Prioritising primary care respiratory research needs: results from the 2020 International Primary Care Respiratory Group (IPCRG) global e-Delphi exercise

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Abstract

Respiratory diseases remain a significant cause of global morbidity and mortality and primary care plays a central role in their prevention, diagnosis and management. An e-Delphi process was employed to identify and prioritise the current respiratory research needs of primary care health professionals worldwide. 112 community-based physicians, nurses and other healthcare professionals from 27 high, middle and low-income countries suggested 608 initial research questions, reduced after evidence review by 27 academic experts to 176 questions covering diagnosis, management, monitoring, self-management and prognosis of asthma, COPD and other respiratory conditions (including infections, lung cancer, tobacco control, sleep apnoea). 49 questions reached 80% consensus for importance. Cross-cutting themes identified were: a need for more effective training of primary care clinicians; evidence and guidelines specifically relevant to primary care, adaption for local and low resource settings; empowerment of patients to improve self-management; and the role of the multidisciplinary healthcare team.

Introduction

Chronic respiratory diseases (CRDs) impose a significant burden on global health[1]. The Global Burden of Disease Study 2019 suggested that respiratory conditions[1] account for 7.7million deaths per year [1]. CRD and respiratory infections (including tuberculosis) account for the third and fourth causes of death after cardiovascular disease and cancer [2,3]. Smoking is the second most important risk factor for global disease burden (GBD) while indoor and outdoor air pollution are included in the top ten risk factors [2]. Furthermore, the number of Disability Adjusted Life Years (DALYs) for CRD has increased by 20% since 1990 [2,3]. Commentaries by the GBD highlight the gap between current policies, activity and burden and the importance of universal health coverage[3].

Primary care has a core role in the prevention, diagnosis and management of all respiratory diseases [4]; indeed, respiratory symptoms are the most common reason for primary care consultations [5]. However, significant evidence gaps remain, with a corresponding lack of evidence-based guidelines, quality standards and training to support primary care practice [5]. Progress is further challenged by the diversity of healthcare issues presented in primary care and the various models adopted for primary care worldwide [6,7]. Prioritising research needs helps guide researchers, research funders, and policymakers and will ultimately improve clinical guidelines and patient care globally. Although relevant prioritisation studies exist [8,9], there is still a need for a systematic and transparent approach in the specific area of primary care respiratory research [7], and furthermore to ensure that the priorities are relevant to countries with different risk factor profiles and phases of development [10]. To date, there has been a general lack of investment in primary care respiratory research and an up-to-date specific needs statement will provide impetus to redress that balance [11].

The International Primary Care Respiratory Group (IPCRG) is a clinically-led charity which aims to promote research into the care, management and prevention of respiratory diseases in the community [12]. Its vision is a "world breathing and feeling well through universal access to right care". Current membership includes 34 full and 24 associate member countries [12] representing an estimated 150,000 primary healthcare professionals worldwide from high-, middle- and low-income countries in Europe, Asia, North and South America, Australia, and Africa [12]. In 2010, the IPCRG published its first Research Needs Statement for primary care respiratory research, identifying 145 research questions within five domains: asthma, rhinitis, COPD, smoking and respiratory infections [5]. This was prioritised in 2012 through an e-Delphi exercise culminating in a final list of 62 questions [13]. Now, eight years on, changing needs and contexts require an update.

In this paper, we provide a new agenda for primary care respiratory research, obtaining consensus on the most important respiratory research questions from the perspective of practising primary care healthcare professionals representing a wide range of backgrounds and settings worldwide.

Results

Participants

A total of 112 participants from 27 countries took part in the initial online e-Delphi survey. Participants came from a wide range of backgrounds, roles, and experiences (Table 1). Participants represented all main global regions including Europe (n=46, 41%), Asia (n=37, 33%), Africa (n=14, 12.5%), South America (n=9, 8%), North America (n= 3, 2.7%), and Oceania (n=3, 2.7%). There were similar numbers of high-income and low- and middle-income countries (LMICs) represented, but with a higher proportion of participants from LMICs (n=67, 60%). Appendix 1 provides further detail on the distribution of participants within high-, middle- and low-income countries.

Women accounted for 58% (n=65) of the participants, and most (n= 90, 80.3%) were between the ages of 25 to 54 years. While some participants worked in hospital settings (also treating community patients) (n=16, 14.3%), the majority worked mainly in primary care or community settings (n=74, 66.1%). Overall, 65 (58%) were family physicians, 13 (11.6%) hospital doctors, 12 (10.7%), clinician researchers, 11 (9.9%) were nurses, and 8 (7.1%) were other healthcare workers. 66 (58.9%) participants reported being in their roles for more than ten years, and 72 (64.3%) had respiratory-related special interests or qualifications. Rounds 2 and 3 included 52 and 34 of the original respondents respectively with a generally similar demographic distribution to round 1 except in round 3 where a larger proportion of women remained than in previous rounds (n=22, (65%) women), a lower proportion of family physicians (n=14, (41%)), but a greater proportion with more experience (n=25 (73%) reported 10 or more 'years' experience in their role). The income distribution of countries was generally similar throughout the 3 rounds.

e-Delphi round	Round 1	Round 2	Round 3
Table 1: Demographic characteristics of participants for e-Delphi rounds 1, 2 and 3			
Characteristic	N (%)	N (%)	N (%)
Number of participants	112 (100.0)	52 (100.0)	34 (100.0)
Gender			
Male	47 (42.0)	21 (40.4)	12 (35.0)
Female	65 (58.0)	31 (59.6)	22 (65.0)
Age in years			
25-34	28 (25.0)	14 (27.0)	9 (26.5)
35-44	36 (32.1)	17 (32.7)	10 (29.4)
45-54	26 (23.2)	10 (19.2)	9 (26.5)
55-64	18 (16.1)	9 (17.3)	5 (14.7)
65 and over	4 (3.6)	2 (3.8)	1 (2.9)
Role			
Doctor: Family Physician	65 (58.0)	25 (48.2)	14 (41.0)
Doctor: Hospital Doctor	13 (11.7)	6 (11.5)	3 (8.8)
Doctor: Other	3 (2.7)	2 (3.8)	2 (6.0)
Doctor: Clinician Researcher	12 (10.7)	5 (9.6)	3 (8.8)
Nurse: Hospital Nurse	3 (2.7)	4 (7.7)	4 (11.8)
Nurse: Community Nurse	2 (1.8)	0 (0.0)	0 (0.0)
Nurse: Other	6 (5.4)	5 (9.6)	4 (11.8)
Other Healthcare Worker	8 (7.1)	5 (9.6)	4 (11.8)
Years of Experience			
< 5 years	22 (19.6)	11 (21.3)	7 (20.5)
5- 10 years	24 (21.5)	7 (13.4)	2 (6.0)
> 10 years	66 (58.9)	34 (65.3)	25 (73.5)
Additional Respiratory Qualifications or Special Interest			
Yes	72 (64.3)	35 (67.3)	21 (62.0)
No	40 (35.7)	17 (32.7)	13 (38.0)
Work Setting			
Hospital	26 (23.2)	15 (29.0)	11 (32.4)
Primary Care/ Community	74 (66.1)	29 (55.7)	16 (47.1)
Other	12 (10.7)	8 (15.3)	7 (20.5)
Region			
Africa	14 (12.5)	5 (9.7)	4 (11.8)
Asia	37 (33.0)	21 (40.4)	12 (35.3)
Europe	46 (41.1)	18 (34.6)	12 (35.3)
North America	3 (2.7)	2 (3.8)	1 (2.9)
Oceania	3 (2.7)	2 (3.8)	1 (2.9)
South America	9 (8.0)	4 (7.7)	4 (11.8)
Country Classification*			
High-income	45 (40.2)	23 (44.2)	15 (44.1)
Upper middle-income	34 (30.4)	12 (23.0)	10 (29.4)
Lower middle-income	24 (21.4)	14 (27.0)	7 (20.5)
Low-income	9 (8.0)	3 (5.8)	2 (6.0)

* *Source: World Bank Country Classifications by income level: 2018-2019* [14].

***Responses to the initial survey (round 1)***

<u>*Question 1 (most common conditions):*</u>

Asthma was the most frequently mentioned respiratory condition encountered by respondents in their clinical practice (17.2%), followed by COPD (15.2%). However, as a clustered group of conditions, respiratory infections (TB, pneumonia, URTI, bronchitis/bronchiolitis, influenza) were mentioned most often (34.8% of all responses). Respiratory symptoms such as cough and dyspnoea rather than specific clinical conditions were mentioned in 6.7% of responses.

<u>*Question 2 (most important conditions)*</u>

Although respiratory infections as a clustered group of conditions were perceived to be the most clinically important (29.9%), asthma was reported to be the most important single condition (25.7%), followed by COPD (24.5%), Figure 2 illustrates the proportional distribution (percentages) of most clinically important respiratory conditions.

