# Chronic respiratory diseases

# A handbook for pharmacists



#### Chronic respiratory diseases

FIP Practice Transformation Programme on NCDs



2022



### Colophon

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## Executive summary

Chronic respiratory diseases (CRDs) impose significant health and economic burdens on individuals, healthcare systems and society overall. Asthma and chronic obstructive pulmonary disease (COPD) are two common CRDs and their global prevalence has been rising over the years. While the prevalence of asthma and COPD is slightly higher in high-income countries, mortality rates attributed to asthma and COPD have been significantly higher in low- and middle-income countries. As healthcare delivery undergoes a paradigm shift towards a people-centred care approach to optimising therapy and health outcomes, pharmacists are well-positioned to play a unique and complementary role in an interprofessional collaborative care model to manage CRDs.

People-centred care is anchored on the patient as a key stakeholder in the care process and emphasises shared decision-making between patients and their healthcare teams. <u>FIP Development Goal 15</u> focuses on people-centred care, aiming at collaborative interprofessional strategies and people-centred professional services to support the prevention, screening, clinical management and therapeutic optimisation of non-communicable diseases (NCDs) and long-term conditions (LTCs), including CRDs. The International Primary Care Respiratory Group (IPCRG) has outlined eight patient-centred statements on quality asthma care. In addition, the IPCRG has also suggested the SIMPLES tool for difficult-to-manage asthma. Pharmacists can be guided through these statements and tool to develop and implement quality pharmaceutical care and collaborate with healthcare providers in managing CRDs.

Pharmacists have been working on identifying and assessing symptoms, referring patients for a definitive medical diagnosis, recommending the most appropriate treatment (non-prescription medicines) to control symptoms, reviewing medicines, identifying unhealthy lifestyles and providing lifestyle counselling, helping patients avoid risk factors (e.g., smoking cessation service), educating patients and their caregivers about their disease, counselling on how to promote nasal and respiratory hygiene, educating on the correct use of inhaler devices, and supporting adherence to therapy. In summary, pharmacists have been involved in disease management, pharmacotherapy and non-pharmacological interventions.

These unique roles in the integral management of CRDs support the integration of pharmacists into the interprofessional collaborative care team. The management of CRDs such as asthma and COPD is complex and multifaceted, requiring a collaborative approach with other healthcare professionals, ensuring consistent communication to optimise health and treatment outcomes for people living with CRDs. While research has shown promising outcomes of pharmacist-involved collaborative care models in the management of asthma and COPD, continual engagement in research to improve and enhance care quality is essential.

With an emphasis on people-centred care for CRD management, pharmacists should also be mindful of ethical considerations such as respecting and safeguarding data privacy and confidentiality. Pharmacists should respect patients' values, beliefs and preferences when developing care plans and goals. Pharmacists are also well-positioned to build rapport and trust with patients to develop care plans that account for their lifestyles.

Opportunities for pharmacists to engage in CRD management are many, ranging from medication management to collaborative care in enhancing overall health. However, the success of integrating pharmacists in a collaborative care team requires in-depth analysis of facilitators and barriers to the implementation of pharmacist-led or pharmacist-involved care. With continual research to overcome barriers to implementation, advocacy of pharmacists' role and structured training, pharmacists will be well-positioned to work collaboratively with other healthcare professionals to deliver effectiveness, efficiency and quality to address the rising global health and economic burdens of CRDs.

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## Foreword

#### By the president and the chief executive officer of the International Primary Care Respiratory Group

The United Nations Sustainable Development Goals prioritise universal health coverage (UHC) and commit to reducing the impact of non-communicable diseases (NCDs) as well as communicable diseases. This handbook is an important enabling tool to achieve those goals because it makes the case for the inclusion of care for chronic respiratory diseases (CRDs) as part of UHC and demonstrates the important role pharmacists have in achieving this.

Respiratory health is often notably absent from NCDs discussions and initiatives despite the many detriments on the global population: tobacco use, air pollution, occupational exposures, poverty, infections such as tuberculosis and pneumonia, and family history all worsen our ability to do something as fundamental as breathe and live well. However, respiratory health is also a cause for hope and optimism. We have safe and effective inhaled medicines for asthma when used correctly, and there is also a growing body of evidence for a range of effective and <u>cost-effective interventions to support people with chronic obstructive pulmonary disease (COPD)</u>, including treating tobacco dependence. Pharmacists can play an important role in supporting people with CRDs if they are provided with opportunities as part of funded respiratory pathways and capabilities through training and education, and if they are motivated by feeling respected by their clinical peers, patients and the public.

In many countries, particularly in low- and middle-income countries, the only interaction the public has with healthcare is with their pharmacist, and this may include life-saving interventions such as management of acute attacks of CRD and treating tobacco dependence, so it is in everyone's interest that this interaction is of high quality. Therefore, the International Primary Care Respiratory Group (IPCRG) is delighted to have collaborated on this handbook with FIP and to share our open access resources and tools that we know can be helpful for pharmacists. We have been working with primary care teams for two decades, promoting an interdisciplinary approach to optimise the management of CRDs, including medication management through shared decision making. We have many examples of transformational work that can be achieved by pharmacists to improve respiratory care. These include: offering education about how we breathe and why we get breathless; taking responsibility for identifying and supporting people who are misusing inhaled medicines or not adhering to their regimens, including teaching inhaler technique; initiating behaviour change with people with asthma who are over-reliant on episodic care, including short-acting beta-agonists; vaccinating people with CRDs at risk of influenza, pneumonia or COVID-19; and taking every opportunity to support someone at risk of <u>COPD to quit smoking</u>. Where it works best, there is an acknowledgement at policy, organisational and personal level of the value pharmacists can bring as part of the respiratory care pathway. By contrast, where there are challenges, pharmacists may be operating in isolation from each other and from the healthcare system, and are often excluded from educational and improvement initiatives.

We urge you to consider how you can improve your community's respiratory health, and enhance your engagement, so that we can all live in a world where everyone is breathing and feeling well through universal access to the right care.

Siân Williams, CEO and Ee Ming Khoo, president, IPCRG <u>www.ipcrg.org</u>

## Foreword

Chronic respiratory diseases are long-term conditions that affect the airways and lungs, causing various symptoms in the respiratory tract.<sup>1</sup> Asthma and COPD are two common CRDs that affect hundreds of millions of people worldwide.<sup>2</sup> The Global Burden of Disease study estimates that in 2019 there were 262 million people worldwide living with asthma and that this condition caused 461,000 deaths.<sup>3, 4</sup> A recent systematic review estimated that in 2019 there were 391.9 million people worldwide living with COPD.<sup>5</sup> This disease is the third leading cause of death worldwide,<sup>6</sup> and accounted for 3.2 million deaths in 2019.<sup>3</sup> Over 80% of the deaths occurred in low- and middle-income countries.<sup>7</sup>

Asthma and COPD are mainly triggered by exposure to risk factors such as tobacco smoke, occupational exposure to noxious agents, indoor and outdoor air pollution, allergens, unhealthy diet, inadequate physical activity, stress and respiratory infections, among others.<sup>8,9</sup>.

