that measures cough severity and many other health domains relating to cough). In the revised multivariate analysis (Table 3), anxiety (GAD7) and cough-specific health status (LCQ) were significantly related to costs (p < .001 and .037, respectively), with costs increasing as severity increased on both measures. Other variables, including duration of cough, were not significantly related to costs. Exploratory analyses were undertaken to determine the impact of anxiety and cough-specific qualityof-life on the components of total costs in which total costs were split into costs of tests, costs of consultations, and other costs. Anxiety and cough-specific quality were predictive of costs of consultations (p < .001 and .053) and of other costs (p = .001 and < .001) but not the costs of tests, respectively.

Discussion

We investigated healthcare utilization and cost in chronic cough for 12 months prior to and after the first specialist cough clinic consultation. The mean cough-related cost accrued was £1,663 per patient, and diagnostic investigations were the largest contributor, at 57% of all costs. Univariate analysis suggested cost was related to duration of cough, diagnosis of unexplained cough, cough severity, healthrelated quality-of-life, and objective cough frequency. Multivariate analysis indicated that anxiety and health-related quality-of-life best predicted healthcare cost.

This is, to the best of our knowledge, the first study to investigate healthcare cost in chronic cough. The healthcare costs are considerable and relate largely to diagnostic investigations and associated clinic consultations. This is consistent with clinical guidelines which advocate a combination of investigations and treatment trials for investigating patients. The costs of most treatments are low since they are largely generic, widely available, and are often used short- to medium-term. Our findings should facilitate the investigation of healthcare cost in chronic cough in future studies.

In univariate analysis, cough-related healthcare cost was associated with duration of cough, diagnosis of unexplained cough, cough severity VAS, cough-related health status, and objective cough frequency. A longer duration and more severe cough are likely to lead to more healthcare utilization for investigations and management. Furthermore, an unexplained cough is also likely to lead to more investigations to establish a diagnosis. These are all plausible associations with cost, and they increase confidence in our estimate of healthcare cost associated with cough. Female gender was not associated with cost. This may be because, as expected, our study population was largely female, and the male sample size may have been too small for analysis. Furthermore, whilst female patients are more likely to seek medical attention for their cough, the approach to investigating patients in specialist clinics is not gender-specific. We did not find a difference in cost between patients referred from primary vs. secondary care. This needs investigating in larger studies in future. In multivariate analysis, only cough-related quality-of-life and anxiety were associated with healthcare cost. It is likely that factors such as cough frequency and severity are reflected in LCQ scores. As our data suggests that diagnostic investigations and clinical consultations comprise the majority of healthcare cost, future studies should investigate the relationship between clinical characteristics and contributors of costs in a larger number of patients.

Our data suggest that anxiety and the burden of cough may influence healthcare utilization and cost in chronic cough. The prevalence of psychological morbidity was lower than that reported in previous studies^{5,7}. Previous studies used different tools, the Hospital Anxiety and Depression Scale, State Trait Anxiety Inventory, and Center for Epidemiologic Studies Depression Scale^{5,7}. We used PHQ9 since it has been reported to have a good sensitivity, specificity, reliability, and is validated in physically ill populations and is recommended by the National Institute of Clinical Excellence (NICE)^{11,22–25}. We also used the GAD7 which has also been reported to have a good reliability and construct, factorial, and criterion validity¹⁵. In our study, the presence of more significant anxiety symptoms assessed with the GAD7 was predictive of healthcare utilization and cost. A study by French et al.⁶ found that worry about cough indicating a serious illness was the main reason why patients sought medical attention. Another study by Cornford²⁶ reported healthcareseeking patients with chronic cough were more worried compared to non-healthcare-seeking counterparts. Other adverse consequences of cough, such as syncope and urinary incontinence, impact quality-of-life and are also important reasons for seeking medical attention^{6,26,27}. Future studies should evaluate whether the LCQ and GAD7 questionnaires can identify patients who utilize high levels of healthcare and whether earlier interventions can achieve better outcomes for patients and healthcare organizations.

No association was found between EQ-5D-5L and health-care cost. Polley et al.²⁸ reported that EQ-5D had a weak relationship with cough-related health status in chronic cough. A lack of correlation between EQ-5D scores and healthcare cost does not preclude the possibility that the instrument is able to detect improvements in quality-of-life arising from treatment of cough. Nevertheless, it is possible that EQ-5D is not particularly sensitive to the impact cough has on patients' quality-of-life. Appropriate methods to capture the cost-effectiveness of antitussive therapy on quality-of-life are urgently needed given the rapid developments in new therapies recently^{8,9,29}.

Very little data is available on the cost of chronic cough. One study from Malawi estimated the cost of chronic cough to be \$3.9 (2015 USD), which should be set against annual per capita consumption of \$107 USD at the time and the different spectrum of causes of cough in this setting³⁰. The cost

associated with chronic cough in our study was less than we expected since this condition involves numerous consultations, investigations, and treatments. We did capture assessments that secondary care patients underwent before review at the specialist clinic. Most of our patients underwent chest radiograph, spirometry, CT scans, ENT review, and multiple trials of therapy. It should be noted that the trials of therapy for cough involve low-cost generic medication. Furthermore, the NHS tariffs for investigations and consultations are modest. The costs associated with chronic cough in the UK are only slightly less than for COPD. Data from the UK on COPD indicates annual costs of management of £2,108 (2011 GBP)³¹. A study in the UK reported annual costs of managing severe uncontrolled eosinophilic asthma to be £861 (2017 GBP)³¹.

There are limitations with our study. The patients were recruited from a tertiary specialist cough clinic and a study with a broader population is required. We assessed a relatively small number of patients and there was significant missing data with objective cough frequency and the EQ-5D-5L measurements. Nevertheless, we were able to demonstrate an association between objective cough frequency and healthcare cost in univariate analysis. In addition, the cough severity VAS and EQ-5D-5L values in our study population were comparatively similar to those reported in chronic cough, and chronic obstructive pulmonary disease and cystic fibrosis, respectively^{9,32,33}. We assessed healthcare cost 12 months prior to referral to the specialist clinic and therefore may not have captured all costs in patients with a longer duration of cough. We did not assess the cost of general practice consultations since we did not have access to primary care records for out of area patients and many were referred by secondary care physicians. Our estimate of healthcare cost is likely to be an underestimate and, therefore, further, more detailed studies are required. We did not assess the employment and social cost related to cough since this was beyond the scope of this study.

Conclusions

In conclusion, chronic cough is associated with moderate healthcare cost and diagnostic investigations are the main contributor. Anxiety and cough-related health status were associated with healthcare cost. Further studies are needed to confirm the healthcare costs associated with cough and investigate the optimal clinical and cost-efficient management protocols for patients with chronic cough.

Transparency

Declaration of funding

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Declaration of financial/other relationships

JS is reporting no potential competing interest other than the investigator research grant from Merck & Co., Inc. SC and AS are reporting no



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Author contributions

Conception and design: SB, PC, JS, and MP; Data collection: PC, SC, and AS; Data analysis: PC, SB, JS, and MP; Interpretation of data: PC, SB, JS, MP, and AS; Drafting manuscript: PC, SB, JS, and MP; Revised manuscript: PC, JS, SC, AS, MP, and SB.

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ORCID

Peter S. P. Cho (D) http://orcid.org/0000-0001-8689-8541 Surinder S. Birring (i) http://orcid.org/0000-0003-2525-6291

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