Figure 2 Proportional distribution of respiratory conditions identified by participants as most clinically important
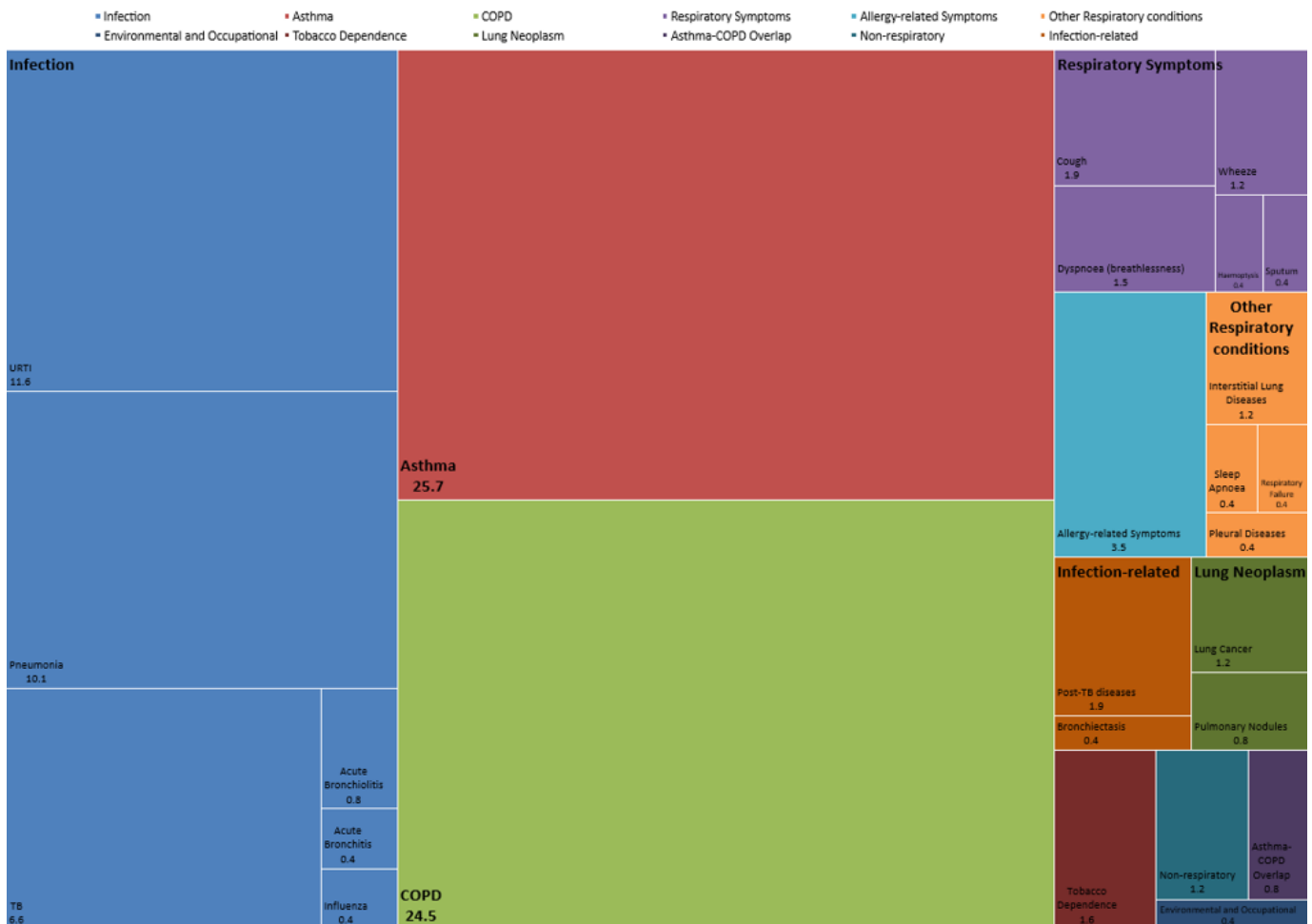
Topics names followed by the percentage share of responses. The area of each box represents the proportion of each condition as a percentage of all mentioned conditions.

Suggested research questions (question 3) and the Evidence Verification Stage

A total of 608 research questions were suggested by participants and grouped into 19 topics representing common categories of respiratory conditions. After verification and review by the expert group, and removal of duplicates, 176 research questions were finalised, categorised pragmatically into 14 topics and entered into the remaining two e-Delphi rounds. Figure 3 illustrates the proportional distribution (frequencies) of respiratory research questions as finalised by experts in the Evidence Verification Stage. The greatest proportion of questions were related to the management of COPD, followed by asthma self-management, asthma management, COPD diagnosis and screening, tuberculosis in primary care, and tobacco control.

Figure 3 Proportional distribution of final research questions across the 14 topics after the Evidence Verification Stage

Topics names followed by the number of final research questions. The area of each box represents the proportion of each topic as a percentage of all research questions.

Consensus and ranking

Overall, 80% consensus was reached in 49 (27.7%) of the 176 rated questions. Asthma accounted for 19 (38.8%) of these questions while COPD accounted for 17 (34.7%) questions. Two questions (4%)

reached a consensus of 100%: "What is the best way to manage chronic/ persistent cough in primary care?" and "What are the best ways to monitor asthma in primary care?". Furthermore, 20 (40%) questions reached 90-99% consensus, while 27 questions (55.1%) reached a consensus of 80-89%. Table 2 lists the top 10 questions by consensus scores. Detailed rankings within asthma, COPD and other respiratory conditions are provided in Tables 3 to 5. Appendix 3 lists all 176 questions with their scores.

Table 2: Top 10 primary care research respiratory priorities

Top 10 primary care research respiratory priorities			
Question	Category	Consensus (%)*	Mean rating 0-5
What is the best way to manage chronic/ persistent cough in primary care?	Chronic/ persistent cough management	100	4.71
What are the best ways to monitor asthma in primary care?	Asthma monitoring	100	4.44
What steps could be taken to prevent exacerbations and progression of asthma?	Asthma management	97.1	4.38
How can brief advice be used more effectively to increase motivation to quit, and what elements are most efficient for a busy primary care practitioner?	Tobacco Control management	97.1	4.38
How should we best manage COPD in patients with cardiovascular diseases, arrhythmias and uncontrolled hypertension?	COPD management	97	4.35
What are the most effective strategies for ensuring sustained good inhaler techniques among asthma patients?	Asthma self-management	94.2	4.38
What methods could be used to enhance adherence to asthma controller therapy?	Asthma management	94.1	4.5
How could we improve COPD 'patients' adherence to inhalers? Which are the best methods to teach about inhaler use and how can we incorporate them in daily clinical practice?	COPD self-management	94.1	4.5
What is the best way to engage people with asthma in self-management?	Asthma self-management	94.1	4.44
How can we best educate healthcare professionals to improve early recognition and diagnosis of COPD?	COPD diagnosis	94.1	4.44

Questions rated on a Likert scale (0, not important -5, very important). * % rating 4 (important) or 5 (very important).

Table 3: Consensus on the research priorities in asthma

	Rank	Question	Consensus (%)*	Mean Rating
Asthma				
Diagnosis	1	How could asthma be diagnosed earlier in primary care?	88.3	4.26
	2	How could asthma be diagnosed in settings with limited availability of diagnostic tests?	85.3	4.38
	3	What practical algorithms could distinguish between recurrent wheeze/ asthma and other acute respiratory diseases for young children?	85.3	4.24
Management	1	What steps could be taken to prevent exacerbations and progression of asthma?	97.1	4.38
	2	What methods could be used to enhance adherence to asthma controller therapy?	94.1	4.5
	3	What is the most effective management for acute exacerbation of asthma in children?	91.1	4.29
	4	How could guidelines be adapted to manage asthma in Lower-Middle- Income Countries (LMICs)?	88.2	4.35
	5	What is the role of intermittent therapy, such as SABA, ICS/SABA and ICS/LABA, in the management of asthma?	88.2	4.26
	6	When and how should asthmatic patients be stepped down from ICS?	85.3	4.09
	7	What is the best way to select drug therapy in children with asthma?	82.3	4.12
Monitoring	1	What are the best ways to monitor asthma in primary care?	100	4.44
	2	What are the best clinical tools to monitor asthmatic and allergic children in primary care in LMICs?	82.3	4.18
Self-management	1	What are the most effective strategies for ensuring sustained good inhaler techniques among asthma patients?	94.2	4.38
	2-a	What is the best way to engage people with asthma in self-management?	94.1	4.44
	2 -b	What is the best way to support patients to improve their adherence to asthma medications?	94.1	4.44
	4	What are the best ways for health care professionals to engage patients in supported self-management and empower them to take control of their asthma?	94.1	4.24
	5	What are 'physicians' barriers to supporting patients to effectively self-manage their asthma in low resource settings?	88.3	4.15
	6	What educational interventions are effective and cost-effective for children /families with asthma?	88.2	4.21

	7	What strategies/adaptations can help empower people with limited health literacy to effectively self-manage their asthma?	85.3	4.09

Questions rated on a Likert scale (0, not important -5, very important). * % rating 4 (important) or 5 (very important).

SABA=Short-acting inhaled beta-agonists, ICS=Inhaled Corticosteroids, LABA=Long-acting beta-agonists

Table 4: Consensus on the research priorities in COPD

	Rank	Question	Consensus (%)*	Mean Rating
COPD				
Diagnosis	1	How can we best educate healthcare professionals to improve early recognition and diagnosis of COPD?	94.1	4.44
	2	How should we best diagnose COPD in settings where good quality spirometry is not available or not affordable?	91.2	4.32
	3	What are the most cost-effective and efficient approaches for identifying COPD, especially in low-resource settings?	88.3	4.26
	4	How effective are public awareness/education campaigns to improve awareness and earlier diagnosis of COPD?	82.3	4.26
Management	1	How should we best manage COPD in patients with cardiovascular diseases, arrhythmias and uncontrolled hypertension?	97.0	4.35
	2	How to tailor the current COPD management guidelines to suit those with comorbidities?	94.1	4.38
	3	How can we manage COPD patients with comorbidities in primary care using a personalised approach to reduce adverse reactions and limit disease progression?	91.2	4.38
	4	What is the optimal strategy for identifying and treating COPD exacerbations in primary care?	91.2	4.35
	5	Does shared care between primary care physicians and specialists improve the management of COPD patients and reduce exacerbations?	88.3	4.21
	6	How best could COPD treatments be tailored to suit different COPD phenotypes?	88.3	4.15
	7	How should COPD be managed in low- and middle-income countries, including rural community settings?	88.2	4.18

	8	How do primary care clinicians use spirometry findings to inform the ongoing management of COPD?	85.3	4.03
Monitoring	1	How do primary care clinicians use measures of disease progression in COPD to inform the care they provide? What is the impact of using measures of disease progression on quality of care and clinical outcomes?	88.3	4.15
Self-management	1	How could we improve 'patients' adherence to inhalers? Which are the best methods to teach about inhaler use and how can we incorporate them in daily clinical practice?	94.1	4.5
	2	How cost-effective are e-Health interventions, mobile and online applications (including wearables) in self-monitoring, symptoms control and adherence to medications in patients with COPD?	91.2	4.29
	3	What are the best engaging and supporting strategies for health care professionals to help improve self-management of COPD?	88.2	4.24
Prognosis	1	Is the early identification of COPD beneficial to patients in the long-term?	85.3	4.32

Questions rated on a Likert scale (0, not important -5, very important). * % rating 4 (important) or 5 (very important).