Given the prevalence and the health-economic burden that CRDs can place on both patients and health systems, actions are needed to prevent these diseases from developing in the first place and, where present, to prevent their exacerbation. Efforts to reduce the burden of CRDs should focus on better disease management, especially improving access to healthcare and improving adherence to evidence-based interventions and treatments. Pharmacy-based, people-centred care goes beyond medicines use management and optimising their effectiveness and safety, as pharmacists have an essential role in promoting well-being and healthy living, educating patients about the triggers of respiratory disease, and providing ways to avoid and manage exacerbations. Pharmacists have an important role to play in promoting healthy lifestyles and preventing risk factors.

FIP has completed work in the area of CRDs, including three digital events on <u>The contribution of pharmacists</u> in non-communicable diseases: Asthma and COPD (15 January 2020), <u>Delivering asthma right care: For</u> community pharmacists (5 July 2021), and <u>Delivering asthma right care: For hospital pharmacists</u> (15 July 2021), the last two in collaboration with the IPCRG. FIP also has also contributed to the knowledge on the impact of air pollution on health, including four digital events on <u>The impact of air pollution on respiratory health and</u> vulnerability to COVID-19. What can community pharmacists do to help? (14 September 2020), <u>Outdoor and</u> indoor air pollution: Short- and long-term impacts on health (15 June 2021), <u>Community pharmacy roles</u>, services and tools to minimise the impact of air pollution on health (12 August 2021), and <u>Leveraging</u> pharmacists to minimise the impact of air pollution on health (12 August 2021), and <u>Leveraging</u> pharmacists in this area, and that professional organisations, including FIP, support practitioners to adopt and provide services for patients living with CRDs.

In the framework of FIP's work on NCDs, and particularly as part of FIP's Practice Transformation Programme on NCDs initiated in 2021, FIP has collaborated with an international group of experts, the IPCRG and the European Society of Clinical Pharmacy (ESCP) to develop this practice-support handbook and its <u>companion</u> <u>guide on the knowledge and skills</u> required to deliver a range of proposed interventions in the area of CRDs. These tools highlight the important role that pharmacists can play in identifying individuals living with CRDs, preventing risk factors, identifying CRD symptoms, helping patients avoid risk factors (e.g., smoking cessation service), educating patients and their caregivers about the disease, counselling on how to promote nasal and respiratory hygiene, educating on the correct use of inhaler devices, promoting adherence to therapy, and providing support to ensure the safe and effective use of medicines by people living with asthma or COPD, especially in managing medication that may require closer monitoring by a healthcare professional.

In addition, pharmacists can play a key role in supporting a paradigm shift in terms of the management of asthma, from the current over-reliance and excessive use of short-acting beta-2-agonists, to an approach that focuses on the management of inflammation and the prevention of exacerbations using inhaled corticosteroids in asthma and appropriate bronchodilation in COPD.

Overall, through the provision of person-centred pharmaceutical services, pharmacists play a key role in the healthcare system, contributing to ensuring healthy lives and promoting well-being, as well as promoting more effective, rational and economic use of medicines for people living with CRDs.

In summary, pharmacists, through their unique skillsets in varied practice settings, can contribute to the prevention, care and management of CRDs, by supporting people living with asthma or COPD through different roles, including:

- Health promotion and education
- Early detection
- Triage and referral
- Disease management
- Treatment optimisation
- Helping to shape public policies
- Interprofessional collaborative practice
- Research

The <u>Global Alliance Against CRDs (GARD)</u> vision is "a world where all people breathe freely". GARD focuses especially on the needs of people with CRDs in low- and middle-income countries. This is also the aspiration of FIP's Practice Transformation Programme on NCDs, under which this handbook is being published. This programme aims to provide tools and strategic support to FIP member organisations to develop and implement pharmacy services that can have a sustained positive impact in the prevention, screening, management and treatment optimisation of NCDs, for improved health outcomes and health systems efficiency and sustainability. While the project will have a particular focus on low-and-middle-income countries, it will encourage implementation by countries of all income levels.

Numerous examples of evidence-based interventions by pharmacists around the world that have led to positive health and economic outcomes for patients living with CRD are described throughout this handbook. FIP looks forward to working together with its member organisations and individual pharmacists around the world towards the optimisation and/or expansion of pharmacists' scope of practice in CRD, to better serve patients and health systems, and improve the respiratory well-being of our communities.

We want to thank the authors and the large group of experts from around the world who have reviewed and contributed to this publication. We also appreciate the valuable support and collaboration of the IPCRG, which not only contributed directly to this publication and kindly authorised FIP to include some of the tools it developed and validated, but also formally supported this programme by participating in our Expert Advisory Group. We are also grateful for the support and collaboration of the ESCP in reviewing this publication. FIP sincerely appreciates this important recognition of the role of pharmacists in chronic respiratory diseases.

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vagL

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## **1** Introduction

## 1.1 Definition and characteristics of CRDs: asthma and chronic obstructive pulmonary disease

Chronic respiratory diseases are long-term conditions that affect the airways and lungs, causing various symptoms in the respiratory tract. Asthma and chronic obstructive pulmonary disease (COPD) are two common chronic respiratory diseases that affect hundreds of millions of people worldwide.<sup>2</sup> Although asthma and COPD present different pathophysiologies, their main clinical manifestations are similar (cough, wheeze and difficulty breathing).

