

## SUPPLEMENT

The International Primary Care Respiratory Group (IPCRG)  
Research Needs Statement 2010

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Received 7th March 2010; accepted 11th March 2010

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**Abstract**

**Aim:** Respiratory diseases are a public health issue throughout the world, with high prevalence and morbidity. This Research Needs Statement from the International Primary Care Respiratory Group (IPCRG) aims to highlight unanswered questions on the management of respiratory diseases that are of importance to practising primary care clinicians.

**Methods:** An informal but inclusive consultation process was instigated in 2009. Draft statements in asthma, rhinitis, COPD, tobacco dependence, and respiratory infections were circulated widely to IPCRG members, other recognised experts, and representatives from a range of economic and healthcare backgrounds. An iterative process was used to generate, prioritise and refine research questions in each section.

**Results:** Two overarching themes emerged. Firstly, there is a real need for research to be undertaken within primary care, which recruits patients representative of primary care populations, evaluates interventions realistically delivered within primary care, and draws conclusions that will be meaningful to professionals working within primary care. Secondly, international and national guidelines exist, but there is little evidence on the best strategies for implementing recommendations. Disease-specific research questions focus on effective and cost-effective ways to prevent disease, confirm the diagnosis, assess control, manage treatment, and empower self-management. Practical questions about how to deliver this comprehensive agenda in diverse primary care settings are highlighted.

**Conclusions:** We hope that this Research Needs Statement will be used by clinicians and patients campaigning for answers to relevant questions, by researchers seeking funding to provide answers to these questions, and by funding bodies to enable them to prioritise research agendas.

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H Pinnock *et al.* *Prim Care Res J* 2010; **19**(Suppl 1): S1-S20.

doi:10.4104/pcrj.2010.00021

**Keywords:** asthma, rhinitis, COPD, smoking, tobacco dependence, respiratory, infections, IPCRG, research, strategies, primary care, guideline implementation, delivery of care

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## 1. Introduction

### 1.1. The importance of primary care respiratory research

The core agenda of primary care research is to provide the evidence base for clinical and organisational issues relating to the treatment of common diseases, management of chronic diseases, and identification of risk groups.<sup>1</sup> Respiratory disease exemplifies all these agendas. In many countries, respiratory symptoms are the commonest reason for presentation to primary care, encompassing both acute infections (pneumonia and the familiar if ill-defined 'chest infections') and long-term conditions such as asthma, rhinitis, and chronic obstructive pulmonary disease (COPD). Primary care clinicians worldwide have an important role in respiratory health promotion which includes vaccination programmes and smoking cessation.

Effective evidence-based medicine needs to be underpinned by methodologically robust research that answers questions that are relevant, recruits from representative populations, and acknowledges the diversity of contexts in which clinicians practise. From a primary care perspective, there are important gaps in the evidence base for common respiratory conditions which we highlight in this document. By excluding the elderly and those with co-morbidity, disease-focused research may be of direct relevance to only a minority of the patients seen in a typical primary care practice.<sup>2</sup> Furthermore, global diversity (geographic, climatic, economic) and differences in healthcare organisation mean that evidence from one healthcare system may not be transferable to another.

### 1.2. Methodology

This Research Needs Statement from the International Primary Care Respiratory Group (IPCRG) aims to highlight unanswered questions of importance to practising primary care clinicians. The extensive list of contributors is testament to the broad range of countries represented.

The decision to update previous IPCRG Research Needs Statements<sup>3,4</sup> was discussed by the IPCRG research committee in June 2009. As a result, an informal but inclusive consultation process was instigated. Summaries of early discussions were compiled by lead authors for asthma, allergic rhinitis, COPD, tobacco dependence, and respiratory infections. These were circulated to IPCRG members with a known interest in these areas and then more widely to recognised experts and representatives from a range of economic and healthcare backgrounds. An iterative process was used to generate, prioritise and refine research questions in each section. Finally, penultimate drafts were sent to the Senate members – who represent the 17 member and 21 associate member countries of the IPCRG – for further comment.

### 1.3. The role of the IPCRG Research Needs Statement

Thus this paper presents the research needs identified by an international group of respiratory-interested primary care professionals. We hope that the statement will be used by clinicians and patients campaigning for answers to relevant questions, by researchers seeking funding for work that will answer these questions, and by funding bodies to enable them to prioritise research agendas. It sits within the context of the draft World Health Organisation (WHO) research agenda for non-communicable diseases, which not only prioritises chronic respiratory diseases and

tobacco control, but also specifically emphasises the core role of primary care in the management of long-term conditions.<sup>5</sup>

It also reflects, in the specific context of respiratory disease, the broad themes of generic primary care research priorities, including organisation of accessible, community-based, integrated care, clinical problem solving (encompassing diagnosis, treatment and management), and a comprehensive, holistic, patient-centred cost-effective approach.<sup>1</sup> A core message of all primary care research agendas (clearly echoed in this document) is the need for research undertaken within primary care, recruiting patients representative of primary care populations, evaluating interventions realistically delivered within primary care, and drawing conclusions that will be meaningful to professionals working within primary care.

### 1.4. Generic research questions

There are national and/or international guidelines available to inform management of all the conditions discussed in this document, but a common theme voiced by each of the section contributors was the concern that recommendations were poorly implemented and that research was needed to identify barriers and understand strategies to facilitate cost-effective implementation within different healthcare systems.<sup>6</sup>

#### Research questions:

- What sources of information do primary care clinicians use when assessing and treating patients with asthma, allergic rhinitis, COPD, smoking dependence, respiratory infections?
- What does the general practitioner (GP) really want from a guideline?
- What are the barriers to, and facilitators of, implementation of guidelines?
- What are the most effective ways of educating and updating primary care clinicians in the management of respiratory disease?
- Are guidelines applicable all over the world in the primary care setting?

## 2. Asthma

Its high prevalence makes asthma a worldwide public health issue.<sup>7</sup> Globally, more than 300 million people of all ages suffer from asthma, of whom more than 250,000 die each year.<sup>8</sup> This is not only of concern in (typically higher-income) countries where prevalence is greatest,<sup>7</sup> but is also a challenge in low- and middle-income countries, where most asthma-related deaths occur.<sup>9</sup>

Improving the prevention and management of asthma is thus a high priority for primary healthcare in all countries. The Brussels Declaration advocates a ten point plan of action to improve evidence-based asthma management, emphasising the importance of including evidence from real life studies in treatment guidelines<sup>10,11</sup> – an issue relevant to management of asthma throughout the world.

To promote high quality care, international and national asthma guidelines are updated regularly<sup>12-14</sup> using evidence-based

methodology,<sup>15,16</sup> though the paucity of evidence from patients managed in primary care is acknowledged.<sup>14</sup> By contrast, the IPCRG asthma guidelines aimed to highlight the special conditions in, and the evidence base from, primary care.<sup>17</sup>

This statement identifies research needs that should be given high priority in order to improve asthma care from the perspective of practising primary care clinicians.