Table 5: Consensus on the research priorities in other respiratory conditions

	Topic	Rank	Question	Consensus (%)*	Mean Rating
Other respiratory conditions					
Diagnosis	TB	1	What are the best methods to increase detection of tuberculosis cases in primary health care or at the community level?	91.2	4.21
	Allergic Rhinitis and Other Allergic Conditions	2	What tools could help the primary care clinician differentiate between allergic and non-allergic rhinitis, rhinosinusitis, common cold and other clinically similar conditions?	88.2	4.24
	Infections in Primary Care	3	What are the best tools to help in triaging patients with respiratory infections to guide the use of antibiotics in community settings?	85.3	4.24
	Lung cancer in Primary Care	4-a	What is the best diagnostic algorithm for lung cancer for helping primary care doctors identify those at increased risk?	85.3	4.15
	Sleep Apnoea	4-b	What is the best-validated screening tool for sleep-related breathing disorders, especially Obstructive Sleep Apnoea in the primary care setting?	85.3	4.15
Management	Other respiratory-related questions	1	What is the best way to manage chronic/ persistent cough in primary care?	100	4.71
	Tobacco Control	2	How can brief advice be used more effectively to increase motivation to quit, and what elements are most efficient for a busy primary care practitioner?	97.1	4.38
	Tobacco Control	3	What combination of interventions (e.g. brief advice, cost-free medications, adjunct counselling) are most effective for increasing patient quit rates in primary care practice?	91.2	4.32
	Tobacco Control	4	What are the most effective models (including primary healthcare or specialist smoking cessation teams) for providing smoking cessation support services in different cultural and/or socioeconomic settings?	91.2	4.26
	Tobacco Control	5	How can primary care clinicians in different countries be made more aware of strategies	88.3	4.15

			to prevent smoking in young people and pregnant women?		
Monitoring	Tobacco Control	1	How effective is monitoring patients following a quit attempt? What questions or simple instruments could be used to assess the risk of relapse in primary care consultations?	91.2	4.21
Self-management	Other respiratory-related questions	1	What are the most effective strategies to improve self-management of chronic respiratory diseases in primary care?	88.2	4.24
	Other respiratory-related questions	2	What are the most effective strategies to improve shared decision and adherence when managing chronic lung diseases in primary care?	82.3	4.03

Questions rated on a Likert scale (0, not important -5, very important). * % rating 4 (important) or 5 (very important).


Qualitative analysis of cross-cutting themes from the initial questionnaire

A thematic analysis of the original 608 questions contributed by participants produced six cross-cutting themes relevant to primary care clinicians (Table 6) (Figure 4). Despite the availability of relevant evidence, the first main theme highlights a need for education and accessible guidelines tailored for the primary care context reflecting a lack of awareness by some primary care clinicians of current recommendations about how to manage respiratory conditions. The second main theme provides insight into gaps in evidence for diagnosing and treating respiratory conditions in primary care. Themes 3 and 4 focus on the need for locally relevant information, both in terms of local evidence to inform decisions but also locally relevant and practical solutions for primary care, and particularly in low resource settings. The final two areas of interest were the need to improve patient empowerment to manage their own conditions, and the growing importance of the wider multidisciplinary healthcare team.

Table 6: Cross-cutting themes from qualitative analysis of open-ended round 1 questions

Theme	Comments	Example of question received
Lack of awareness of published evidence regarding respiratory disease management	Many participants demonstrated lack of knowledge of the available evidence regarding screening, diagnosing, and managing respiratory conditions in primary care	*"What is the best way to diagnose Asthma?"*
The need for better evidence on prevention, diagnosis and treatment of respiratory conditions in primary care	Some questions suggested a genuine gap in evidence and guidelines relevant to specific topics	*"What is the role of spirometry in the diagnosis of asthma at different age groups?"*
Need for information applicable to local healthcare provision/resources	Participants indicated a need for evidence, guidelines and epidemiological studies that directly related to their local populations.	*"What are the best feasible and effective asthma management guidelines that are appropriate for resource-poor settings?"*
Simple and accessible tests for screening, diagnosing and monitoring	A large proportion of suggested research questions demonstrated a need to explore or develop tests that are simple and feasible to perform in primary care to diagnose or manage respiratory conditions	*"How could point-of-care testing be used effectively in screening for COPD?"*
Effective approaches to empower patients	There was a significant emphasis on the need to explore tools and methods that could be used in primary care to empower patients with respiratory conditions in managing their own conditions.	*"What are the best self-management strategies for patients with chronic cough?"*
Role of multidisciplinary healthcare teams	Participants expressed interest in exploring the role of various health care professionals in the diagnosis, monitoring and management of respiratory conditions in primary care.	*"What is the role of community pharmacists in improving the prognosis of COPD patients?"*

Figure 4 Summary of the 6 themes and sub-themes from the qualitative analysis of research questions
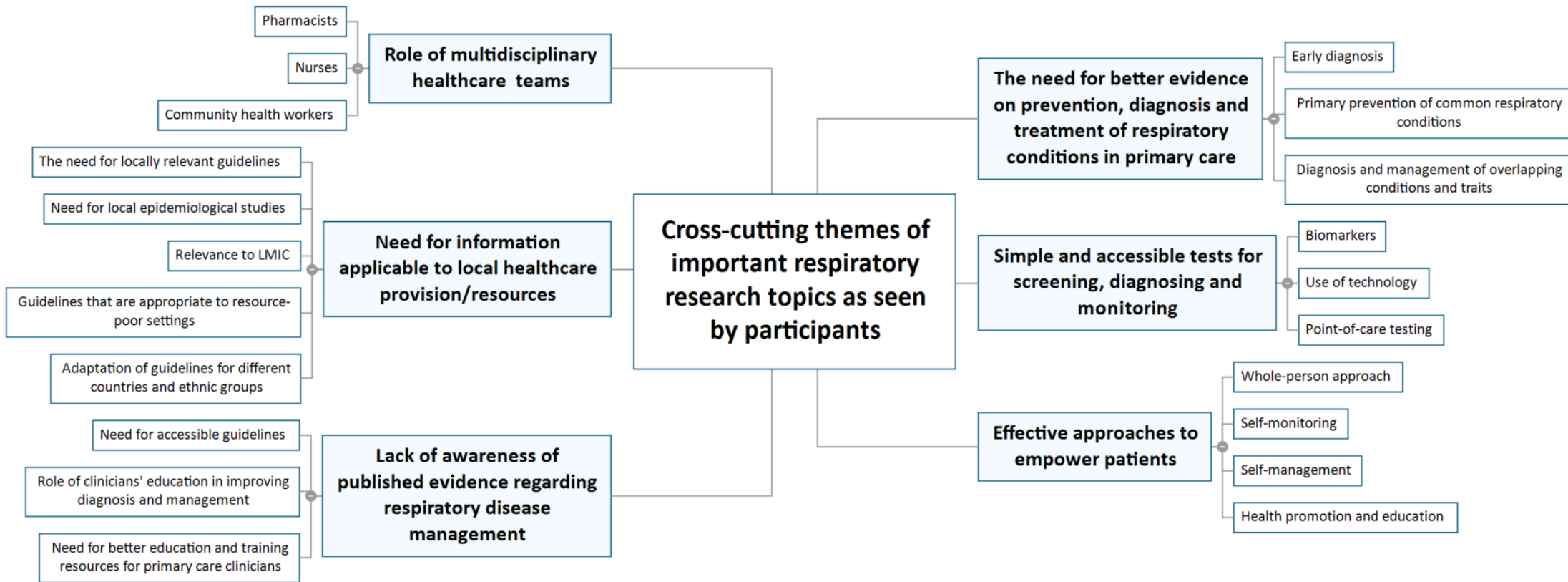
Discussion

We have used the e-Delphi method to rank the global priorities for respiratory research in primary care by drawing on the views and experiences of primary healthcare professionals from a wide range of settings and backgrounds. This supersedes the previous 2012 IPCRG priorities [13] and uniquely provides a primary care perspective on respiratory problems.

Whilst respiratory infections as a clustered group of conditions remained the most frequent and clinically important reason for consultation in primary care, COPD and asthma were considered the most frequent and clinically important individual conditions. This reflects both our previous findings [13] and the current global burden [15]. TB was highlighted more frequently than in the 2012 IPCRG priority exercise, reflecting greater involvement of clinicians from LMICs.

Whilst the most common research questions suggested by participants related to the diagnosis, management and self-management of COPD and asthma, there were a significant number of questions relating to tobacco control, reflecting a worldwide lack of progress in this area, especially in LMIC countries [10,16]. However, after the consensus building stages of the e-Delphi, the most highly ranked research priorities (Table 2) concerned the management of chronic cough, brief advice for smoking cessation, management of multimorbidity, adherence to inhalers, monitoring of asthma and earlier diagnosis of COPD. The findings reflect the wide range of problems encountered in primary care, from prevention through to management of complexity, and emphasises the need for influencing behaviour change amongst both patients and clinicians. Many questions also related to how best to implement known effective interventions.