According to the <u>Global Initiative for Asthma (GINA)</u>, asthma is described as "a heterogeneous disease, usually characterised by chronic airway inflammation. It is defined by the history of respiratory symptoms such as wheeze, shortness of breath, chest tightness and cough that vary over time and in intensity, together with variable expiratory airflow limitation."<sup>8</sup> Asthma occurs in the presence of airway inflammation, smooth muscle contraction, epithelial sloughing, mucous hypersecretion, bronchial hyperreactivity and mucosal oedema.<sup>8</sup> Common triggers of asthma which can lead to airway inflammation and bronchoconstriction include allergens exposure (e.g., pollen, moulds, feathers and animal hair, dust mites and cockroaches, food allergens), airway irritants (e.g., temperature change, air pollution, noxious chemicals, smoke), respiratory infections, stress, exercise and some medicines (e.g., beta-blockers, aspirin and other non-steroidal anti-inflammatory medicines).<sup>8,10</sup>

Based on symptom severity and lung function tests, asthma can be classified into four categories: intermittent, mild persistent, moderate persistent and severe persistent. Asthma severity is not static and a patient's condition may change over time. In addition, patients with asthma may be classified according to the triggers that cause asthma exacerbation, such as allergic (immunoglobulin E mediated), non-allergic (often triggered respiratory infections or no apparent cause), occupational, aspirin-exacerbated respiratory disease, exercise-induced bronchoconstriction, and cough variant asthma.<sup>8, 11</sup>

COPD is described by the <u>Global Initiative for Chronic Obstructive Lung Disease (GOLD)</u>, as "a common, preventable and treatable disease that is characterised by persistent respiratory symptoms and airflow limitation that is due to airway and/or alveolar abnormalities usually caused by significant exposure to noxious particles or gases and influenced by host factors including abnormal lung development".<sup>9</sup> Chronic and progressive dyspnoea, cough and sputum production are the most common symptoms experienced by patients living with COPD.<sup>9</sup>

COPD develops progressively over time, mainly resulting from an interaction of risk factors. Exposure to tobacco, occupational exposure to noxious agents (e.g., dust, fumes or chemicals), indoor air pollution (including from biomass combustion) and ambient air pollution have been reported as leading risk factors for the development of COPD.<sup>5</sup> Other factors include hereditary alpha-1-antitrypsin deficiency (a genetic condition which can cause COPD at a young age), age and gender, events occurring *in utero* and premature birth affecting lung growth and development, lower socioeconomic status, asthma and airway hyper-reactivity, chronic bronchitis and history of severe childhood respiratory infections.<sup>7,9</sup>

COPD is a preventable and treatable heterogeneous disease with several clinical manifestations. COPD classification into groups of distinct phenotypes could guide the therapeutic approach, disease management and prognosis.<sup>12</sup> Small airway disease, emphysema (parenchymal tissue destruction), chronic bronchitis, alpha-1-antitrypsin deficiency, frequent exacerbators (patient with two or more acute exacerbations per year triggered predominantly by respiratory viruses and bacteria),<sup>13</sup> asthma-COPD overlap, eosinophilic versus non-eosinophilic phenotype, and phenotyping beyond the lungs (comorbidities) are some of the most commonly known COPD phenotypes.<sup>2, 12</sup>

Patients with COPD often suffer from other chronic conditions such as cardiovascular diseases, osteoporosis, musculoskeletal disorders, lung cancer, anxiety and depression, cognitive impairment, metabolic syndrome and diabetes, gastrointestinal diseases, bronchiectasis, pulmonary fibrosis and obstructive sleep apnoea. The presence of comorbidities has a significant impact on COPD morbidity and mortality, and huge economic

consequences for healthcare systems.<sup>14</sup> The management of comorbidities according to their respective treatment guidelines is essential for slowing the progression of COPD.<sup>7, 9, 15</sup>

Although asthma and COPD present different features and symptoms of airway inflammation and airway obstruction resulting from different mechanisms, there are also patients that may have persistent airflow limitation with several features of both asthma and COPD conditions, presenting asthma-COPD overlap.<sup>8, 16</sup> Acknowledging the overlap in symptoms, instead of labelling patients with either asthma, COPD or overlap diagnoses, an alternative characterisation approach using <u>treatable traits</u> has been proposed including specific patient features that can be targeted individually (see Section 8.5).<sup>17</sup>

Chronic respiratory disease treatment differs according to the condition and the severity of the symptoms, focusing on the appropriate management of the inflammatory dimension of the disease and, also the dilation of airways to improve respiratory capacity. The treatment of asthma and COPD demands a long-term and systematic approach.<sup>2</sup> Avoiding the triggers is fundamental to controlling these chronic respiratory conditions.

### 1.2 Asthma and COPD prevalence and impact

Asthma is a global public health problem affecting 1–18% of the world's population.<sup>8</sup> Its prevalence varies considerably among different countries, with some of the highest rates seen in countries such as Australia (21.5%), Sweden (20.2%), the UK (18.2%), Netherlands (15.3%) and Brazil (13.0%), and much lower prevalence rates in some African (e.g., Burkina Faso with 2.3%) and Asian countries (e.g., Vietnam with 1.0% and China with 1.4%).<sup>18-20</sup> It seems that the higher prevalence of asthma observed in high-income countries (HICs) is linked to environmental conditions, urbanisation and westernised lifestyle, where there is greater exposure to risk factors,<sup>19, 20</sup> but also better diagnostic opportunities. In low- to middle-income countries (LMICs) there might be a severe underdiagnosis due to a lack of spirometry and doctors, and priorities on communicable diseases (e.g., tuberculosis).

The latest Global Burden of Disease study, led by the Institute for Health Metrics and Evaluation, estimates that in 2019 there were 262 million people worldwide living with asthma and that this condition caused 461,000 deaths.<sup>3, 4</sup> The prevalence and impact of asthma are continuously increasing, especially in urban areas.<sup>21-23</sup> It is estimated that by 2025, about 400 million people worldwide will have developed asthma.<sup>19, 21</sup>

Asthma is the most common chronic disease in childhood and its prevalence is increasing in many countries.<sup>4,</sup> <sup>24, 25</sup> Maternal obesity and weight gain during pregnancy, maternal smoking during pregnancy, birth by Caesarean section, use of some medicines during pregnancy (e.g., paracetamol and antibiotics), maternal vitamin D deficiency, and the social environment to which children are exposed, are some of the factors that could increase asthma risk in children.<sup>8</sup>

Asthma is responsible for a substantial global health-economic burden in terms of direct, indirect and intangible costs.<sup>4, 19, 25</sup> Hospitalisation and medication are the main drivers of direct costs. A high percentage of indirect costs include work- and school-related losses, and early mortality.<sup>19</sup> Intangible costs are associated with immeasurable losses, such as a decrease in quality of life, increases in pain or suffering, limitation of physical activities and job changes.<sup>4, 19</sup> The global asthma costs have significant differences across countries. For example, annual direct costs could be varied from less than USD 150 per patient in the United Arab Emirates to more than USD 3,000 per patient in the United States.<sup>19, 25</sup> In LMICs in particular, the indirect burden on patients is considerable as showed in the <u>FRESH AIR</u> programme. This study concluded that although quite limited worktime was missed due to chronic lung diseases (asthma, COPD, or asthma-COPD overlap) in low-resource settings, the disease-related productivity and activity impairment was significant.<sup>26</sup>