### 2.1. Prevention

Various factors in early life have been associated with the recent increasing prevalence of asthma, although effective primary prevention strategies remain to be established.<sup>18</sup> Although environments vary between and within different countries, exposure to smoke (including tobacco and indoor bio-mass fuel and coal burning) is a universal factor which impacts on the severity of asthma symptoms and the response to treatment,<sup>19,21</sup> making reduction of exposure to smoke an important issue for primary care (see section 5). Occupational asthma is common, potentially preventable, but poorly recognised.<sup>22</sup>

#### Research questions:

- What are the important environmental risk factors (including indoor bio-mass fuel smoke, cigarette smoking and environmental pollution, aeroallergens, dietary and lifestyle factors) in different countries and what preventative measures can reduce effectively the prevalence and severity of asthma?
- Are primary care physicians aware of the allergens and respiratory irritants in their area? Are they aware of the preventive measures against such asthma triggers?
- What strategies will improve detection and prevention of occupational asthma in primary care?

### 2.2. Diagnosis

The diagnosis of asthma can be difficult, especially in patients with mild or intermittent disease seen in primary care, resulting in both under-diagnosis and over-diagnosis.<sup>23-26</sup> Misdiagnosis might be due to inadequate professional training and/or interest, or limited healthcare resources.<sup>27,28</sup>

Under-diagnosis may be due to patients not consulting or not having access to clinical advice or diagnostic resources, or physicians' failure to consider the diagnosis when presented with non-specific symptoms (e.g. cough). Small children may be misdiagnosed with pneumonia or recurrent bronchitis.<sup>29</sup> In countries where asthma is taboo, patients may seek another diagnosis rather than be labelled as "asthmatic".<sup>30</sup> The characteristic variability of asthma means that there is a low sensitivity of objective measurements in patients during asymptomatic periods.<sup>31,32</sup>

The common clinical scenario of 'wheeze infants' poses a particular challenge for primary care. The diagnosis is based on the history, signs and symptoms,<sup>33,34</sup> and whilst the presence of atopy may strengthen the probability of asthma, diagnostic spirometry is not practical under the age of 5 years.<sup>35</sup>

The IPCRG guidelines suggest a range of symptom-based tools

and investigations including peak flow monitoring, spirometry, reversibility testing and challenge tests,<sup>36</sup> and a recent international statement summarises the technical details.<sup>37</sup> Information on the sensitivity, specificity, positive and negative predictive value of such tools in primary care settings is needed to inform best practice. Such data will need to be context-appropriate, not only reflecting diverse primary care populations but also recognising the different availability of diagnostic tools in different countries.

#### Research questions:

- How can asthma be diagnosed earlier in primary care?
- What is the role of symptom-based tools for diagnosing asthma in primary care?
- What are the reliability, validity and feasibility of different diagnostic tools such as spirometry, peak-flow measurement, challenge tests, exhaled nitric oxide and allergy testing in the diagnosis of asthma in primary care?
- What are the cut-off values for abnormal spirometry (lower limit of normal), reversibility tests and diurnal variation of peak-flow measurement across a broad range of age groups and ethnicity?
- How can rural and remote areas or developing countries diagnose and manage asthma with limited or no availability of diagnostic tests?
- What is the reliability of a medication trial for diagnosing asthma in different ages, how should such tests be performed, using which treatments and for how long?

#### Children:

- To what extent are small children with recurrent wheeze misdiagnosed in primary care and with what consequences for morbidity?
- What practical algorithms could distinguish between recurrent wheeze/asthma and other acute respiratory diseases including pneumonia for young children presenting to primary care?
- Is it possible to predict persisting asthma in children with wheeze in primary care?

### 2.3. Management, assessment of severity, asthma control and treatment

Studies have consistently demonstrated widespread poor asthma control, implying that the management of asthma could be improved.<sup>38-41</sup> Guidelines highlight the importance of developing a partnership between the doctor and the patient<sup>12-14,36</sup> so that regular professional review and monitoring of people with asthma is combined with appropriate treatment recommendations and self-management education to enable patients to achieve treatment goals.<sup>42</sup>

The dual concepts of asthma severity and asthma control have been widely discussed.<sup>43-45</sup> Recent guidelines have changed their emphasis from classification of severity to the goal of achieving asthma control,<sup>12</sup> prioritising the objective assessment of control.

Structured morbidity scores can be used to quantify patients' reports of their asthma symptoms over a period of time.<sup>46-54</sup> Although such questionnaires have been validated for research purposes, few have been validated for assessing individual asthma control in a clinical context. Suboptimal control is associated with concomitant rhinitis, other co-morbidities, smoking, poor inhaler technique and poor concordance with treatment,<sup>40</sup> but there is further need for studies enrolling patient populations seen in primary care to inform practice.<sup>40</sup>

Management should reflect the heterogeneity of asthma. Children and adults may have persistent or episodic asthma, triggered by viral infections, allergens or exercise.<sup>12,33</sup> Asthma in pregnancy requires proactive management to optimise outcomes for mother and baby.<sup>14</sup> Asthma and rhinitis often co-exist in the same patient.<sup>55</sup> Other important co-morbidities which may invite alternative approaches – often overlooked by disease-specific guidelines but of significance to primary care clinicians – include COPD, cardiovascular disease, gastro-oesophageal reflux, obesity, psychological morbidities and dysfunctional breathing.

Pharmacotherapy for asthma includes regular 'controllers' (or 'preventers') which improve control and reduce the risk of exacerbations, and as-required 'reliever' medications which reverse airflow limitation and reduce symptoms. Guidelines, which are based on an extensive pharmacological evidence base, emphasise early regular treatment with a 'controller', though allergen avoidance may also be a consideration. Randomised trials suggest that inhaled corticosteroids (ICS) are the most efficacious 'controller', with no clinically relevant side effects at low to moderate doses.<sup>12-14,36</sup> Efficacy trials of alternative 'controllers' (e.g. anti-leukotrienes, LTRAs) in moderate asthma conclude that ICS produce better outcomes, though whether this is true for all patients with mild or intermittent asthma is debated.<sup>56-57</sup>

Such trials do not address the practical issues that impact on effectiveness in real-life primary care practice such as inadequate inhalation technique,<sup>58</sup> perceived side effects of steroids,<sup>59</sup> patient preference for regular treatment, and the impact of adherence.<sup>60</sup>

#### Research questions:

##### *Monitoring and assessing asthma control:*

- What simple tools enable assessment of asthma control, and is their use acceptable and feasible in primary care?
- Is an assessment of severity needed in addition to an assessment of asthma control in primary care?
- What is the role of lung function testing in regular monitoring of asthma patients in primary care?
- What is the role of nitric oxide, mannitol challenge testing (or other innovative techniques) in the monitoring of asthma in primary care?
- What is the validity and usefulness of questionnaires for assessing quality of life (or other outcomes) when used for individual patients in routine primary care clinical practice.
- Why do patients accept suboptimal asthma control, and

how can we address the reasons?

- How do co-morbidities impact on asthma control and management?

##### *Adherence:*

- What is the impact of patients' comprehension of the disease, use of different treatment strategies, treatment cost (in high income and low income countries and between social groups) and concern about side effects of inhaled steroids on adherence to prescribed treatment?
- How may these issues of adherence be addressed (especially in sub-groups such as the adolescent patient with asthma)?

##### *Inhalation technique and usage:*

- How can good and poor inhaler technique be identified and what is the best strategy for ensuring good inhaler technique?
- What is the most cost effective approach to inhaler devices?
- What strategies are needed to counteract the taboos associated with inhaler usage in some countries?