Additional cross-cutting themes included questions involving the role of the multidisciplinary team, the need for locally relevant data and guidance, empowerment of patients to be involved in their own healthcare, and use of simple accessible tests for diagnosis and monitoring. A further theme identified the need for more effective clinical education for delivering best practice care.

Compared with our previous prioritisation exercise [13], there were a greater number of participants, fewer with an academic focus, and more from LMIC settings. In addition, open-ended questions were sought from a wider range of healthcare professionals without restriction on broad topic areas. This approach was reflected in our findings, with a more diverse range of research questions and the inclusion of additional topics e.g. TB, sleep apnoea and lung cancer. New topics emerged as priorities, such as the need for research about shared and multidisciplinary care, and the need for greater

understanding about the role of inhaled corticosteroids in management of COPD and asthma. However, some research topics remained important including the need for simple and accessible tools and tests, improvement of patient self-management skills (including inhaler adherence), and the most efficient and effective ways to promote smoking cessation in busy primary care settings. Research questions about comorbidities have progressed from simple description to the management of people with multimorbidity. Training and education of primary care professionals remains an important topic.

Since the last IPCRG research prioritisation exercise, there have also been a number of other relevant respiratory research prioritisation exercises [16–19]. although all are narrower in scope, focussing on specific conditions or geographical settings. The exercise specific to Portugal was based on the previous IPCRG research needs and set in primary care [17]. Similar to our recent findings, they emphasised the importance of methods of empowering patient self-management, to optimise adherence to asthma and COPD medication and inhaler technique, and to reduce inappropriate antibiotic prescribing [17]. The patient-led EARIP asthma programme also prioritised optimising self-management support and medication adherence/inhaler technique but also highlighted the need for simple diagnostic tools and relevant training for healthcare professionals[18]. Another project-focused prioritisation publication considered specifically the research needs in LMIC countries in South Asia, prioritising research questions relevant to COPD awareness and early identification [19]. The James Lind alliance projects are more specific, and the current COPD exacerbation project is yet to report[20].

Strengths and limitations of the study

A major strength of this study is the large sample size and diverse representation of the participants from high-, middle- and low-income countries. While most participants in this study were primary care physicians, there was a representation of other healthcare professionals, including secondary care doctors with relevant experience, nurses, pharmacists, academic clinicians, and other healthcare workers. Not surprisingly, two-thirds of participants reported an additional respiratory qualification or special interest in respiratory care, which may have affected generalisability, but only a few had a special interest in research.

One of the objectives of this study was to cover the breadth of respiratory conditions relevant to primary care. The bottom-up approach adopted with the open-ended questions helped to identify all important conditions observed in practice, including TB, lung cancer, interstitial lung diseases and sleep apnoea. A thorough evidence review stage was added to ensure that questions were refined and validated against current evidence by academic subject experts, thus avoiding duplication, questions already researched, or those not feasible for research. Furthermore, using qualitative methods to analyse 'participants' responses in depth enabled us to triangulate the e-Delphi prioritisation and introduced an additional perspective on respiratory research gaps. This helped to highlight important issues beyond specific respiratory conditions that could be helpful in improving the care of respiratory patients in primary care globally.

Unfortunately, due to limited time and resources, it was not feasible to involve members of the public and patient groups or other stakeholders within this study. Their views should now be sought to provide further insight and alternative perspectives.

The COVID-19 pandemic emerged at the end of round two (the first rating stage of the e-Delphi exercise). This is likely to have influenced participation (although we reached a 65% response rate between the rating rounds 2 and 3) and could explain changes in demographics between the stages. Furthermore, this might have influenced the views of participants in the final rating of priorities.

Finally, full generalisability cannot be ensured, as we were only able to accept participants who had access to the internet and could complete the survey in English (including through

self-arranged translators), which could be more of a problem in the primary care setting compared with secondary care.

Implications for research and practice

It is widely accepted that the only way to achieve the United Nations Sustainable Development Goals, including a reduction in tobacco use, reduction in premature mortality from chronic respiratory diseases and improving wellbeing, is by orienting health systems towards primary care and supporting universal access [21]. However, this access needs be good quality primary healthcare [22]. Therefore, this study has identified clear knowledge gaps for primary care which need to be addressed and tailored to the preferences of local primary care professionals.

Questions and themes elicited from this study can now be used to guide researchers and funders when planning research and allocating resources. Respiratory research has hitherto been relatively poorly funded, but it is clear from our work that more funding is urgently required and focussed on greatest need. Our prioritised list of research questions generated by practising healthcare professionals ensures relevance and improves the chance of effective implementation. Research inspired by these priorities will contribute to the improvement in the respiratory health of patients in primary care, both locally and globally.

The requirement for prioritised respiratory research needs relevant to primary care is vital now more than ever [23]. The COVID-19 pandemic has led to unprecedented pressure on healthcare systems globally and prompted a re-organisation of the healthcare landscape [24]. This has impacted the way primary healthcare is being delivered worldwide, with the use of remote and telephone consultations increased substantially [25,26]. COVID-19 has introduced a significant impact on the core competencies of primary care, which is affecting the continuity of care and changing the way primary healthcare will be provided in the near and distant future [27]. As COVID-19 has created new opportunities and innovations in medical research [28,29], it will be important to tailor prioritised primary care respiratory research needs to fit into this new era of medical research. It is crucial, therefore, to allow for any new and dynamic changes in primary care when shaping prioritised primary care respiratory research.

The findings of this study also suggest a need to invest in evidence implementation with the publication of locally relevant primary care guidance, supported by effective methods of

translation into practice. This exercise has also signposted to areas of training needs for primary care professionals.

Finally, addressing these key areas of research will have wider implications for primary care because many of the respiratory research needs are generalisable to other conditions.

Conclusions

This e-Delphi exercise provides a prioritised list of respiratory-related research questions which can be used by funders and researchers to commission and conduct research studies relevant to primary care clinicians globally. The findings also emphasise the need for primary care relevant guidance supported by effective approaches to achieve implementation. By driving this research agenda, we anticipate a shift in research funding and activity to improve the respiratory health and healthcare of patients managed in primary care worldwide.

Methods

Overview of the e-Delphi processes

An e-Delphi exercise with three rounds was undertaken to build consensus on the most important priorities for respiratory research in primary care [30,31]. It commenced in May 2019 and was completed in August 2020 (

Figure *1*) and included research questions suggested by practising primary healthcare professionals from across the world, with input from a panel of experts to verify and refine these questions, and

two further rounds to rate the priorities. In addition, the open comments from the first Delphi round were analysed qualitatively to identify cross-cutting themes.

Figure 1 Flow diagram of the research prioritisation process
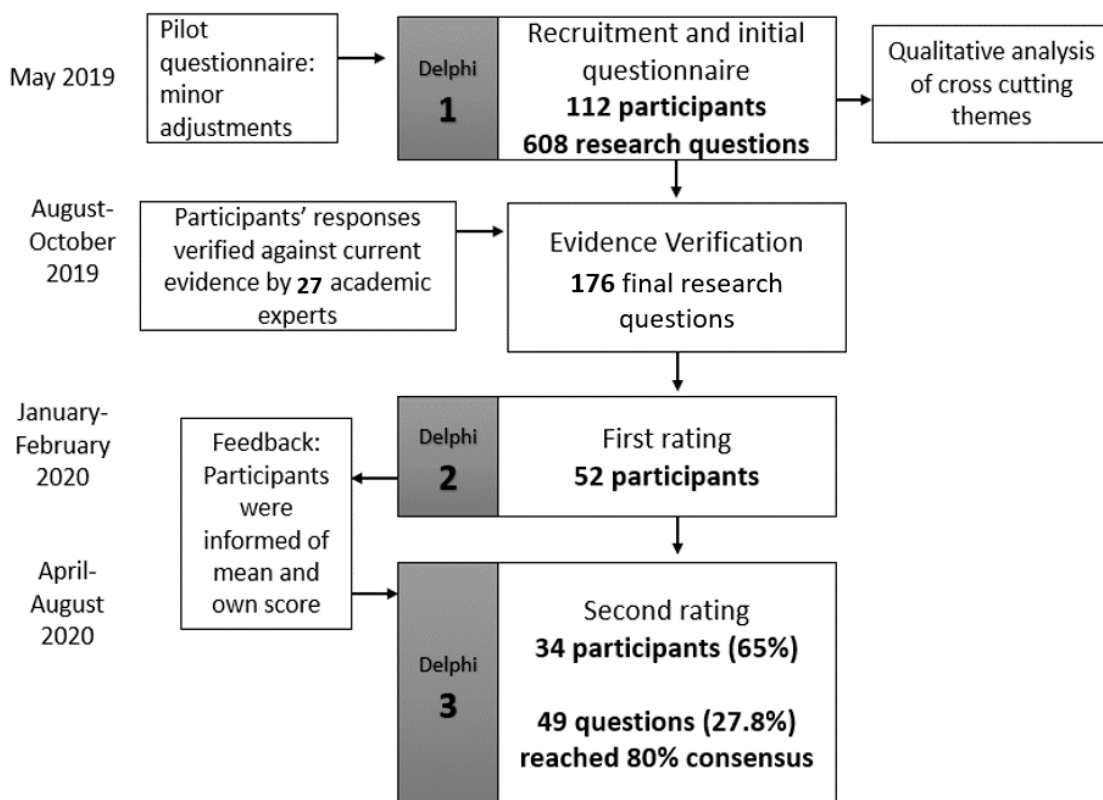
Recruitment

National coordinators from all IPCRG member countries were asked to purposively select and invite (by email) clinicians (doctors, nurses and any other healthcare professionals) working with respiratory patients in community settings in their countries to represent a broad range of views and experience. Specific inclusion criteria included the ability to complete online surveys in English and working in/with primary care settings to deliver care to patients with respiratory conditions.

e-Delphi 1: initial open-ended questionnaire

All data were collected through the *Jisc Online Survey* tool [32]. The initial questionnaire included three open questions seeking opinions on the most *common* respiratory conditions encountered in their clinical practice; the most *clinically important* conditions (in terms of burden and impact) and to suggest research questions relevant to their stated conditions for which they perceived evidence to be lacking (see box). Participants were asked to consider the following domains: diagnosis, management, monitoring, self-management, and prognosis. This questionnaire was piloted for clarity and ease of use by members of the IPCRG Research Committee and amended accordingly.