Worldwide, asthma costs are increasing, closely connected with comorbidities, age and asthma severity. According to the Global Asthma Report 2018 published by the <u>Global Asthma Network</u>, efforts to reduce the economic burden of asthma should focus on increasing awareness of the impact of asthma and its risk factors, taking actions to prevent the triggers, and better disease management, especially improving access to healthcare and improving adherence to evidence-based therapies.<sup>20, 25</sup> The Global Asthma Report 2018 also indicated that the "development and implementation of national and regional asthma strategies can improve evidence-informed disease management among healthcare providers and use of medicines among patients".<sup>25</sup>

These efforts are especially needed by healthcare workers, policymakers and patients in low-resource settings. $^{26}$ 

For COPD, the prevalence data vary greatly with estimates of less than 6% of the population having a diagnosis of COPD. Standardised methodology with the Burden of Obstructive Lung Diseases (BOLD) programme have improved estimates of COPD. Current estimates indicate a prevalence of 10.1% and a substantial prevalence in never-smokers of 3 to 11%.<sup>9</sup> Based on BOLD and other epidemiological studies, it is estimated that in 2010 there were 384 million people worldwide living with COPD. A recent systematic review, based on the GOLD definition, estimated that the global prevalence of COPD was 10-3% in 2019, accounting for 391.9 million cases among people aged 30–79 years. Most cases were in LMICs (315.5 million [246.7–399.6]; 80.5%), although prevalence was slightly higher in HICs.<sup>5</sup> COPD is the third leading cause of death worldwide,<sup>6</sup> and accounted for 3.2 million deaths in 2019.<sup>3</sup> Over 80% of the deaths occurred in LMICs.<sup>7</sup> With the increase in smoking and the ageing population, the prevalence of COPD is expected to rise over the next 40 years and, by 2060 there may be over 5.4 million deaths every year.<sup>9</sup> The prevalence of COPD is often directly related to the prevalence of tobacco smoking and also related with the exposition to outdoor, occupational and indoor air pollution. According to GOLD, the prevalence of COPD is appreciably higher in smokers and ex-smokers compared with non-smokers, in patients over 40 years of age compared with those under 40 years, and in men compared with women.<sup>9</sup>

The economic burden of COPD is enormous and will continue to grow as the population ages.<sup>2</sup> In the European Union, the direct cost of COPD comprises 6% of total healthcare costs (EUR 38.6bn annually) and accounts for 56% of the total costs of treating respiratory diseases.<sup>27</sup> The costs attributable to COPD in the USA are expected to increase by over USD 800.9bn per year over the next 20 years.<sup>9</sup>

## 1.3 Pharmacists' integration in CRD care: current and future

With the aim of reducing the global burden of CRD, the <u>Global Alliance Against Chronic Respiratory Diseases</u> (<u>GARD</u>), an alliance of national and international organisations, medical and scientific societies, institutions and agencies, supported by the World Health Organization (WHO) through provision of technical leadership and secretariat support, defined four strategic objectives:

- Advocacy to raise the recognition of the importance of CRDs at global and country levels, and to advocate the integration of the prevention and control of such diseases into policies across all government departments;
- 2. **Partnership** to promote partnering for the prevention and control of CRDs;
- 3. **National plans on prevention and control** to support the WHO in assisting countries to establish and strengthen national policies and plans for the prevention and control of CRDs using WHO-endorsed approaches and methods; and
- 4. **Surveillance** to support the WHO in monitoring CRDs and their determinants, and to evaluate progress at country, regional and global levels.<sup>28</sup>

The GARD vision is "a world in which all people breathe freely", with a special focus on the needs of people with CRDs in LMICs.<sup>1</sup> Based on this, and taking into account that pharmacists are an essential part of the healthcare team, the untapped potential of pharmacists' contribution to reduce the burden of CRDs is huge.

Due to their knowledge, education, ability to provide person-centred care and competency level, pharmacists have an important role in the prevention, screening, referral, management and treatment optimisation of CRDs, as well as patient education, contributing to reducing disease burden and improving patient outcomes.<sup>29, 30</sup> Given their accessibility, community pharmacists, in collaboration with other members of the healthcare team, are ideally placed to offer these services.

Pharmacist-delivered asthma care programmes have been shown to improve asthma control.<sup>31, 32</sup> Collaborative interventions can significantly improve self-reported asthma control and asthma-related quality of life in patients that have been identified as having suboptimal management of their asthma.<sup>33</sup>

The four categories of COPD-interventions are primary prevention, early detection, therapy management and long-term health management.<sup>34</sup>

Improvement in inhaler technique, medication adherence and smoking cessation are some examples where pharmacists can have a major role in educating patients.<sup>34</sup> A randomised control trial on pharmacist-led COPD interventions has shown the potential to improve medication adherence which, in turn, increases quality of life, decreases pulmonary exacerbations and reduces utilisation of acute healthcare resources.<sup>35</sup>

The IPCRG's Asthma Right Care strategy agreed on eight patient-centred statements about good quality asthma care in primary care. Table 1 shows what people living with asthma deserve, according to the IPCRG. Pharmacists can have a role in statements 2, 4, 5, 6 and 7.

| Categories           | Statements  |
|----------------------|---|
| Diagnosis            | <ol> <li>A timely, accurate and formal/objective diagnosis of their asthma by their primary<br/>healthcare team.<br/>[The IPCRG has addressed this through the asthma diagnosis jigsaw project.]</li> </ol>   |
| Management           | <ol> <li>To receive adequate inhaler treatment for their asthma according to the best practice recommendations for their level of disease severity. [The IPCRG is currently doing this with <u>Asthma Right Care</u> — addressing overreliance on short-acting beta-2 agonists/oral steroids, and underuse of inhaled corticosteroids.]</li> <li>To participate in the choice of treatment for their asthma, including the decision between different options of inhaler devices.</li> <li>To have appropriate inhaler technique training and to agree an asthma action plan shared with their healthcare providers.</li> <li>To receive counselling and treatment if they are tobacco-dependent, a yearly flu vaccination and COVID-19 vaccination.</li> </ol> |
| Review               | <ol> <li>Follow-up appointments at acceptable intervals for the management of their asthma that must include structured assessment of control, well-being and evaluation of future risk.</li> <li>That their -difficult-to-manage asthma is evaluated by their primary healthcare team following a structured approach in order to identify any solvable questions before they are referred to secondary care. [The <u>SIMPLES tool</u>, see Table 2, could be used to review a patient with -difficult-to-manage asthma.]</li> </ol>   |
| When things go wrong | 8. To have easy and timely access or referral to a primary or secondary healthcare professional who is skilful in asthma management whenever their symptoms cannot be self-managed or when their asthma cannot be managed in primary care.  |