##### *Non-pharmacological management and management of co-morbidities:*

- What is the impact of non-pharmacological strategies – e.g. breathing modification, allergen avoidance techniques – in the management of asthma symptoms?
- Does the detection and treatment of co-morbidities (anxiety and depression, obesity) improve outcomes for people with asthma?

##### *Treatment:*

- How do ICS and LTRAs compare with regards to effectiveness and side-effects in patients with mild and moderate asthma in real-life primary care practice?
- What is the most effective add-on therapy option to ICS in different sub-groups of asthma?
- How and when should regular medication be stepped down or stopped?
- Can specific asthma phenotypes be identified in primary care and what are the implications for treatment and management in primary care?

##### *Children:*

- What is the impact of different treatments for wheezing in young children in primary care?

## 2.4. Management of acute asthma

Guidelines offer advice on the assessment, therapeutic management and organisation of care for acute asthma, though audits consistently show that compliance with recommendations is poor.<sup>61-64</sup> Although the management of acute asthma in different countries is dependent on resources and the organisation of care, a key skill for primary care in any healthcare setting is objective assessment of severity.<sup>12-14,36</sup> Most exacerbations seen in primary care are moderate,<sup>61,63</sup> but prompt recognition of life-threatening attacks, appropriate management, and close supervision of severe asthma may prevent deaths.

**Research questions:**

- How can services be configured to ensure that front-line clinical staff assess and manage acute asthma attacks according to evidence-based practice?
- What is a practical approach to the assessment of the severity of acute asthma in primary care in settings with limited diagnostic resources?
- What is the preferred management (including appropriate inhalation device) of moderate exacerbations in primary care, including in clinical situations where treatment options are limited?
- What are the indications for referral to an emergency unit?
- How should acute severe asthma be managed in settings where emergency departments and hospitals are not accessible?
- What is the importance of co-morbidity (especially psychological morbidity) and socio-economic factors in identifying those at risk of very severe attacks?

**2.5. Self-management**

Asthma is a variable condition and patients need advice to help them understand their illness and their own particular triggers, recognise changes in their control, and to act appropriately. There is an extensive evidence base demonstrating that the provision of self-management education supported by written action plans as part of regular asthma reviews improves outcomes.<sup>65-67</sup> Although this approach – known as ‘guided self-management’ – is endorsed by guidelines,<sup>12-14,36</sup> there is evidence of widespread underuse in clinical care.<sup>68,69</sup> Despite evidence from primary care studies,<sup>70-73</sup> there is a perception that such plans may not be appropriate for people with mild disease.<sup>69</sup> There is a paucity of evidence to inform implementation of self-management education,<sup>14</sup> though some evidence that a link with routine reviews is important.<sup>73-77</sup> Specifically, there is a need for more knowledge about the contents of the plans in relation to the asthma severity and individual requirements.

**Research questions:**

- How can guided self-management be implemented in real life primary care practice?
- Why are professionals reluctant to provide asthma action plans to their patients, and how may this be overcome?
- What are effective approaches to developing a partnership with the patient?
- What are the important components of self-management education, and how can they best be conveyed to the patient/family in routine practice?
- How should action plans accommodate the different asthma treatment schedules?
- How, and to what degree, are asthma action plans implemented in various communities, especially in low and middle income countries, and how do they impact on asthma morbidity and mortality?

- How might asthma action plans be tailored for different ethnic groups, taking into account their cultural beliefs and practices?

**2.6. Organisation of asthma care**

The organisation of asthma care differs between countries depending on economic factors, health care systems and traditions. In some countries, nurses with a special interest in asthma work independently or in co-operation with GPs managing asthma patients.<sup>78</sup> Modern information technology offers new opportunities for remote consulting,<sup>79-81</sup> and tele-monitoring of asthma,<sup>82</sup> which may facilitate convenient care or overcome accessibility problems in remote areas.<sup>83</sup>

**Research questions:**

- Are any models of health care better than others in terms of clinical and cost-effectiveness for the management of asthma?
- What is the influence of cultural and ethnic beliefs towards asthma and how do these beliefs affect outcome in management of asthma in these communities?
- What is the role of mobile technology, web-resources and remote consultations in the management of patients in primary care?

**3. Allergic rhinitis**

Allergic rhinitis affects over 600 million people of all ages, and globally is increasing in prevalence.<sup>55</sup> It causes a greater impairment of quality of life than asthma,<sup>84</sup> a disease which it may precede or accompany in up to 80% of cases.<sup>85</sup> Together, allergic rhinitis and asthma represent an important socioeconomic burden.<sup>86,87</sup>

Recent reports have highlighted the unmet needs of people with allergic rhinitis,<sup>88</sup> and argued for increasing adherence to guideline recommendations. However, guidelines for the management of allergic rhinitis need to reflect the primary care context if they are to be adopted in primary care.<sup>6</sup> We propose a series of research topics selected to meet current and future needs in primary care.

**3.1. Epidemiology**

Widespread under-diagnosis means that there is still insufficient data about the epidemiology of allergic rhinitis.<sup>89-92</sup>

**Research questions:**

- What is the hidden burden of undiagnosed allergic rhinitis in different countries?

**3.2. Diagnosis**

Globally, allergic rhinitis is under-diagnosed, mis-diagnosed, and therefore, under- and mis-treated and managed.<sup>93</sup>

Under-diagnosis may occur as patients' assumption that they are suffering from the common cold is reinforced by a friend, or the pharmacist from whom they purchase over-the-counter (OTC) medication.<sup>93</sup> Reliance on self-diagnosis is common, with a delay of many years before seeking professional advice.<sup>94</sup>

When the symptoms become severe, or home remedies fail,<sup>95</sup>

and the patient consults their primary care clinician,<sup>96-98</sup> failure to take an adequate medical history, perform a clinical examination, and initiate appropriate diagnostic tests means the diagnosis may be still be overlooked.<sup>99</sup> Heavy demand for GPs' services may lead to trivialisation of rhinitis.<sup>99</sup> Although a pattern of symptoms that make a diagnosis likely has been proposed,<sup>55</sup> there is no short, validated, symptom-based instrument to assist diagnosis in primary care.

In regions where local 'pollen calendars' are available, a good history is usually sufficient to identify the allergen with a reasonable degree of reliability, though intermittent symptoms from variable levels of house dust mite allergen can cause confusion. Unfortunately, such seasonal information is not universally available.

Skin prick testing is the "gold standard" of allergy testing, and is recommended to support the clinical assessment of those with persistent or moderately severe disease, uncontrolled with conventional medication,<sup>55</sup> reserving the expensive allergen-specific IgE test for situations when (or where) skin testing is not possible.

#### Research questions:

- What are the common local indoor and outdoor allergens, and what is the local 'pollen / allergen calendar' for allergenic pollens, fungi (moulds), dusts and other aero-allergens?
- What tools (e.g. validated, symptom-based questionnaires for rhinitis or screening for atopy<sup>100</sup>) could help the primary care clinician differentiate between allergic and non allergic rhinitis, rhino-sinusitis, the common cold and other clinically similar conditions?
- What are the essential components of physical examination in primary care?
- What is the value of, and how feasible are, skin-prick tests and other tests in the diagnosis and management of allergic rhinitis in primary care in diverse healthcare settings? Does performance of these tests affect clinical outcomes?
- What is the availability of OTC remedies in different countries, and the diagnostic and management skills of those who sell or advise on their administration?