BOX   Round 1 open ended questionnaire to participants

1. What are the most common respiratory conditions encountered in your clinical practice? Please list 5 to 8 conditions.

2. Amongst those, which conditions are the most clinically important in your daily clinical practice (please consider the burden and impact of these conditions)?

3. Please list 10 questions relevant to the above conditions that you would like to see answered but currently cannot find enough evidence for them in the literature? Please carefully consider the following areas: diagnosis, management, monitoring, self-management and prognosis.

Evidence verification stage

To ensure that the questions suggested by participants reflected genuine evidence gaps and were answerable as research questions, 27 academic experts (Appendix 2) with topic-specific expertise related to primary care, associated with the IPCRG, reviewed and verified evidence against the

questions suggested by participants, refining and grouping similar questions, removing duplicates and adding questions where appropriate (including referring to unanswered questions from the previous prioritisation exercise[5,13]) to produce a final list of relevant and answerable questions.

e-Delphi round 2: first rating stage

All participants from the e-Delphi round 1 were invited to rate each question from the final list of research questions through two e-Delphi rating stages. During the first rating stage, participants rated each question on a 5-point Likert scale from 1 to 5 based on clinical importance (1= Not at all important to 5= Very important).

e-Delphi round 3: second rating stage

All participants from the e-Delphi round 2 were invited to re-rate the same list of questions from the previous round. At this stage, each participant was asked to consider the mean score, their individual score and any justification/comments provided by the participants on the questions in e-Delphi round 2, before re-rating the questions. Consensus for the e-Delphi was defined in round 3 for any question when 80% or more of participants rated it as 4 or 5 (important or very important).

Statistical analysis

Descriptive statistics were used to present the characteristics of participants and responses. Treemap charts were used to present the relative proportions of conditions mentioned in the questions. All questions were ranked by consensus score within three main topics: Asthma, COPD and Other, and within each topic, further ranked within 5 domains: prevention, diagnosis, management, self-management, monitoring and prognosis. The mean rating score was used in the final ranking to separate questions with the same consensus score. In the few cases where the consensus score and the mean rank score were identical, questions were listed in alphabetical order. All analyses were carried out using the analysis functions in the *Jisc Online Survey tool* and Microsoft Excel.

In-depth qualitative analysis of cross-cutting themes from the initial questionnaire

The qualitative analysis focussed on the raw open-ended research questions received in the initial questionnaire and aimed to highlight cross-cutting needs, issues and possible solutions relevant to the care of respiratory patients in primary care. Thematic analysis was carried out by AAA using NVIVO 12 software. Three other authors (RJ, PA, KL) independently reviewed the data, which was followed by a discussion between these four authors to reach an agreement on the final themes.

Ethics

This study was approved by the University of Birmingham Ethics Committee (ERN_19-0303B).

from GSK, grants and personal fees from Novartis, grants from MundiPharma, grants from TEVA, outside the submitted work, all paid to his institution; and Janwillem Kocks holds 72.5% of shares in the General Practitioners Research Institute.

Karin Lisspers has received personal fees for lectures and educational activities from AstraZeneca, Novartis, Boehringer Ingelheim and Chiesi and served on advisory boards arranged by AstraZeneca, GlaxoSmithKline, Novartis and Boehringer Ingelheim.

Luis Moral has received payment for participating in educational activities, consultancy, or support to attend clinical meetings from Hero España, Merck-Allergopharma, ALK-Abelló, Laboratorios Jofre-Roig, Laboratorios Leti, Faes Farma, Novartis, Inmunotek, GSK, and Alter.

David Price has board membership with Amgen, AstraZeneca, Boehringer Ingelheim, Chiesi, Circassia, Mylan, Mundipharma, Novartis, Regeneron Pharmaceuticals, Sanofi Genzyme, Teva Pharmaceuticals, Thermofisher; consultancy agreements with Amgen, AstraZeneca, Boehringer Ingelheim, Chiesi, GlaxoSmithKline, Mylan, Mundipharma, Novartis, Pfizer, Teva Pharmaceuticals, Theravance; grants and unrestricted funding for investigator-initiated studies (conducted through Observational and Pragmatic Research Institute Pte Ltd) from AstraZeneca, Boehringer Ingelheim, Chiesi, Circassia, Mylan, Mundipharma, Novartis, Pfizer, Regeneron Pharmaceuticals, Respiratory Effectiveness Group, Sanofi Genzyme, Teva Pharmaceuticals, Theravance, UK National Health Service; payment for lectures/speaking engagements from AstraZeneca, Boehringer Ingelheim, Chiesi, Cipla, GlaxoSmithKline, Kyorin, Mylan, Mundipharma, Novartis, Regeneron Pharmaceuticals, Sanofi Genzyme, Teva Pharmaceuticals; payment for the development of educational materials from Mundipharma, Novartis; payment for travel/accommodation/meeting expenses from AstraZeneca, Boehringer Ingelheim, Mundipharma, Mylan, Novartis, Thermofisher; funding for patient enrolment or completion of research from Novartis; stock/stock options from AKL Research and Development Ltd which produces phytopharmaceuticals; owns 74% of the social enterprise Optimum Patient Care Ltd (Australia and UK) and 74% of Observational and Pragmatic Research Institute Pte Ltd (Singapore); 5% shareholding in Timestamp which develops adherence monitoring technology; is peer reviewer for grant committees of the Efficacy and Mechanism Evaluation programme, and Health Technology Assessment; and was an expert witness for GlaxoSmithKline.

Hilary Pinnock has in the last 3 years was paid by Teva to write a piece on supported self-management for their website Organisations with which she is involved, or conferences/meetings at which she has spoken receive multi-company sponsorship

Dermot Ryan has in the last 3 years received payment for participating in educational activities, consultancy or support to attend clinical meetings from: AZ,BI, GSK, Chiesi, Novartis, Trudell, Meda, Regeneron and Medscape. He is a board-member of the Primary care and allied health section of the European Academy of Allergy and clinical Immunology and vice president of the Respiratory Effectiveness Group.

Björn Ställberg has received honoraria for educational activities and lectures from AstraZeneca, Boehringer Ingelheim, GlaxoSmithKline, Novartis, MEDA and TEVA and has served on advisory boards arranged by AstraZeneca, Novartis, GlaxoSmithKline, Boehringer Ingelheim and MEDA**.**

Stanley Szefler has served as a consultant for Boehringer-Ingelheim, Genentech, GlaxoSmithKline, AstraZeneca, Propeller Health, Sanofi, and Regeneron; and received a grant from Propeller Health. All payments were made to his University.

Alice Turner has grants for respiratory research from AstraZeneca, Chiesi and CSL Behring, and has additional consultancy or honoraria for educational work for GSK and Boehringer Ingelheim.

Steph Taylor holds grants related to COPD and asthma from the NIHR.

Ioanna Tsiligianni has in the last 3 years received payment for participating in educational activities, consultancy or received grants from: AstraZeneca, Boehringer Ingelheim, GlaxoSmithKline, Novartis and ELPEN. She is the Editor in Chief of the npjPCRM.

Osman Yusuf holds a grant related to respiratory health from the NIHR.

Amanda Barnard, Rachel Adam, Arwa Abdel-Aal, Dhiraj Agarwal, Izolde Bouloukaki, Niels Chavannes, Andy Dickens, Mercedes Escarrer, Frederik van Gemert, Shamil Haroon, Alex Kayongo, Bruce Kirenga, Daniel Kotz, Esther Metting, Cliodna McNulty, Chris Newby, Sophia Papadakis, Sally J Singh, David Weller, Siân Williams, and Aizhamal K. Tabyshova have no conflict of interest.

Contributorship

AAA designed, conducted and analysed the study with supervision from RJ. AB, FG, JK, KL, CN, IT, SW and OY advised on the protocol and materials. SW facilitated the recruitment and response of participants and advised on interpretation and write-up of the paper. PA, KL, RJ and RA advised on the interpretation of qualitative component. PA, AB, IB, JvB, NC, AD, FvG, ME, SH, AK, BK, KL, CN, CMN, EM, LM, SP, HP, DP, DR, SS, JCS, BS, SJS, ST, IT, AT, DW, and SW provided academic expertise in refining the research questions. AAA and RJ wrote the final draft with input from all authors.

References

1. Soriano, J. B. *et al.* Prevalence and attributable health burden of chronic respiratory diseases, 1990–2017: a systematic analysis for the Global Burden of Disease Study 2017. *Lancet Respir. Med.* (2020) doi:10.1016/S2213-2600(20)30105-3.

2. Abbafati, C. *et al.* Five insights from the Global Burden of Disease Study 2019. *The Lancet* (2020) doi:10.1016/S0140-6736(20)31404-5.