Table 1. The IPCRG's eight people-centred statements: What people with asthma deserve

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Specifically, pharmacists can adopt the SIMPLES tool suggested by the IPCRG in reviewing people with difficult-to-manage asthma. The SIMPLES tool represents factors to check while reviewing asthma control (Table 2).

| SIMPLES           | Description   |
|-------------------|---|
| Smoking           | Check current smoking status and for smokers, ask about current smoking habits and encourage smoking cessation. For non-smokers, ask about exposure to second-hand tobacco smoke. |
| Inhaler technique | Check accurate use of inhaler (i.e., correct inhaler techniques) and assess choice of inhaler.  |
| Monitoring        | Monitor asthma control through assessment of symptoms and activity limitations.   |
| Pharmacotherapy   | Assess medication adherence, medicines-related problems, and patients' understanding of their medicines.  |
| Lifestyle         | Assess any exacerbating and trigger factors for asthma.   |
| Education         | Check patients' understanding of asthma and its related treatment.  |
| Support           | Identify support from family in patients' management of asthma and assist family to support patients' self-management.  |

#### Table 2. The IPCRG SIMPLES tool for reviewing difficult-to-manage asthma

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In summary, through the provision of person-centred services, pharmacists play a key role in primary healthcare in partnership with other primary care services in the community, including GPs, primary care nurses, rehabilitation teams and respiratory teams in hospitals, contributing to ensuring healthy lives and promoting respiratory well-being, as well as promoting more effective, rational and economical use of medicines by people living with asthma or COPD.

## 2 Clinical manifestations of CRDs

### 2.1 Characteristics of CRDs: asthma versus COPD

Asthma is a variable chronic inflammatory disease of the airways leading to bronchial constriction, which can make its diagnosis and management challenging. It can lead to sporadic breathing difficulties, and the airflow limitation may resolve spontaneously or in response to medication and may sometimes be absent for weeks or months.<sup>36,37</sup> However, patients can experience episodic flare-ups (exacerbations) of asthma that may be life-threatening and carry a significant burden on patients and the community.<sup>8</sup> Asthma exacerbations are a major factor responsible for morbidity and even mortality, increases in healthcare costs, and, in some patients, a greater progressive loss of lung function.<sup>38</sup> Figure 1 shows the anatomy of a normal airway, an airway of a person with asthma and an airway during an asthma attack.

#### Figure 1. Anatomy of airways



Pathology of asthma. Shutterstock

Pharmacists as healthcare providers should focus on the potential asthma triggers, including smoking tobacco, air pollution, viral respiratory tract infections, environmental allergens (e.g., pollen "season"), and stress, among others (see Figure 2). These are risk factors that could lead to disease development or that could lead to asthma exacerbation. Understanding which characteristics are associated with an increased risk for asthma development and exacerbation is an important step to help pharmacists figure out how to be part of preventing these situations.

#### Figure 2. Key asthma triggers



Beta-blockers and non-steroidal anti-inflammatory drugs.
 1. Esposito S, et al. BMC Pulm Med 2014;14:130; 2. Beigelman A, et al. Curr Opin Allergy Clin Immunol 2014;14:137–142; 3. See K, et al. Singapore Med J 2015 epub; 4. Vernon M, et al. J Asthma 2012;49:991–998; 5. Global Initiative for Asthma. Global Strategy for Asthma Management and Prevention, 2016. Available from: www.ginasthma.org; 6. Lim FL, et al. PLoS One 2015;10:e0124905.

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COPD is characterised by persistent respiratory symptoms and by airflow obstruction that is due to airway or alveolar abnormalities commonly caused by exposure to smoking tobacco and air pollution.<sup>12</sup> Inflammation in COPD is predominantly localised to peripheral airways and lung parenchyma, where a number of processes such as fibrosis and collapse of peripheral airways cause the airways to become narrow, which leads to air trapping, destruction of parts of the lung and mucus blocking the airways.<sup>7, 39</sup>

COPD may be punctuated by periods of acute worsening of respiratory symptoms, often referred as acute exacerbations of chronic obstructive pulmonary disease (AECOPD), which account for the greatest proportion of the total COPD burden on healthcare systems<sup>40</sup>. AECOPD or COPD flare-ups are episodes of symptom worsening that have significant adverse consequences for patients and are often caused by a respiratory infection.<sup>7</sup> COPD exacerbations are heterogeneous events related to increased airway inflammation, mucus hypersecretion and gas trapping. These are characterised by "transient periods of increased symptoms of dyspnoea, sputum purulence and sputum volume, but they may also encompass minor symptoms of nasal blockage/discharge, wheeze, sore throat, cough, fever, chest tightness or discomfort, fatigue/reduced energy, sleep disturbance or limited physical activity".<sup>13</sup>

Table 3 outlines the main differences and similarities between asthma and COPD.

| Characteristics                | Asthma   | COPD  |
|--------------------------------|--|---|
| Lung function<br>abnormalities | Bronchial reversibility or airway<br>hyperreactivity41   | Non-reversible chronic obstruction <sup>12,40</sup> |
| Age group                      | <ul> <li>Atopic in childhood (early onset<br/>asthma)</li> <li>Non-atopic for adult onset<br/>asthma<sup>42</sup></li> </ul> | ≥ 40 years old9                                     |