### 3.3. Rhinitis and asthma

Rhinitis and asthma co-exist in a large proportion of patients, with rhinitis often preceding asthma.<sup>85,101</sup> In atopic children, the presence of allergic rhinitis is a risk factor for asthma, with a time interval of about a year before the development of asthma symptoms,<sup>102</sup> offering a potential window of opportunity when early detection and appropriate management of rhinitis may prevent the progression to asthma.

Co-morbid rhinitis is associated with increased asthma symptoms, increased exacerbations and hospital admissions,<sup>103-105</sup> with some evidence that concomitant treatment can improve control.<sup>106,107</sup>

#### Research questions:

- Are clinicians aware of the asthma-rhinitis link, and to what extent do they seek information about allergic

rhinitis when seeing asthmatic patients?

- Does early and aggressive treatment of atopic children with allergic rhinitis (e.g. with topical nasal steroids, and/or immunotherapy) prevent the progression to asthma?
- What (combinations of) management strategies for treating rhinitis improve asthma control, and/or improve quality of life?
- Does nitric oxide measurement have a role in the diagnosis and management of patients with allergic rhinitis in primary care?

### 3.4. Management

The main goal of treatment is to achieve control of the disease,<sup>55</sup> but tools capable of assessing the control of both upper and lower airways diseases are lacking.<sup>108</sup> The ARIA guideline proposes a classification based on both severity of symptoms and whether symptoms are intermittent and persistent.<sup>55</sup>

Guidelines provide evidence-based recommendations to inform the management of allergic rhinitis under the headings 'allergen avoidance', 'pharmacological treatment', and 'specific immunotherapy'.<sup>55,109-111</sup> Allergen avoidance can be effective for reducing the symptoms of allergic rhinitis,<sup>112-115</sup> though single interventions may be insufficient to control symptoms.<sup>116</sup> Non pharmacological measures with some efficacy include saline douches,<sup>55,117-120</sup> rhinophototherapy,<sup>121</sup> nasal filters,<sup>122</sup> pollen-blocker creams,<sup>123</sup> or cellulose powder.<sup>124</sup> Facemasks and eyeglasses may offer some protection,<sup>125</sup> and probiotics may influence symptoms of allergic diseases.<sup>126,127</sup>

Guidelines describe a stepped approach to pharmacological treatment with (second generation) antihistamines and topical nasal corticosteroids as first line treatment, which may be combined with leukotriene-receptor antagonists, cromolyn, short-term topical or systemic decongestants, intranasal antihistamines, and intranasal anticholinergics for additional symptom relief.<sup>55,128,129</sup> Practical questions about how to identify patients who would most benefit from treatment,<sup>96</sup> and the management of people with co-morbidity, remain to be answered.

Despite advice that they have a limited role in the management of allergic rhinitis, systemic steroids are frequently used in the management of allergic rhinitis in many parts of the world. Depot corticosteroids are popular for practical reasons, and a recent systematic review suggested a potentially useful role in patients suffering from intermittent but severe rhinitis, though the lack of safety data raises concerns about adverse effects.<sup>130,131</sup>

Although a consensus is emerging that immunotherapy should be considered for patients with moderate to severe allergic rhinitis who have not responded to optimal medical therapy and allergen avoidance,<sup>132</sup> a greater understanding is required of its effectiveness and safety in different primary health care settings.

#### Research questions:

*Monitoring and assessing control:*

- What questions for use in primary care practice will determine rhinitis control, and identify those at risk of

worsening symptoms and/or onset of co-morbid asthma?

- Is the ARIA classification<sup>55</sup> useful in guiding prescribing in primary care?

*Non-pharmacological management and management of co-morbidities:*

- What role does allergen identification and avoidance have in the management of rhinitis? Does this vary according to the geographic, climatic and demographic context?
- To what extent do patients with allergic rhinitis use alternative medicines? (e.g. homeopathy, herbal treatment etc)
- What is the acceptability to patients and impact on the morbidity of rhinitis / asthma of physical measures (e.g. nasal douches, nasal lubricants, closing windows at night)

*Inhalation technique and usage:*

- What is the best technique for using nasal sprays? What do doctors, pharmacists, and patients know of correct nasal inhalation technique?

*Treatment:*

- What is the cost-effectiveness of different treatment regimens in healthcare systems with diverse socio-economic and financial status?
- How should patients with other respiratory conditions (e.g. asthma, COPD, sleep apnoea), or other co-morbidities (e.g. hypertension, diabetes mellitus, heart disease, liver disease) or physiological states (e.g. pregnancy, extremes of age) be managed?
- What evidence is there for the safety and efficacy of systemic steroids in the treatment of rhinitis? Are there differences between existing systemic therapies (e.g. oral, intra-muscular?)
- For which patients is immunotherapy (sublingual or injection) appropriate, safe and cost effective? Should such treatment always involve a referral for a specialist care?

### 3.5. Self-management, and over-the-counter treatment

Patients often rely for many years on 'over-the-counter' medication with limited effectiveness and may experience adverse effects (e.g. drowsiness with first generation antihistamines,<sup>133-135</sup> rhinitis medicamentosa with prolonged use of topical decongestants) to which the GP should be alert. Incorrect use of medication (e.g. topical nasal steroid sprays), inadequate dosages, and poor compliance, all contribute to treatment failure. Pharmacists and primary care clinicians have an important role in providing information and treatment.<sup>136-138</sup>

#### Research questions:

- What non pharmacological remedies do patients use to treat their rhinitis?
- What strategies can be used to reduce the risk of side-effects from self-treatment?
- How can compliance with treatments be improved?

- Are patients' information needs being met, with accurate, easily accessible, and culturally sensitive resources?<sup>137,138</sup>

### 3.6. Organisation of care

Despite specific recommendations from the World Allergy Organisation about inclusion of an allergy module within the undergraduate medical curriculum,<sup>139</sup> studies demonstrate significant shortfalls in undergraduate allergy training,<sup>140</sup> considerable scope for improvement in clinicians' awareness and management of allergic rhinitis,<sup>99,141</sup> and pressure to shorten allergy training programs,<sup>141</sup> thus threatening standards of care for allergic diseases.

Allergy service provision needs to encompass both primary care and allergy specialists with good collaboration between sectors,<sup>112</sup> though division of responsibility will vary in different healthcare systems.

#### Research questions:

- What is the current state of knowledge about the diagnosis and management of rhinitis in primary care?
- What are the educational needs of primary care clinicians, and how may these be met? Can an educational intervention improve awareness and clinical skills of GPs and improve clinical outcomes in allergic rhinitis?
- What is the optimal balance between generalist care and specialist allergy care in different healthcare systems?

## 4. COPD

COPD is a major public health problem. The prevalence of COPD varies between countries depending on smoking habits, indoor air pollution and the spectrum of age within the population; but globally, COPD was responsible for 3.7million deaths in 2005,<sup>5</sup> and will rank as the 4th leading cause of death by 2030.<sup>142</sup>

International and national guidelines focus attention on preventing COPD, case finding and/or screening to promote early diagnosis, proactive treatment of symptoms, and attention to supportive and end-of-life care needs.<sup>143-148</sup> Primary care physicians play a key role in all these aspects of COPD management.

Seven years ago, the IPCRG developed a statement of COPD research needs from the perspective of primary care.<sup>4</sup> Since then some of the questions identified have been addressed while others have not. The purpose of this section is to update the previous statement and develop a series of research questions pertinent to primary care practice in the new decade.