3. Abbafati, C. *et al.* Global burden of 369 diseases and injuries in 204 countries and territories, 1990–2019: a systematic analysis for the Global Burden of Disease Study 2019. *Lancet* (2020) doi:10.1016/S0140-6736(20)30925-9.

4. Gibson, G. J., Loddenkemper, R., Sibille, Y. & Lundbäck, B. The European Lung White Book. *Eur. Respir. Soc.* (2013) doi:10.1183/2312508X.10003015.

5. Pinnock, H. *et al.* The International Primary Care Respiratory Group (IPCRG) Research Needs Statement 2010. *Prim. Care Respir. J.* (2010) doi:10.4104/pcrj.2010.00021.

6. Rudan, I. *et al.* Setting priorities in global child health research investments: assessment of principles and practice. *Croat. Med. J.* (2007).

7. Yoshida, S. Approaches, tools and methods used for setting priorities in health research in the 21st century. *J. Glob. Health* (2016) doi:10.7189/jogh.06.010507.

8. Bousquet, J. *et al.* Prioritised research agenda for prevention and control of chronic respiratory diseases. *European Respiratory Journal* (2010) doi:10.1183/09031936.00012610.

9. Vardavas, C. I. *et al.* H2020 funding for respiratory research: Scaling up for the prevention and treatment of lung diseases. *European Respiratory Journal* (2019) doi:10.1183/13993003.01417-2019.

10.   Abbafati, C. *et al.* Global burden of 87 risk factors in 204 countries and territories, 1990–2019: a systematic analysis for the Global Burden of Disease Study 2019. *Lancet* (2020) doi:10.1016/S0140-6736(20)30752-2.

11.   Williams, S. *et al.* Respiratory research funding is inadequate, inequitable, and a missed opportunity. *The Lancet Respiratory Medicine* (2020) doi:10.1016/S2213-2600(20)30329-5.

12.   IPCRG. IPCRG- About Us. https://www.ipcrg.org/aboutus (2020).

13.   Pinnock, H. *et al.* Prioritising the respiratory research needs of primary care: The international primary care respiratory group (IPCRG) e-Delphi exercise. *Prim. Care Respir. J.* (2012) doi:10.4104/pcrj.2012.00006.

14.   World Bank Data Team. New country classifications by income level: 2018-2019. *The World Bank Group* (2018).

15.   Soriano, J. B. *et al.* Global, regional, and national deaths, prevalence, disability-adjusted life years, and years lived with disability for chronic obstructive pulmonary disease and asthma, 1990–2015: a systematic analysis for the Global Burden of Disease Study 2015. *Lancet Respir. Med.* (2017) doi:10.1016/S2213-2600(17)30293-X.

16.   Institute for Health Metrics and Evauation. Global Burden of Disease Compare. *University of Washington* (2019).

17.   Araújo, V., Teixeira, P. M., Yaphe, J. & Correia De Sousa, J. The respiratory research agenda in primary care in Portugal: A Delphi study. *BMC Fam. Pract.* (2016) doi:10.1186/s12875-016-0512-1.

18.   Masefield, S. *et al.* The future of asthma research and development: A roadmap from the European Asthma Research and Innovation Partnership (EARIP). *European Respiratory Journal* (2017) doi:10.1183/13993003.02295-2016.

19.   Rudan, I. *et al.* Setting research priorities for global respiratory medicine within the national institute for health research (NIHR) global health research unit in respiratory health (RESPIRE). *J. Glob. Health* (2018) doi:10.7189/jogh.08.020314.

20.   NIHR. James Lind Alliance. https://www.jla.nihr.ac.uk/ (2020).

21.   Hone, T., Macinko, J. & Millett, C. Revisiting Alma-Ata: what is the role of primary health care in achieving the Sustainable Development Goals? *The Lancet* (2018) doi:10.1016/S0140-6736(18)31829-4.

22.   Ghebreyesus, T. A. How could health care be anything other than high quality? *The Lancet Global Health* (2018) doi:10.1016/S2214-109X(18)30394-2.

23.   Williams, S. & Tsiligianni, I. COVID-19 poses novel challenges for global primary care. *npj Primary Care Respiratory Medicine* (2020) doi:10.1038/s41533-020-0187-x.

24.   Tanne, J. H. *et al.* Covid-19: How doctors and healthcare systems are tackling coronavirus worldwide. *BMJ* (2020) doi:10.1136/bmj.m1090.

25.   Thornton, J. Covid-19: How coronavirus will change the face of general practice forever. *The BMJ* (2020) doi:10.1136/bmj.m1279.

26.   Trethewey, S. P., Beck, K. J. & Symonds, R. F. Video consultations in UK primary care in response to the COVID-19 pandemic. *British Journal of General Practice* (2020) doi:10.3399/BJGP20X709505.

27. Verhoeven, V., Tsakitzidis, G., Philips, H. & Van Royen, P. Impact of the COVID-19 pandemic on the core functions of primary care: Will the cure be worse than the disease? A qualitative interview study in Flemish GPs. *BMJ Open* (2020) doi:10.1136/bmjopen-2020-039674.

28. Magan, A. A., Plastow, R. & Haddad, F. S. Impact of COVID-19 on research. *Bone Jt. Res.* (2020) doi:10.1302/2046-3758.98.BJR-2020-0344.

29. Harper, L. *et al.* The impact of COVID-19 on research. *J. Pediatr. Urol.* (2020) doi:10.1016/j.jpurol.2020.07.002.

30. Sumsion, T. The Delphi Technique: An Adaptive Research Tool. *Br. J. Occup. Ther.* (1998) doi:10.1177/030802269806100403.

31. Hsu, C. & Sandford, B. The Delphi Technique: Making Sense of Consensus. *Pract. Assessment, Res. Eval.* (2007) doi:10.1016/S0169-2070(99)00018-7.

32. Online Surveys. Jisc online survey tool. https://www.onlinesurveys.ac.uk/ (2020).

Appendices:

Appendix 1 Distribution of participants and countries based on income classification*

High-Income	Number of Participants	Upper Middle-Income	Number of Participants	Lower Middle-Income	Number of Participants	Low-Income	Number of Participants
Australia	3	Malaysia	5	India	2	Ethiopia	4
Belgium	2	Brazil	6	Bangladesh	6	Mozambique	1
Canada	3	China	8	Kyrgyzstan	11	Uganda	4
Chile	3	Romania	10	Angola	2		
France	1	Turkey	5	Cape Verde	3		
Germany	1						
Greece	5						
Ireland	1						
Macao	5						
Netherlands	4						
Norway	2						
Portugal	7						
Sweden	2						
United Kingdom	6						
Number of participants from High-income countries: n (%)	45 (40.2)	Number of participants from Upper middle-income countries: n (%)	34 (30.4)	Number of participants from Lower middle-income countries: n (%)	24 (21.4)	Number of participants from low-income countries: n (%)	9 (8)
Number of high-income countries: n (%)	14 (52)	Number of upper middle-income countries: n (%)	5 (18.5)	Number of lower middle-income countries: n (%)	5 (18.5)	Number of low-income countries: n (%)	3 (11)
				Number of participants from LMIC: n (%)	67 (59.8)		
				Number of LMIC countries: n (%)	13 (48)		

Source: World Bank Country Classifications by income level: 2018-2019 [14].

Appendix 2: List of experts who contributed to the Evidence Verification Stage by topic

Condition	Expert names	Country
Asthma diagnosis and screening	Jaime Correia de Sousa	Portugal
	Karin Lisspers	Sweden
Asthma management and prognosis	Amanda Barnard	Australia
	Björn Ställberg	Sweden
	Stanley J. Szefler	USA
Children with asthma	Mercedes Escarrer	Spain
	Louis Moral	Spain
Asthma self-management	Hilary Pinnock	UK
	Steph Taylor	UK
COPD diagnosis and screening	Rachel Jordan	UK
	Andy Dickens	UK
COPD management	Alice Turner	UK
	Shamil Haroon	UK
	Ioanna Tsiligianni	Greece
	Job FM van Boven	Netherlands
Multi-morbidity	Ioanna Tsiligianni	Greece
COPD self-management/pulmonary rehabilitation	Sally Singh	UK
	Niels Chavannes	Netherlands
COPD prognosis	Professor Peymané Adab	UK
	Rachel Jordan	UK
Infections/ pneumonia (in primary care)	Cliodna McNulty	UK
Allergic rhinitis/ other allergic conditions	Dermot Ryan	UK
	Mercedes Escarrer	Spain
	Louis Moral	Spain
Lung cancer (in primary care)	David Weller	UK
TB (in primary care)	Bruce Kirenga	Uganda
	Alex Kayongo	Uganda
Tobacco control	Daniel Kotz	Germany
	Sophia Papadakis	Greece
Air pollution	Niels Chavannes	Netherlands
	Alice Turner	UK
Health economics:	Job FM van Boven	Netherlands
Sleep Apnoea	Izolde Bouloukaki	Greece
Lung Fibrosis/ ILD/ occupational lung diseases	David Price	UK
Other respiratory conditions/ general	Björn Ställberg	Sweden
	Karin Lisspers	Sweden
	Jaimie Correia de Sousa	Portugal

Appendix 3 Full list of the 176 respiratory research questions finalised by experts in the Evidence Verification stage