#### Table 3. A comparison of the main characteristics of asthma and COPD

| Characteristics         | Asthma  | COPD   |
|-------------------------|---|--|
| Gender                  | <ul> <li>Asthma is more common in men<br/>than in women before puberty<sup>43</sup></li> <li>After puberty, many studies show<br/>that asthma is significantly more<br/>prevalent in women (10.4%) than in<br/>men (6.2%)<sup>44</sup></li> </ul>   | <ul> <li>COPD is more prevalent in men (11.8%) than in women (8.5%)<sup>9</sup></li> <li>COPD diagnosis in women has been neglected because it has been considered predominantly a disease of men. However, because of an increase in smoking or ongoing exposure to biomass fuel smoke in many countries, COPD prevalence now seems to be more similar between women and men.<sup>45</sup></li> </ul>   |
| Causes and risk factors | <ul> <li>Individual factors:</li> <li>Genetics and family history</li> <li>Gender</li> <li>Gestation period (e.g., maternal obesity and weight gain during pregnancy, maternal smoking during pregnancy, use of some medicines during pregnancy such as paracetamol and antibiotics, maternal vitamin D deficiency, and the social environment to which children are exposed could increase asthma risk in children)</li> <li>Birth characteristics (e.g., birth by Caesarean section, premature or low birth weight)</li> <li>Not having been breastfed as a baby</li> <li>Allergic conditions (e.g., eczema and rhinitis)</li> <li>Environmental factors:</li> <li>Urbanisation and lifestyle factors</li> <li>Exposure to environmental allergens and irritants (e.g., indoor and outdoor air pollution, house dust mites, moulds, and occupational exposure to chemicals, fumes or dust)</li> <li>Obesity in children and adults</li> <li>Tobacco smoking or exposure to second-hand smoke</li> <li>Respiratory viral and bacterial infections (patients with asthma may be more susceptible to viral and bacterial respiratory infections as a result of impaired mucosal and systemic immune defence)</li> <li>Diet</li> <li>Exposure to stress</li> <li>Occupational risk factors (e.g., work environment).<sup>8, 36, 38, 46</sup></li> </ul> | <ul> <li>Individual factors:</li> <li>Tobacco exposure and exposure to second-hand smoke</li> <li>Occupational exposure to dusts, fumes or chemicals</li> <li>Asthma in childhood</li> <li>Severe respiratory infections in childhood that prevent maximal lung growth</li> <li>α1-Antitrypsin deficiency (COPD phenotype) can cause COPD at a young age</li> <li>Environmental factors:</li> <li>Indoor air pollution (e.g., biomass fuel and coal, which is used for cooking and heating in LMICs, with high levels of smoke exposure).<sup>7, 32</sup></li> </ul> |

| Characteristics  | Asthma   | COPD   |
|--|--|--|
| Common triggers  | <ul> <li>Vary from person to person, but can include the following:<sup>7, 8, 13</sup></li> <li>Respiratory viral infections</li> <li>Exercise</li> <li>Allergen exposure (e.g., dust, grass and tree pollen)</li> <li>Changes in weather</li> <li>Laughter or stress</li> <li>Irritants such as perfumes, car exhaust fumes, smoke</li> </ul> | <ul> <li>Triggered predominantly by: <sup>7, 13</sup></li> <li>Respiratory viruses and bacteria</li> <li>Air pollution</li> <li>Ambient temperature</li> </ul>   |
| Cells endotype/<br>inflammatory and cellular<br>mechanisms | Eosinophilic inflammation is a<br>characteristic feature of asthmatic<br>airways <sup>47</sup>   | The inflammation in COPD is<br>characteristically described as<br>neutrophilic.<br>Although COPD is typically characterised<br>by neutrophilic inflammation, the<br>eosinophilic endotype is not rare.<br>Approximately 25% to 40% of patients with<br>COPD have the eosinophilic endotype <sup>48</sup> |

## 2.2 CRDs phenotypes

#### 2.2.1 Asthma phenotypes

Asthma is an inflammatory condition that is highly complex, multifactorial and associated with an immunemediated process.<sup>37</sup> It is currently divided into different phenotypes, with age at onset as a relevant differentiating factor,<sup>49</sup> and other characteristics (e.g., demographic, clinical and pathophysiological).<sup>8</sup> Some of the most common phenotypes for asthma are described in Table 4.

#### Table 4. Asthma phenotypes

| Phenotype   | Characteristics  |
|---|--|
| Allergic asthma (early-onset atopic asthma)                       | Most asthma patients are atopic and have an allergic<br>pattern of inflammation in their airways, which extends<br>from the trachea down to peripheral airways. This is the<br>most easily recognised asthma phenotype. <sup>8, 50</sup>                                 |
| Non-allergic asthma   | Between 10 and 30% of patients have asthma that is not associated with allergies. <sup>8, 51</sup>   |
| Adult-onset (late-onset) asthma; including<br>occupational asthma | Adult-onset asthma (with an incidence of adult-onset<br>asthma peaks in middle-aged women, in whom smoking is<br>a higher risk) is a common phenotype and a major burden<br>to healthcare systems. <sup>49</sup>   |
| Asthma with obesity   | Obese or non-eosinophlic asthma: inflammation is not<br>prevalent and occurs most commonly in overweight<br>women. <sup>47</sup>   |
| Cough asthma  | Patients with this phenotype typically do not complain of wheeze.44  |
| Aspirin-exacerbated respiratory disease (AERD)                    | In this phenotype, asthma is precipitated or worsened by<br>medicines that inhibit cyclo-oxygenase 1 (enzyme involved<br>in degradation of proinflammatory leukotrienes). AERD is<br>typically more severe and uncontrolled than other forms<br>of asthma. <sup>44</sup> |
| Exercise-induced bronchoconstriction                              | Some patients experience bronchoconstriction in response<br>to exercise. This phenotype occurs in individuals who<br>experience typical asthma symptoms shortly after<br>finishing exercise that lasts for up to one hour  |

| Phenotype | Characteristics   |
|-----------|---|
|           | afterwards. <sup>44</sup> Exercise-induced bronchoconstriction can<br>develop in people who do not have a history of known<br>asthma. |

#### 2.2.2 COPD phenotypes

COPD results from long-term exposure to harmful gases and particles combined with individual factors. Common COPD phenotypes are described in Table 5.

#### Table 5. COPD phenotypes

| Phenotype   | Characteristics   |
|---|---|
| Small airway-predominant<br>disease               | This phenotype is characteristic of early stages of COPD, observing a reduction<br>in total bronchiolar area and a reduction in the number of small conducting<br>airways, however, it becomes more prevalent over time as the disease<br>progresses to more severe COPD. <sup>12</sup>   |
| α1-Antitrypsin deficiency                         | $\alpha$ 1-Antitrypsin is a proteinase inhibitor that protects the lung tissue from damage by neutrophil elastase. This deficiency can be either homozygous or heterozygous with a prevalence of 1%–4.5% and 17.8%, respectively. Younger individuals, smokers and workers exposed to occupational risk factors with the $\alpha$ 1-antitrypsin gene mutation are at a higher risk of COPD. <sup>12</sup> |
| Emphysema   | Emphysema refers to parenchymal tissue destruction. This phenotype occurs in a significant proportion of smokers. <sup>12</sup>   |
| Chronic bronchitis                                | Chronic bronchitis is characterised by chronic cough with the production of sputum resulting from inflammation in the airways. It is associated with an increased extent of dyspnoea, increased frequency of exacerbations, airway obstruction and increased airway wall thickening. It is also associated with cardiovascular comorbidities and sleep apnoea. <sup>12</sup>                              |
| Asthma-COPD overlap                               | Asthma-COPD overlap is "characterised by persistent airflow limitation with several features usually associated with asthma and several features usually associated with COPD". <sup>8, 9, 12</sup>   |
| Frequent exacerbations                            | This phenotype is characterised by the worsening of a patient's respiratory symptoms, with two or more acute exacerbations per year triggered predominantly by respiratory viruses and bacteria. <sup>12</sup>  |
| Eosinophilic versus<br>non-eosinophilic phenotype | The eosinophilic phenotype has been increasingly recognised as a distinct COPD phenotype. Although eosinophil counts as biomarker to start or de-escalate inhaled corticosteroids, their role in the pathophysiology of COPD is not fully clear yet. <sup>52</sup>  |
| Phenotyping beyond the lungs<br>(comorbidities)   | In this phenotype, patients with COPD suffer from other comorbidities that have<br>a significant impact on COPD, and approximately two thirds of patients with<br>COPD die from these other diseases. Identifying these subpopulations might<br>lead to therapeutic interventions that could affect patients' health<br>significantly. <sup>12</sup>  |