### 4.1. Prevention

Primary care physicians have a key role in primary prevention, by identifying patients at high risk for COPD and promoting smoking cessation for both individual patients and for communities and populations (see also section 5).<sup>149</sup> Worldwide, the use of biomass combustion is a major contributor to respiratory illness especially in women.<sup>150</sup> It is estimated that 40-45% of the COPD burden in women in developing countries can be attributed to indoor smoke from solid fuels.<sup>151</sup> The prevention of the unventilated use of biomass fuel in developing countries is complex and requires



political and societal measures outside the remit of the primary care team.<sup>152</sup> However, locally-tailored measures to decrease indoor smoke exposure are the subject of an IPCRG / Global Alliance against Chronic Respiratory Diseases (GARD) demonstration project in Vietnam involving nurses and health workers.<sup>153</sup>

Guidelines recommend immunisation against influenza and pneumococcal infection to prevent exacerbations, and many countries offer proactive immunisation programmes.

#### Research questions:

- In the context of COPD, what are the key questions that assess smoking history accurately, provide a sensitive and specific assessment of tobacco addiction, and motivation for smoking cessation?
- What is the impact (e.g. on smoking cessation rates, identification of COPD) of routinely undertaking spirometry in smoking cessation consultations?
- What is the impact of locally-tailored community-level measures to decrease exposure to indoor smoke and reduce harm?
- What organisational approaches (e.g. primary care registers, public health campaigns) are most effective in facilitating good uptake of seasonal flu vaccination?

#### 4.2. Diagnosis of COPD in primary care

COPD is both under-diagnosed and over-diagnosed in primary care.<sup>27,154</sup> Guidelines base the classification of severity on post-bronchodilator spirometry, and recommend a threshold forced expiratory volume in one second/forced vital capacity (FEV<sub>1</sub>/FVC) ratio less than 0.7 to confirm a diagnosis of COPD.<sup>143-148</sup> This fixed ratio cut-off has the advantage of simplicity but does not allow for the natural reduction in the ratio due to lung ageing, thus risking under-diagnosis in younger patients and over-diagnosis in the elderly.<sup>35</sup> The use of the lower limit of normal (LLN) may improve diagnostic precision but accurate reference ranges are needed in the older patients.<sup>155</sup>

Primary care spirometry has been criticised as being underused,<sup>156,157</sup> and in many countries is not available outside specialist centres. Concerns about the quality of spirometry<sup>158</sup> have recently been addressed by a UK document recommending standards for spirometry undertaken in primary care practice.<sup>35</sup>

Validated questionnaires have been developed to support the diagnosis of COPD.<sup>159-161</sup> Practical experience with these tools is limited and it is not yet clear how such questionnaires can best be used in clinical practice – e.g. to identify patients for spirometry, or to replace spirometry in low income countries where spirometry is not available.

Early diagnosis and subsequent reduction in exposure to smoke could prevent progress to severe disease leading to calls for screening smokers and/or active case finding.<sup>159,162</sup> International guidelines advise spirometry in all people with respiratory symptoms and/or smoking exposure.<sup>143,163,164</sup> Such initiatives are likely to be the responsibility of primary care services, but the clinical and cost effectiveness of different strategies (screening or case-finding, questionnaire or spirometry testing, based in primary care or linked

with occupational health, health insurance screening) have yet to be established. It is likely that different approaches will be appropriate in different healthcare economies.<sup>162,165</sup>

#### Research questions:

##### Primary care diagnosis:

- What is the best way to identify and diagnose COPD in primary care? Does this incorporate history, age, symptoms and spirometry?
- Can the use of a simple validated questionnaire<sup>159-161</sup> improve the accurate identification of COPD in different countries (including those without access to spirometry)?
- When a primary care approach to the diagnosis of COPD is applied, what is the diagnostic yield compared to currently accepted diagnostic criteria?<sup>143-148</sup>

##### Spirometry and assessment:

- What are the essential parameters (e.g. FEV<sub>1</sub>/FVC and/or FEV<sub>1</sub>/FEV<sub>6</sub>, inspiratory measurements) of spirometry in primary care?
- What is an appropriate standard of spirometry training for primary care clinicians?
- Is it best to use a fixed ratio or the LLN for the diagnostic FEV<sub>1</sub>/FVC threshold? What are the characteristics of patients in the community who are diagnosed with COPD according to the fixed ratio formula and not according to the LLN?
- Should a CXR always be done as part of an initial assessment, regardless of the severity of COPD at diagnosis?

##### Screening or case finding:

- What is the extent of under- (and over-) diagnosis of COPD in primary care communities in different countries, and to what extent are patients who smoke, (or exposed to burning bio-mass fuels), proactively screened for COPD?
- Which approach to early COPD diagnosis in primary care is underpinned by the strongest clinical and health economic evidence base (questionnaires and/or spirometry, screening or case finding)?

#### 4.3. Management

Relief of symptoms, reduction in exacerbation frequency and improved quality of life are the major goals in the management of people with COPD.<sup>143-148</sup> Recent work suggests that the qualitative difference between 'bad days' and 'exacerbations' may be quantifiable, thus supporting the concept of 'COPD control'<sup>166</sup> – though the significance of this in clinical practice has yet to be established. The BODE index,<sup>167</sup> while increasingly important in staging COPD in secondary care practice, involves measurements not routinely available in primary care. The ADO index may be more practical,<sup>168</sup> and the DOSE index has been developed in primary care and intended for use in routine clinical practice.<sup>169</sup>

A number of validated questionnaires measuring dyspnoea,<sup>170,171</sup> COPD control,<sup>172,173</sup> and impact on quality of life<sup>174-176</sup> have been

developed, and although some have been recommended for clinical use none have been validated in this context. Practical considerations (such as length, and mode of administration) will affect feasibility, and floor and ceiling effects will be important in primary care where the population ranges from very mild sub-clinical disease to severely disabling end-stage COPD.

International and national guidelines summarise and make therapeutic recommendations based on the extensive pharmacological and pulmonary rehabilitation evidence base.<sup>143,145-148</sup> and the IPCRG guidelines for COPD management provide a primary care perspective.<sup>144</sup> Pragmatic primary care trials with minimum exclusion criteria are needed to assess effectiveness in the diverse populations and healthcare systems in which primary care operates globally.

A range of conditions (e.g. musculoskeletal disorders, heart disease, depression, anxiety, diabetes and osteoporosis/fractures) commonly co-exist with COPD.<sup>177-180</sup> These co-morbid diseases not only impair and restrict the activity of COPD patients, but also affect the therapeutic options.<sup>181,182</sup> There is limited evidence to inform primary care clinicians responsible for managing patients with co-morbidity.

#### Research questions:

##### Monitoring COPD:

- Which measurements (spirometry, breathlessness scores,<sup>171</sup> exercise tolerance,<sup>183</sup> symptom/control scores,<sup>172,173</sup> COPD-specific<sup>174,176</sup> or generic Quality of Life questionnaires<sup>175</sup>) are feasible, and provide useful information for routine monitoring and assessing effectiveness of treatment in primary care worldwide?
- Are composite measures (such as the DOSE index<sup>169</sup> or ADO-index<sup>168</sup>) feasible in primary care within a range of health care settings, and valid when compared with established indices (e.g. BODE<sup>167</sup>)?