Topic	Question	Consensus score	Mean Rank
Asthma diagnosis and screening	How could asthma be diagnosed earlier in primary care?	88.3	4.26
8 questions	What practical algorithms could distinguish between recurrent wheeze/ asthma and other acute respiratory diseases for young children?	85.3	4.24
	How could asthma be diagnosed in settings with limited availability of diagnostic tests?	85.3	4.38
	What is the role of spirometry in the diagnosis of asthma at different age groups?	79.4	4.15
	What is the best way to diagnose exercise-induced asthma in primary care?	61.8	3.65
	What tools could be used in community pharmacies to assess the probability of asthma?	41.2	3.32
	How could the implementation of pocket guidelines help the diagnosis of asthma?	44.1	3.53
	How could we achieve an international consensus on the definition of asthma?	76.5	4.06
Asthma management and prognosis	What is the role of intermittent therapy, such as SABA, ICS/SABA and ICS/LABA, in the management of asthma? (SABA=Short-acting inhaled beta-agonists, ICS=Inhaled Corticosteroids, LABA=Long-acting beta-agonists)	88.2	4.26
14 questions	When and how should asthmatic patients be stepped down from ICS?	85.3	4.09
	What is the most effective management for acute exacerbation of asthma in children?	91.1	4.29
	What is the best way to select drug therapy in children with asthma?	82.3	4.12
	What are the best ways to manage post-viral asthma?	52.9	3.62
	Are there any new non-inhaled asthma medications that are effective in the treatment of asthma?	41.2	3.53

	Are there any new cost-effective care models that are effective in managing asthma in a primary care setting?	70.6	3.91
	How could biomarkers be used in clinical practice for managing asthma?	47.1	3.56
	What methods could be used to enhance adherence to asthma controller therapy?	94.1	4.5
	What are the best ways to monitor asthma in primary care?	100	4.44
	What steps could be taken to prevent exacerbations and progression of asthma?	97.1	4.38
	How could guidelines be adapted to manage asthma in Lower- Middle- Income Countries (LMIC)?	88.2	4.35
	What are the best clinical tools to monitor asthmatic and allergic children in primary care in LMIC?	82.3	4.18
	What is the importance of different clinical phenotypes in the prognosis of asthma with early onset in childhood?	67.7	4.06
Asthma self-management	What educational interventions are effective and cost-effective for children /families with asthma?	88.2	4.21
18 questions	What is the best way to support patients to improve their adherence to asthma medications?	94.1	4.44
	What are the most effective strategies for ensuring sustained good inhaler techniques among asthma patients?	94.2	4.38
	What is the best way to engage people with asthma in self-management?	94.1	4.44
	What self-monitoring techniques are appropriate for people with mild intermittent asthma?	73.6	3.97
	What is the best way to support accurate recognition among asthma patients of worsening of signs and symptoms (e.g. questionnaires and novel biomarkers)?	70.6	3.88
	What strategies/adaptations can help empower people with limited health literacy to effectively self-manage their asthma?	85.3	4.09

	Would universal, international, validated, shared, self-management plans help in improving the management of patients with asthma?	52.9	3.62
	Which patients are most likely to need support to self-manage?	52.9	3.62
	What are 'patients' barriers to effectively self-managing their asthma in low resource settings?	79.5	4.12
	What are 'physicians' barriers to supporting patients to effectively self-manage their asthma in low resource settings?	88.3	4.15
	What are the best ways for health care professionals to engage patients in supported self-management and empower them to take control of their asthma?	94.1	4.24
	What is the role of pharmacists in supporting asthma self-management?	50	3.62
	What is the role of community health workers in supporting asthma self-management?	61.7	3.76
	What is the potential for digital options in improving recognition of asthma deterioration?	70.6	3.94
	Are digital options effective in improving adherence to medications and self-management among asthma patients compared to traditional modes of delivery?	70.6	3.94
	What is the impact of over-the-counter availability on the use of asthma medications?	53	3.68
	What are the best ways to discourage over-reliance on beta-agonists in patients with asthma?	67.7	3.97
COPD diagnosis and screening	Which are the best methods to identify Asthma-COPD Overlap Syndrome (ACOS) in primary care?	73.5	3.94
12 questions	What are the most effective approaches for optimising uptake of invitations for COPD screening?	70.6	3.82

	Is the early identification of COPD beneficial to patients in the long-term?	85.3	4.32
	What are the most cost-effective and efficient approaches for identifying COPD, especially in low-resource settings?	88.3	4.26
	How should we best diagnose COPD in settings where good quality spirometry is not available or not affordable?	91.2	4.32
	Is it feasible to use microspirometry to assess lung function amongst those with poor coordination or low cognitive ability?	55.8	3.56
	What are the clinical characteristics of patients diagnosed by microspirometry alone, compared with those diagnosed using quality diagnostic spirometry?	52.9	3.68
	Is lung function measured by spirometry stable over time and is there a need for multiple measurements before diagnosis?	50	3.59
	What is the burden and epidemiology of COPD in settings with no current information?	50	3.59
	What are the reference values for countries with no current relevant information?	58.9	3.82
	How can we best educate healthcare professionals to improve early recognition and diagnosis of COPD?	94.1	4.44
	How effective are public awareness/education campaigns to improve awareness and earlier diagnosis of COPD?	82.3	4.26
COPD management	How to best manage patients with Asthma-COPD Overlap Syndrome (ACOS)?	70.6	3.94
43 questions	How existing guidelines for asthma and COPD should be modified for the diagnosis and management of occupational Asthma-COPD Overlap Syndrome (ACOS)?	58.8	3.71
	How should asthma-COPD overlap be monitored?	70.5	3.82
	What are the most effective and cost-effective therapies for people with mild or case-found/screen-detected COPD?	76.4	4

	What are the optimal care pathways for the management of people with screen-detected COPD?	67.6	3.82
	Can we effectively manage different COPD types with appropriate treatments?	88.3	4.15
	In end-stage COPD patients, what are the benefits/ risks of de-prescribing inhaled therapy?	52.9	3.59
	What is the cost-benefit analysis of LABA/ICS in developing countries?	58.9	3.65
	How can we best apply personalised approaches to tailor the most appropriate treatments to patients with COPD (triple therapy versus dual versus mono-therapy vs ICS/LABA, co-morbidities, etc.?)	64.7	3.82
	When should ICS be stopped when they are already in use in COPD?	79.4	4.15
	How do we individualise the decision of choosing an inhaler based on patients characteristics taking into consideration advantages, disadvantages and inhalers specific characteristics?	70.6	3.94
	How could we improve 'patients' adherence to inhalers? Which are the best methods to teach about inhaler use and how can we incorporate them in daily clinical practice?	94.1	4.5
	What is the optimal strategy for identifying and treating COPD exacerbations in primary care?	91.2	4.35
	How should we best manage asymptomatic patients with emphysema on Computed tomography (CT)?	38.3	3.35
	What are the factors leading to ICS overuse in the treatment of COPD in primary care? How could this be minimised?	64.7	3.74
	Does shared care between primary care physicians and specialists improve the management of COPD patients and reduce exacerbations?	88.3	4.21
	Are educational interventions for community health agents about care for	70.6	3.97

	patients and families of COPD patients cost-effective?		
	How effective are multidisciplinary approaches involving primary health care centres, community pharmacies and community centres in improving the clinical outcome for patients with COPD?	64.7	3.85
	How frequently, and using which approach, should we monitor COPD patients in the community? Should this vary by severity?	67.7	3.85
	What is the role of community pharmacists in improving the prognosis of COPD patients?	38.2	3.35
	What are effective treatments for biomass-related COPD and how should biomass-related COPD be managed?	53	3.65
	How should COPD be managed in low- and middle-income countries, including rural community settings?	88.2	4.18
	Are micro-spirometers an adequate substitute for spirometry for monitoring the progression of COPD in primary care?	67.6	3.85
	Can portable particulate monitors be used to prevent exacerbations and prevent deterioration of health for patients with COPD?	52.9	3.59
	How effective and cost-effective is a point of care C-reactive protein (CRP) testing (or other biomarkers) for guiding therapy for preventing and treating exacerbations of COPD in primary care?	55.9	3.59
	How effective are biomarkers in assessing adherence to COPD treatments?	47.1	3.59
	How do primary care clinicians use spirometry findings to inform the ongoing management of COPD?	85.3	4.03
	How do primary care clinicians use measures of disease progression in COPD to inform the care they provide? What is the impact of using measures of disease progression on quality of care and clinical outcomes?	88.3	4.15

	What should be the referral criteria for secondary care for patients with COPD?	73.5	3.91
	What is the prognostic value of eosinophils and other novel biomarkers in predicting exacerbations?	58.8	3.71
	What is the role of eosinophils in the treatment effect of ICS?	44.2	3.5
	How effective and how safe is the use of eosinophil level to step-down ICS treatment?	58.9	3.68
	Can Fractional Exhaled nitric oxide (FeNo) be used in primary care to identify ICS-responsive patients?	47.1	3.47
	How can we adapt care to patients with low health literacy?	73.5	3.91
	What is the impact of financial restrictions on COPD management and adherence to medications?	64.7	3.68
	How useful is the ABCD assessment tool for classifying and managing patients? Are there better ways to classify COPD patients?	73.6	3.79
	How should we best manage COPD in patients with cardiovascular diseases, arrhythmias and uncontrolled hypertension?	97	4.35
	How can we manage COPD patients with comorbidities in primary care using a personalised approach to reduce adverse reactions and limit disease progression?	91.2	4.38
	How to tailor the current COPD management guidelines to suit those with comorbidities?	94.1	4.38
	How best to improve awareness, early identification and screening of mental health disorders in patients with COPD, and does this improve outcomes?	73.5	3.91
	What is the clinical- and cost-effectiveness of management plans that are implemented based on prognostic score categories, rather than routine care?	52.9	3.62
	Could telephone counselling for patients with COPD help in managing their COPD?	52.9	3.74