## 2.3 Classification of control and severity

#### 2.3.1 Classification of asthma control

Asthma management is mostly based on asthma control. The level of control is the extent to which the manifestations of asthma can be observed in the patient or have been reduced or removed by treatment.<sup>8</sup> It is determined by the interaction between a patient's genetics, traits of the disease process, the treatment, the environment and psychosocial factors. Asthma control is assessed in two domains: symptom control and future risk of adverse outcomes. Patients with poor symptom control are more at risk of exacerbations.<sup>8</sup>

Assessing symptom control is based on the frequency of daytime and night-time asthma symptoms, night waking and activity limitation and, for patients using short-acting beta-2-agonist (SABA) relievers, their frequency of SABA use. The Asthma Control Test (ACT), Asthma Control Questionnaire and other tools may be

used to assess asthma control (see Chapter 4).<sup>8</sup> The GINA symptom control tool can also be used in conjunction with the ACT to determine asthma control. The GINA symptom control tool assesses the following four symptoms experienced by the patient over the four weeks prior to assessment:

- Daytime asthma symptoms (> twice per week)
- Night awaking due to asthma
- Use of SABA reliever (> twice per week)
- Activity limitation due to asthma

The classification of asthma control is described in Table 6.

#### Table 6. Classification of asthma control in adults<sup>8</sup>

|  | Well controlled | Partly controlled/<br>not well controlled | Poorly controlled |
|--|-----------------|---|-------------------|
| Asthma Control Test                                      | ≥20 points      | 16-19 points                              | ≤15 points        |
| Asthma Control Questionnaire                             | < 0.75          | 0.75-1.5                                  | > 1.5             |
| Daytime asthma symptoms in the past four weeks           |                 |   |                   |
| Night awakening due to asthma in the past four weeks     | None            | 1-2                                       | 2.4               |
| Use of SABA as reliever in the past four weeks           | None            | 1-2                                       | 3 -4              |
| Activity limitation due to asthma in the past four weeks |                 |   |                   |

#### 2.3.2 Classification of asthma severity

According to GINA, the definition of asthma severity is based on the concept of "difficulty to treat". This definition is based on retrospective assessment, after at least two to three months of controller treatment, from the treatment required to control symptoms and exacerbations.<sup>8</sup> Severity classification helps in guiding therapeutic decisions and is classified as intermittent, mild persistent, moderate persistent, or severe persistent. Asthma severity is not static and should be reviewed at each visit with reclassification based on the magnitude of treatment needed to control or alleviate the symptoms of asthma. Asthma severity indicates the intensity of the disease process, and changes in asthma severity may related to different environmental exposures, comorbidities or advancing disease.<sup>44</sup> GINA states that asthma severity classification is "clinically useful for severe asthma, as it identifies patients whose asthma is relatively refractory to conventional high dose ICS-LABA and who may benefit from additional treatment such as biologic therapy".<sup>8</sup> The classification of asthma severity is described in Table 7.

| Severity   | Intermittent   | Persistent  |   |   |
|--|--|---|---|---|
|  | Mild   | Mild  | Moderate  | Severe  |
| Main features of<br>symptoms (night<br>waking, activity<br>limitation and<br>frequency of SABA<br>use as the<br>prescribed reliever) | Infrequent (less<br>than once a<br>week) or mild<br>symptoms | Once or more a week<br>with night waking<br>twice or more a month,<br>and activity limitations<br>at least once a month | Every day with night<br>waking once or more a<br>week, and activity<br>limitations at least<br>once a week.<br>Controlled with low<br>dose of inhaled<br>corticosteroids/long-<br>acting beta-2 agonists<br>(ICS-LABA). | Every day with<br>frequent night<br>waking, and daily<br>activity limitations.<br>Uncontrolled despite<br>optimised treatment<br>with high dose ICS-<br>LABA. |

#### Table 7. Classification of asthma severity<sup>8, 43</sup>

#### 2.3.3 Classification of COPD severity

Assessment of COPD severity mainly revolves around the assessment of airflow limitation. Spirometry should be used to determine severity of airflow limitation. GOLD recommends that spirometry should be performed after the administration of an adequate dose of at least one short-acting inhaled bronchodilator in order to minimise variability.<sup>9</sup>

The severity of air flow limitations can be divided into mild, moderate, severe and very severe as per the percentage of FEV1 (forced expiratory volume in one second) predicted:<sup>5</sup>

- Mild: FEV1 ≥80% predicted
- Moderate: 50% ≤ FEV1 <80% predicted
- Severe: 30% ≤ FEV1 <50% predicted
- Very severe: FEV1 <30% predicted

Airflow limitation should also be coupled with assessment of symptoms. Several validated tools such as the COPD Assessment Test and the COPD Control Questionnaire can be used to assess COPD symptoms. The modified British Medical Research Council tool can be used to assess breathlessness symptoms. GOLD recommended the ABCD Assessment Tool (revised) to classify COPD severity based on airflow limitation and symptoms. The revised ABCD Assessment Tool presented in the GOLD can be accessed <u>here</u>.