##### Therapeutic management:

- What is the role of low dose theophylline, especially in low income countries where it may be one of the few treatments available?
- How should people with GOLD mild or moderate COPD<sup>143</sup> be managed in primary care with regard to lifestyle advice (smoking cessation, dietary advice) therapeutic treatment (anti-inflammatory and/or bronchodilators) and physical activity (pulmonary rehabilitation) in order to improve outcomes in different healthcare settings?

##### Co-morbidities:

- Which are the most prevalent co-morbidities in people with COPD in different countries, and what examinations and tests should be undertaken routinely in order to detect co-morbidities?
- To what extent do primary care clinicians screen people with COPD for depression using appropriate validated screening tools?
- What impact does screening for, and taking action (pharmacological and/or physical activity) to prevent, osteoporosis/fractures have on morbidity?

- What are the optimum treatment regimes (including the impact of polypharmacy) for people with COPD and co-morbid conditions such as cardiovascular disease, diabetes or dementia.

#### 4.4. Management of acute exacerbations

Despite evidence-based recommendations on the management of acute exacerbations of COPD,<sup>143-148</sup> there are many unresolved questions for primary care clinicians about definition, prediction, early detection and accurate diagnosis of the cause of exacerbations with the limited diagnostic tools available in the community.<sup>184,185</sup> Although avoidance of costly admissions is a key policy objective in many healthcare systems, and community-based support may enable safe provision of 'hospital-at-home' care,<sup>186</sup> a core skill for primary care clinicians in any healthcare setting is recognition of when to refer for specialist care.

#### Research questions:

- What impact does immediate access to investigations (e.g. CXR, oxygen saturation, CRP) have on the primary care management of people with acute exacerbations of COPD, and the decision to refer?
- Should choice, dose and duration of treatment (oral corticosteroids, antibiotics) be different for different severity of COPD and severity of exacerbations? Is there a role for inhaled steroids in exacerbations of COPD?<sup>187</sup>

#### 4.5. Supported self-management

The importance of empowering self-management is emphasised by guidelines,<sup>143-148</sup> with some evidence that multidisciplinary programmes can be effective in patients with more severe disease.<sup>188</sup> The role and format of self-management education for patients with mild or moderate disease in primary care is less clear.<sup>189</sup> More broadly, it is recognised that people with long-term conditions such as COPD need flexible access to professional support to enable them (and their carers) to manage their own condition.<sup>190</sup> A 'whole systems' approach to supporting self-care<sup>191</sup> focuses attention on the patient's understanding of COPD,<sup>192</sup> the clinician's attitude to patient autonomy, and the accessibility provided by the healthcare organisation.

#### Research questions:

- How can clinical services be organised within different healthcare systems to support self-care?
- What is the optimal format of self-management education (including the information content, individualisation of the plan, written or electronic delivery, professional or lay educators) in order to ensure effective communication with patients (often from deprived communities), facilitation of adherence to treatment, and a positive impact on health status?
- How should the self-management education programme be adapted for different severities of disease and/or different healthcare systems?

#### 4.6. Supportive and palliative care

COPD is implicated in about 5% of deaths.<sup>193</sup> Despite disabling symptoms (especially breathlessness), complex co-morbidity and social isolation,<sup>194-198</sup> the needs of people with very severe COPD are rarely addressed adequately.<sup>194,199</sup> Although 'markers' of a poor prognosis in COPD are well recognised,<sup>200</sup> the outcome for any individual is unpredictable,<sup>201</sup> leading to 'prognostic paralysis' on the part of clinicians.<sup>202,203</sup> Primary care clinicians have an important role in orchestrating proactive supportive care.<sup>204</sup>

##### Research questions:

- What is the best palliative treatment for severe dyspnoea?
- How can primary care clinicians overcome the 'paralysis' that results from the uncertain prognosis in order to deliver proactive supportive care?
- How can health and social care services be developed to meet the needs of people with severe COPD within different cultural and healthcare systems?

#### 4.7. Organisation of COPD care

The organisation of COPD care will differ between healthcare systems. In some countries, evidence that integrated care improves outcomes<sup>205</sup> has led to respiratory specialist nurses taking an increasingly important role especially in supporting self-care for those with on-going complex needs,<sup>206</sup> and providing Hospital-at-Home services during acute exacerbations.<sup>186</sup> Early work suggests that tele-monitoring may have a role in preventing admissions in those with more severe disease.<sup>207</sup>

Pulmonary rehabilitation is acknowledged as an important intervention for people with symptomatic COPD, and recent studies suggest that community programmes can be delivered effectively.<sup>208</sup>

##### Research questions:

- What professional skills are required by clinical teams providing integrated care for people with COPD within diverse healthcare systems?
- What are the core requirements for a community-based pulmonary rehabilitation service?
- What is the role of tele-monitoring? Does it reduce admissions and/or improve the quality of life for people with COPD? For which patients, and under what circumstances, does it work best?
- What are the social care needs? Is it possible to integrate social and clinical care?
- What is the role of the voluntary sector? How can the public profile of COPD be raised?
- How can carers and family members be supported?

### 5. Tobacco dependence

Non-communicable diseases (NCDs) caused an estimated 35 million deaths globally in 2005.<sup>209</sup> This represents around 60% of deaths worldwide and as much as 80% of deaths in low- and middle-income countries. Projections for the next decade suggest that this

will increase by another 17%. NCDs comprise four major disease areas: cardiovascular disease; cancer; chronic respiratory disease; and diabetes.<sup>209</sup> Smoking is a major causal factor in all these disease areas. Prevention of smoking in young people and smoking cessation in adults is thus crucial to reducing premature mortality and morbidity, and improving quality of life for those suffering from NCDs.<sup>210,211</sup>

The IPCRG has published guidance for primary care physicians in their central smoking cessation role.<sup>149,212</sup>

#### 5.1. Prevention

Preventing young people from starting to smoke is one of the six factors identified by the World Bank that can decrease smoking prevalence.<sup>213</sup> Increasing the price of cigarettes,<sup>214</sup> and preventative measures in schools, have been shown to reduce the number of young people who start smoking.<sup>215</sup> Primary care teams can both campaign for and support societal measures to prevent smoking.

Smoking cessation interventions during pregnancy reduce the proportion of women who continue to smoke and diminish perinatal risk.<sup>216</sup> Exposure of children to environmental tobacco smoke increases the incidence of respiratory illnesses such as bronchiolitis, otitis media, and frequency of asthma,<sup>217,218</sup> with consequent excess use of antibiotics.<sup>219</sup>

Smoking is unequally distributed in societies, and increases health inequalities.<sup>220</sup> Many of those who continue smoking have psychiatric problems or other economic or social problems that maintain their choice to continue smoking.

##### Research questions:

###### *Cigarette smoking*

- How can primary care clinicians in different countries be made more aware of strategies to prevent smoking in young people and in pregnancy?
- What is the impact of primary care interventions on exposure of children to environmental tobacco smoke and prevention of smoking in young people?

#### 5.2. National tobacco control policies

The best results for smoking cessation are achieved with a combination of comprehensive national tobacco control policies and programmes,<sup>221,222</sup> together with individual psychological support and medical therapy.<sup>223-225</sup>

Many countries have public campaigns for smoking cessation, but in most countries the place for smoking cessation is not well defined despite the publication of the WHO Framework Convention on Tobacco control.<sup>226</sup> Despite clinical and cost effectiveness, many low- and middle-income countries do not make pharmacological treatments for smoking cessation available.<sup>227</sup> The focus of intervention should be on developing community level education and sustainable non-pharmacological interventions to reduce smoke exposure.