	Are digital applications cost-effective for the management of COPD in patients at high risk for exacerbations?	61.8	3.79
COPD self-management/pulmonary rehabilitation	What are the best engaging and supporting strategies for health care professionals to help improve self-management of COPD?	88.2	4.24
9 questions	How cost-effective are e-Health interventions, mobile and online applications (including wearables) in self-monitoring, symptoms control and adherence to medications in patients with COPD?	91.2	4.29
	How effective are individual self-management compared to group self-management sessions?	53	3.62
	What are the most effective ways to deliver self-management plans to patients in settings with low numbers of doctors and health workers?	79.4	3.88
	What are the patient-related or other barriers that prevent patients from completing pulmonary rehabilitation programmes? What interventions would help to reduce drop-out rates?	64.7	3.82
	What are physician-related barriers to providing self-management support to patients?	79.4	4.03
	What is the effectiveness of alternative forms of exercise (such as Tai Chi, dance etc.) among people with COPD, and what are the most active components of such interventions?	35.3	3.24
	What is the effect of adapted pulmonary rehabilitation on clinical outcomes in low resource settings where pharmacotherapy is less affordable/accessible?	79.4	4.03
	What is the feasibility and effectiveness of offering a choice of activities within a pulmonary rehabilitation programme, compared to traditional only activities, on the uptake and clinical outcomes?	52.9	3.71

COPD prognosis	What is the prognosis of case-found / screened COPD patients, compared to i) those who remain undetected till later in the disease process, and ii) COPD patients diagnosed through usual care?	64.7	3.82
8 questions	What are the characteristics and prognosis of patients with normal spirometry but chronic respiratory symptoms and exacerbation-like events indicative of COPD?	58.9	3.85
	What are the characteristics and prognosis of people with airflow obstruction who have never smoked, compared to ever smokers with or without airflow obstruction?	53	3.71
	Can the performance of COPD risk prediction scores be improved by adding other factors such as clinical measures or assessment of exposure to risk factors?	41.2	3.44
	To what extent are risk prediction scores stable if alternative measures are substituted within them (e.g. different measures of exercise capacity rather than Six-Minute Walk Test)?	38.2	3.44
	What is the validity of existing prognostic scores in different populations, e.g. those with COPD in LMIC, or those with other conditions?	52.9	3.59
	What thresholds or cut-offs should be used for existing prognostic scores, to allow patients to be categorised into clinically meaningful groups?	44.2	3.5
	Does COPD caused by biomass fuel have the same phenotype and prognosis as COPD caused by smoking?	44.1	3.53
Infections in primary care	What are the best tools to help in triaging patients with respiratory infections to guide the use of antibiotics in community settings?	85.3	4.24
5 questions	What is the optimal self-care treatment strategy for acute and chronic sinusitis?	61.8	3.74
	How effective are self-management options for patients with cough and Upper	44.2	3.5

	Respiratory Tract Infections (URTI) in primary care?		
	What is the current understanding of the general public about the causes, illness course and complication rate, and how they can self-care in upper airways infections?	47.1	3.44
	What factors are related to a failure of the flu vaccine response in patients with chronic lung disease?	50	3.71
Allergic rhinitis/ other allergic conditions	What tools could help the primary care clinician differentiate between allergic and non-allergic rhinitis, rhinosinusitis, common cold and other clinically similar conditions?	88.2	4.24
6 questions	What are the best-stratified treatment options for rhinitis (both allergic and non-allergic) that suits variable severities and chronicity?	79.4	3.97
	How best to monitor allergic rhinitis? Self-monitoring (applications) or clinical monitoring? Symptom-based or biomarker-based?	70.6	3.79
	What is the best way to accurately diagnose rhinitis (allergic/non-allergic) in pre-school children (<5 y)?	79.4	3.97
	How best to diagnose and manage rhinitis in low-income countries?	73.5	3.85
	In children and adults with upper viral respiratory tract infection and allergic rhinitis, is the use of oral antihistamines and/or topical nasal steroids beneficial in reducing symptom severity and duration?	61.7	3.79
Lung cancer (in primary care)	What is the best diagnostic algorithm for lung cancer for helping primary care doctors identify those at increased risk?	85.3	4.15
4 questions	What is the current, and potential future role, of biomarkers in early lung cancer detection?	58.8	3.76
	How can primary care best engage with new treatments for lung cancer (such as immunotherapies), and take an active role in community-based management?	35.3	3.41

	How can we ensure that early diagnosis and screening strategies for lung cancer do not increase health inequalities?	73.5	3.85
TB (in primary care)	What are the most useful specific host or pathogen-derived molecular and immunological markers of early tuberculosis (TB) infection?	47.1	3.59
12 questions	What are the genetic correlates of TB susceptibility?	17.7	3
	Is there a better test to detect early non-compliance or resistant cases compared to sputum acid-fast bacilli staining?	50	3.62
	What are the most useful specific host or pathogen-derived molecular and immunological markers for extra-pulmonary tuberculosis?	32.3	3.38
	What is the most effective chemotherapy for treating Latent tuberculosis infection (LTBI)?	44.1	3.62
	What are the best methods to increase detection of tuberculosis cases in primary health care or at the community level?	91.2	4.21
	What are the best ways to improve compliance with treatments in patients with TB?	79.4	4.03
	What are the best ways to prevent exacerbation of post-TB bronchiectasis?	52.9	3.76
	What are the most effective drugs with the fewest side effects for the treatment of Multidrug-resistant TB (TBMDR)?	64.7	3.76
	Is Levofloxacin effective in treating adult close contacts of TB patients who are not immunocompromised?	35.3	3.41
	What are the barriers and challenges of a TB control program for immigrants?	64.7	3.88
	What are the clinical features that could help in predicting prognosis in patients with TB?	58.8	3.76
Tobacco control	How can brief advice be used more effectively to increase motivation to quit, and what elements are most efficient for a busy primary care practitioner?	97.1	4.38

11 questions	What are the benefits of using questionnaires (e.g. 'willingness to 'quit', 'addiction to 'nicotine') in routine clinical practice? Which ones are the most accurate and useful?	70.5	3.88
	How can primary care clinicians in different countries be made more aware of strategies to prevent smoking in young people and pregnant women?	88.3	4.15
	What are the most effective models (including primary healthcare or specialist smoking cessation teams) for providing smoking cessation support services in different cultural and/or socioeconomic settings?	91.2	4.26
	How effective is monitoring patients following a quit attempt? What questions or simple instruments could be used to assess the risk of relapse in primary care consultations?	91.2	4.21
	What are the barriers and facilitators for patients' adherence to smoking cessations treatments?	79.4	4.03
	What are primary care 'patients' knowledge and beliefs regarding the risk of tobacco use and the importance of smoking cessation?	58.8	3.76
	What are the best practices for working with political leaders and business to increase support for smoking cessation?	67.7	3.91
	What are the best practices for treating tobacco dependence in patients with depression?	61.8	3.74
	What are the best practices for increasing primary healthcare 'professionals' knowledge regarding nicotine addiction and evidence-based tobacco treatment?	64.7	3.79
	What combination of interventions (e.g. brief advice, cost-free medications, adjunct counselling) are most effective for increasing patient quit rates in primary care practice?	91.2	4.32

Sleep Apnoea	What is the best-validated screening tool for sleep-related breathing disorders, especially Obstructive Sleep Apnoea in the primary care setting?	85.3	4.15
6 questions	What is the optimal management of patients with sleep-related breathing disorders in the primary care setting?	76.5	3.79
	What are the best strategies to improve adherence to continuous positive airway pressure (CPAP) in the management of patients with sleep apnoea in primary care?	64.7	3.71
	What are the best ways to monitor sleep-related breathing disorders in primary care?	67.7	3.71
	What is the prognosis of patients with sleep-related breathing disorders who are using CPAP and have adequate follow up by a family physician?	52.9	3.56
	What are the most effective strategies to educate family physicians about sleep-related breathing disorders?	58.9	3.65
Other respiratory-related questions	What is the best way to manage chronic/persistent cough in primary care?	100	4.71
20 questions	What are the most effective non-pharmacological methods of managing breathlessness?	73.5	3.94
	Are there simple treatable traits or phenotypic algorithms which are more useful in classifying and managing patients with chronic respiratory disease in primary care?	64.7	3.68
	What are the best ways to help patients with chronic respiratory disease to increase their exercise capacity?	79.4	3.91
	What are the best strategies to involve other healthcare professionals in the management of chronic respiratory diseases in primary care?	67.7	3.88
	What are the barriers and facilitators to early diagnosis, management and treatment of respiratory conditions in primary care?	76.5	3.97

	How can community pharmacists be involved in the care of patients with chronic respiratory diseases?	38.3	3.29
	How useful are Quality of Life questionnaires in the assessment of respiratory diseases?	58.9	3.65
	Which tools should be used to identify patients' health beliefs and understanding of chronic respiratory diseases in primary care?	73.5	3.85
	What are the most effective strategies to improve shared decision and adherence when managing chronic lung diseases in primary care?	82.3	4.03
	What are the most effective strategies to improve self-management of chronic respiratory diseases in primary care?	88.2	4.24
	How can information and communication technologies help in monitoring chronic respiratory diseases?	79.4	4.03
	How could telemedicine strategies help to improve adherence to treatment in patients with chronic respiratory disease in LMIC?	70.6	3.94
	How could e-Health be used in the treatment and monitoring of chronic lung disease?	76.5	3.91
	Are digital options effective for providing access to healthcare or managing health service workload compared to traditional methods?	55.9	3.56
	Which interventions reduce the consequences of outdoor and indoor air pollution on chronic lung disease?	53	3.62
	What is the best way to identify those meriting investigations for Interstitial Lung Disease?	41.2	3.47
	Does earlier diagnosis and intervention improve outcomes for Idiopathic pulmonary fibrosis?	50	3.53
	What are the most effective treatment options to manage bronchiectasis in primary care?	55.9	3.74

	How could we identify patients with bronchiectasis who will progress more rapidly and have a higher burden of the disease?	70.5	3.79