##### Research questions:

- How can awareness of the public health importance of tobacco dependence – both among smokers and the primary care professionals – be raised?

### 5.3. Individual smoking cessation support

The IPCRG has developed guidance specifically for use in primary care internationally, which cites evidence underpinning the provision of brief advice tailored to the person's circumstances and accompanied by appropriate support and treatment.<sup>149,212</sup>

As many as 80% of smokers see their GP once or more per year,<sup>228</sup> giving the primary healthcare team a unique opportunity to identify smokers, assess their motivation to quit and offer help and support. Time is a barrier to primary care smoking interventions; however, brief advice can increase the number of smokers that make an attempt to quit<sup>222,223</sup> even when an attempt had not been planned.<sup>229,230</sup> The impact of brief advice in special populations (e.g. pregnant women,<sup>216,231,232</sup> adolescents,<sup>233</sup> patients with mental health problems,<sup>234-236</sup>) is less clear. Providing support during a quit attempt increases the chance of success up to five-fold.<sup>237</sup> This can be realistically and effectively provided by primary care clinicians within the context of a routine consultation.<sup>237-240</sup>

Prescribing pharmacological therapy to support a quit attempt significantly increases the chance of success when combined with follow-up and psychological support,<sup>225</sup> with a number needed to treat (NNT) to achieve long term cessation of only 10.<sup>241</sup> Nicotine vaccines are under development, and may offer an additional option especially for preventing relapse.<sup>242-244</sup> Primary care teams can review their patients' progress and offer on-going support, though it is not clear which strategies are most effective in preventing relapse.<sup>245</sup>

#### Research questions:

##### Identifying smokers:

- What questions provide the most sensitive and specific assessment of tobacco dependence and motivation to quit, and of the smoker's individual needs?
- What are the benefits of using questionnaires (e.g. 'willingness to quit', 'addiction to nicotine') in routine clinical practice?
- What psychosocial factors (family, alcoholism, depression etc) affect ability to quit and how may these be overcome?

##### Brief advice:

- What is the impact of regular and non-judgmental advice to quit on long-term quit rates?
- 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?
- How can brief advice be implemented in different healthcare systems, and in different clinical (e.g. pregnancy, existing COPD or heart disease, asthma, high risk groups) and psychosocial situations (e.g. those not planning a quit attempt)?

##### Psychological support:

- What are the most effective models (including primary healthcare or specialist smoking cessation teams) of providing smoking cessation support services in different cultural and/or socioeconomic settings?

#### Pharmacological treatment:

- What strategies improve adherence with pharmacotherapeutic agents for smoking cessation?
- What is the clinical and cost effectiveness of nicotine vaccines in assisting smoking cessation and what is their role in primary care populations?

#### Follow-up:

- What questions, or simple instruments, can be used to assess risk of relapse in primary care consultations?

### 5.4. Organisation of services

Many countries have smoking cessation guidelines with evidence-based recommendations for clinical practice, although implementation of guidelines is poor in many countries. GPs who have undertaken a smoking cessation training programme are more effective in promoting smoking cessation.<sup>246</sup>

Proactive telephone quitlines are effective,<sup>247</sup> but their availability, GP referral rates,<sup>248,249</sup> and uptake, varies.<sup>250,251</sup> Internet-based smoking cessation strategies are in their infancy: while access is an advantage, uptake and utilisation remain problematic.<sup>250,252</sup>

#### Research questions:

- What models of providing smoking cessation services overcome known barriers (e.g. time, accessibility, expertise) and are acceptable, feasible, effective and cost-effective in primary care settings worldwide?
- How can the knowledge of primary healthcare professionals about chronic nicotine addiction be increased (including smoking cessation training programmes)?
- What factors increase the uptake and effectiveness of telephone (and internet) quitline services and how may they be optimised?

## 6. Respiratory infections

Respiratory infections are a very common cause of morbidity and mortality globally and are the leading cause of death in low-income countries.<sup>253</sup> Although most patients with acute respiratory tract infections (RTIs) self-manage their illness without seeing a doctor, RTIs remain the most common reason for consulting in primary care, accounting for an estimated 15% of general practice contacts. Most patients are managed within primary care, with the few patients requiring admission representing the 'tip of an iceberg' of illness.<sup>254</sup>

Most human antibiotic use occurs in general practice,<sup>254,255</sup> the majority of patients consulting with common respiratory tract infections. Antibiotics are of minimal benefit to the large majority of patients with the common cold,<sup>256</sup> sore throat,<sup>257</sup> and otitis media.<sup>258</sup> There may be a role for antibiotics in subgroups of patients with rhinosinusitis and acute bronchitis,<sup>259</sup> but clinical tools to identify the subgroups which may benefit from antibiotic treatment are largely lacking. Antimicrobial resistance is promoted by inappropriate use of antibiotics.<sup>255,260,261</sup> Overuse of antibiotics in primary care may lead to increasing resistance both on a local and national level.<sup>255,262,263</sup>

However, failing to use antibiotics in cases where they are needed may lead to increased hospitalisation and mortality.<sup>264</sup> An efficient interface between primary and secondary care is important in the management of respiratory infections.<sup>265</sup> The paucity of evidence from primary healthcare is of concern, since most respiratory infections are managed primarily by primary care clinicians.

This research agenda will focus on infections of the lower respiratory tract, and aims to highlight questions about the assessment and treatment of lower respiratory tract infections (LRTI) in primary care. Upper respiratory tract infections (including sinus, ear and throat infections) are excluded, as is pulmonary tuberculosis (TB), a very important respiratory infection and a global health problem which has recently been addressed by the WHO.<sup>266</sup>

### 6.1. Prevention

Influenza viruses and bacteria such as *Streptococcus pneumoniae* and *Haemophilus influenzae* are the commonest pathogens causing respiratory morbidity in the population,<sup>267-269</sup> and respiratory viral pandemics are a major public health concern. Transmission of LRTI occurs principally in the community, but effective strategies to limit transmission of respiratory infections are incompletely understood.

Vaccinations have an important role in the prevention of respiratory infections.<sup>270</sup> Extensive vaccination schemes, tailored to local conditions, aim to prevent serious infections and associated complications at an individual level and to reduce the incidence of an infectious disease in a population. Primary care has a key role in the prevention of respiratory infections, although predictors of successful uptake and promotion of vaccination and other prevention strategies are largely lacking.<sup>271</sup>

Primary care clinicians also have a key role in smoking cessation interventions – which are important since smoking is a preventable risk factor for community-acquired pneumonia (CAP) and other LRTIs (see section 5).

#### Research questions:

- What are the most effective strategies for prevention and reduction of transmission of LRTIs?
- How can uptake rates for vaccination be improved?
- Is there a role for primary care in smoking cessation, nutritional and other preventative programmes to reduce LRTIs in the community?

### 6.2. Diagnosis

The diagnosis of LRTI and the decision about whether to prescribe antibiotics remains difficult in primary care. Appropriate targeting of treatment relies on prompt and accurate diagnosis. Differentiating bacterial from viral infections is often not possible from the medical history and physical examination alone, suggesting a need for accurate near-patient tests. C-reactive protein (CRP) testing is superior to leucocyte count and erythrocyte sedimentation rate (ESR) in diagnosing LRTI,<sup>272-274</sup> and is available as a near-patient test. A recent randomised trial of its use in LRTI showed a clinically significant decrease in antibiotic prescribing with no detrimental effects on clinical recovery.<sup>275</sup> Although widely used in some

countries, its place in routine primary care diagnosis and assessment of RTIs has not been fully established, and validation of these findings in other countries is warranted. The role and use of other diagnostic tests in the management of LRTI (e.g. X-ray, blood tests, microbiology and virology testing) is currently unclear, with an inadequate evidence base guiding their use in primary care.<sup>276-278</sup>

#### Research questions:

- How can primary care clinicians differentiate between serious and self-limiting LRTIs?
- How can primary care clinicians reliably identify patients who would benefit from antibiotic therapy? What diagnostic criteria are used in deciding on antibiotic treatment in high-, middle- and low-income countries in primary healthcare settings?
- What investigations for respiratory infections are available in primary care in different countries (eg X-Ray, leucocyte count, CRP, ESR, etc) and how does the use of these ancillary tests affect antibiotic use and clinical outcomes in these countries?
- Is it warranted and feasible to use virology testing in primary care?

### 6.3. Vulnerable subgroups and co-morbidities

The elderly with respiratory infections are a particularly vulnerable population. Not only do they have a higher risk of developing LRTIs,<sup>279,280</sup> the increased prevalence of co-morbidity such as cardiopulmonary disease and diabetes puts them at an additional risk of complications.<sup>281-283</sup> This may explain the increased antibiotic prescription rate for older people with LRTI,<sup>284</sup> although large trials underpinning the assumption that the elderly will benefit from antibiotic treatment in acute bronchitis are still lacking.<sup>285</sup> Clinical prediction rules to determine high and low risk elderly patients show promise in assisting primary care clinicians to decide who may be managed at home and who need closer monitoring or hospital care.<sup>286,287</sup>

Morbidity and mortality from respiratory infections are greater in patients with co-morbidities such as COPD, asthma, diabetes, renal failure, alcohol abuse, and immunosuppression.<sup>288,289</sup> Smokers are prescribed antibiotics more frequently than non-smokers, with no apparent benefit.<sup>290,291</sup>

#### Research questions:

- Should management strategies for LRTIs be different in subgroups with various co-morbidities, in smokers, in the elderly, in children, and in pregnant women?

### 6.4. Management

Most patients with a LRTI (even when bacterial infection is confirmed) have a self-limiting condition, but some may go on to develop more serious and life threatening illness such as pneumonia.<sup>288</sup> Overuse of antibiotics (particularly broad spectrum antibiotics) promotes resistance,<sup>255,291,292</sup> and does not reduce (or increase) re-consultation rates.<sup>293-295</sup> Despite interest and research into the effectiveness of

antibiotics in the treatment of RTIs in the community,<sup>296,297</sup> uncertainty persists. Variation in antibiotic prescribing for acute cough is not explained by variation in clinical presentation and is not associated with clinically important differences in recovery.<sup>298,299</sup>

Patients' perceived expectations of antibiotics may drive prescribing.<sup>300</sup> There is some evidence that the use of patient information strategies and deferred prescription strategies can improve patient satisfaction and reduce inappropriate antibiotic use and re-consultation, but further research is needed.<sup>293,300</sup> There is limited evidence of OTC treatment of symptoms associated with LRTI.<sup>301</sup> Cost of treatment may be an issue in low-income countries. Anti-viral drugs are increasingly available but their use in LRTI is unclear.

#### Research questions:

- Which subgroups of patients with LTRIs need antibiotic treatment?
- Which near-patient tests can contribute to cost-effective management of LRTI in primary care by reducing inappropriate antibiotic use without compromising outcomes?
- If antibiotics are used, what are appropriate first-line choices and to what extent do local factors determine antibiotic choice?
- Can deferred prescription strategies reduce antibiotic use without compromising outcomes?
- How should anti-virals be used in primary healthcare?
- Should treatment approaches to LRTI be the same in high-, middle- and low-income countries?
- What is the role of OTC and non-pharmacological therapies in the management of the symptoms of LRTI?
- What is the compliance (adherence and persistence) with different antibiotic treatment regimens? In healthcare systems which allow patients to obtain OTC antibiotics, what is the effect on compliance, on outcomes and on resistance rates? To what extent do people use antibiotic 'left-overs' in the community?
- What determines how long patients wait (delay?) before consulting with their GP?
- Can the use of patient education and information strategies improve patient satisfaction and reduce inappropriate antibiotic use?
- Do primary care clinicians consider the cost of medications to the patient, and does cost and availability of medication affect outcomes?
- Do primary care clinicians follow guidelines such as the British Thoracic Society CAP guidelines<sup>288</sup> or the SIGN LRTI guideline<sup>302</sup> in their daily practice? Does the publication of primary care summaries of guidelines<sup>303</sup> aid implementation of key guideline messages?
- What is the role of primary care in pandemic respiratory infections?

## 7. Conclusion

Respiratory diseases are a public health issue throughout the world, with a high prevalence and morbidity. Primary care has an important role in the management and treatment of respiratory disease and there is a need for research in primary care that is of direct relevance to primary care clinicians and their patients in different countries. International and national guidelines exist, but there is little evidence on the best strategies for implementing recommendations.

- Key asthma questions focus on confirming a diagnosis, assessing control, treatment strategies, encouraging adherence, and empowering self-management. Management of infants and patients with intermittent and/or mild symptoms are a specific challenge.
- Challenges for the care of people with allergic rhinitis include raising the expertise of primary care clinicians, ensuring availability and affordability of suitable self-treatment and prescription medications, and local characterisation of allergens.
- Primary care clinicians have an important role in prevention, identification and management and palliative care of patients with COPD, but practical questions remain about how to deliver this comprehensive agenda in diverse primary care settings.
- The primary care team can and should play a central role in smoking cessation, and outstanding questions focus on mechanisms for encouraging evidence-based primary care cessation services tailored to the needs of different healthcare systems globally.
- Most patients with LTRIs are managed in primary care. There is a need for further epidemiological research, and for evidence to guide the diagnosis and treatment of LRTI, including rational and cost-effective strategies to optimise antibiotic prescribing.

#### Conflict of interest declaration

HP has received fees for lecturing or attending advisory groups from GlaxoSmithKline (GSK), AstraZeneca (AZ), Boehringer Ingelheim (BI), and has been sponsored to attend conferences by AZ and BI/Pfizer.

DR has received sponsorship from, provided lectures for, or delivered consultancy services to: GSK, AZ, Schering-Plough, MerckSharpeDohme, Chiesi, ALK-Abello, Uriach Pharma, Novartis, BI.

NZ has provided expert advice on smoking cessation education programs to Pfizer Pty Ltd and GSK Australia Pty Ltd and has received support to attend smoking cessation conferences.

AL has received salaries as a speaker and member of advisory boards from many different pharmaceutical companies, and is project leader of the Lung Study which was partly funded through a non-demanding grant from AZ. In his clinical practice he is joint-owner of a DXA bone densitometer.

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The contributors to each section are listed below. The authors who led the discussions and writing of the five sections are highlighted (\*). HP led the editing process and combined the five sections into one overarching document assisted by MT and SW.

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