## 2.4 Signs and symptoms

Table 8 shows the most common respiratory symptoms associated with asthma<sup>8, 36, 53</sup> and COPD.<sup>9, 40</sup> The asthma symptoms are intermittent and may occur several times in a day or week, and for some people become worse during physical activity, at night or in the early morning.<sup>36</sup>

#### Table 8. Principal signs and symptoms of asthma and COPD

| Asthma  | COPD   |
|---|--|
| <ul> <li>Wheezing</li> <li>Chest tightness</li> <li>Cough</li> <li>Shortness of breath</li> <li>Variable expiratory airflow limitation</li> </ul> | <ul> <li>Dyspnoea</li> <li>Cough</li> <li>Sputum (phlegm) production</li> <li>Breathlessness or difficulty breathing</li> <li>Chronic cough, often with phlegm</li> <li>Tiredness</li> </ul> |

## **3 Prevention and control of CRDs**

## 3.1 Pharmacists' role in promoting respiratory well-being

Community pharmacists are some of the most easily accessible healthcare providers, typically being the first point of contact for care in the community. As first-line medicines experts, pharmacists have a role in promoting respiratory well-being that commonly involves self-care support, including the use of non-prescription medicines and non-pharmacological measures, and the promotion of adherence to medication.<sup>54</sup> Pharmacists provide counselling and education for patients aiming for respiratory well-being, especially addressing concerns or questions related to respiratory diseases and their prevention, patient training on the correct use of inhalers and inhaler technique assessment, as well as disease management strategies.

Pharmacists can also conduct screening services for asthma/COPD exacerbations, including respiratory function assessment and symptom-control questionnaires, make referrals to physicians as needed, and follow up with patients.<sup>55</sup> Triaging patients and referring them to other healthcare professionals that have the appropriate competence to manage specific situations is in itself an important function of pharmacists.

Other specified services made available by pharmacists include first aid for asthma attacks, guidelines for standard care during the pollen season, vaccine administration and smoking cessation services. In some countries, pharmacists are allowed to prescribe or renew prescriptions for medicines for certain respiratory conditions.<sup>54</sup>

Patient education is a fundamental aspect of CRD management and several studies have looked at the impact of pharmacist-led educational interventions on respiratory well-being, improving asthma/COPD severity and control, quality of life and medication adherence, as well as reducing medicines wastage, hospital admissions and severe exacerbations.<sup>32, 35, 56-60</sup> Proper education reduces exacerbations, decreases morbidity, improves disease control, and increases respiratory well-being and patients' quality of life.<sup>61</sup> The education of patients with chronic respiratory diseases should include the transmission of knowledge by the pharmacist and the acquisition of skills and competencies by the patient.<sup>61</sup> The goal of patient education is to achieve optimal selfcare, better adherence to treatment, increased disease knowledge, recognition of symptoms and thus improved disease control.<sup>62</sup> During the education process, some basic information and skills need to be learnt by people with asthma or COPD.<sup>63</sup>

- Knowing that they have a chronic disease that needs continuous treatment, even if there is no discomfort;
- Knowing the difference between inflammation and bronchoconstriction;
- Differentiating between medicines that control the inflammation and those that relieve the obstruction;
- Recognising the symptoms of the disease;
- Using inhalers correctly;
- Identifying and avoiding triggers as much as possible;
- Monitoring symptoms and peak expiratory flow (PEF);
- Recognising signs and symptoms of worsening of the disease; and
- Acting in the event of a deterioration of their disease to prevent crises or exacerbations.

The IPCRG compiled this type of information into the <u>COPD Right Care</u> wheel. This tool has two sides: side A has a quick helper for prescribing choices, while side B helps to assist with patient consultation and motivational interviewing, and may also be used by pharmacists to help start conversations with patients about what they need to know about COPD (see Figure 3).

Therefore, people living with CRDs need to know:

- Identity what their condition is called;
- **Cause** why they have it (e.g., exposure to tobacco smoke, indoor and outdoor air pollution, allergy);
- Timeline what will happen next;
- **Cure or treat** what we can do about it (e.g., what are the treatments options, including quit smoking, vaccinations, how to use inhalers, eating well, taking other medicines, pulmonary rehabilitation for COPD); and
- **Consequences** knowing how patient choices affect their future (e.g., if a COPD patient does nothing, they may likely reach of a point of disabling breathlessness and need oxygen).

#### Figure 3. COPD Right Care wheel, side B



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Everyday community pharmacists also support respiratory well-being by recommending nonpharmacological measures, such as the use of saline or physiological nasal sprays and nasal washes, that promote nasal hygiene and preserve the protective function of the nose. However, the results of a FIP global survey about mitigating the impact of air pollution on health showed that "advising on the importance of nasal hygiene as a prevention method against the harmful impact of air pollution is not yet fully integrated in community pharmacists' practice as an important measure to promote respiratory well-being".<sup>54</sup> Other forms of non-pharmacological measures recommended by pharmacists include using face masks, helping control the dissemination of respiratory infections and protecting the user from airborne pollutant particles, using gargles and steam inhalations, drinking warm water, using air humidifiers or air purifiers, observing good environmental hygiene, avoiding allergens, and resting.<sup>54</sup>

## 3.2 Promoting healthy lifestyles and preventing risk factors

Given the substantial burden that CRDs can have on both patients and health systems, actions are needed to prevent these diseases from developing in the first place and, where they are presented, prevented from worsening. People-centred care in pharmacy goes beyond medicines use, and pharmacists have an essential role in promoting well-being and healthy living. Health promotion interventions that encourage strategies to prevent the development of CRDs should be considered an essential component of pharmacist-provided care. These efforts are particularly important given that many cases of CRDs or their exacerbations can be prevented through healthy lifestyles and avoidance of exposure to risk factors.

Pharmacists can play an important role in promoting respiratory well-being, making patients aware of the triggers of their respiratory disease, and providing ways to avoid and manage exacerbations. Pharmacists are also available to assist patients through the provision of motivational counselling for those who wish to make and sustain healthy lifestyle changes, especially on smoking cessation. They can also proactively support patients to adopt preventive measures against air pollution and occupational risk factors, encourage respiratory wellness, improve diet and physical activity, and manage stress.

Pharmacists' involvement in CRD prevention can range from the development of educational materials (e.g., flyers or videos), providing general education regarding healthy lifestyles, and providing more comprehensive and long-term counselling on lifestyle changes, to participating in programmes and campaigns (e.g., mitigation of the impact of air pollution on health). Their commitment will depend on their knowledge and skills on the topic and the economic and time resources available to engage with patients.

According to the WHO, primary prevention of CRDs aims at the reduction or avoidance of exposure of individuals and populations to common risk factors, and for this to be started during pregnancy and childhood. Avoidance of direct and indirect exposure to tobacco smoke is essential not only for healthier lungs but as a preventive measure for others NCDs (cardiovascular disease, cancer and diabetes). Other risk factors such as poor nutrition, frequent acute respiratory infections during childhood, and environmental air pollution (indoor, outdoor and occupational) should be addressed.<sup>64</sup>

Chapter 3 will focus broadly on recommendations to prevent patients from developing CRDs or to reduce the risk of exacerbations by promoting healthy lifestyles and preventing risk factors. Pharmacists should consider how it would be best to incorporate these recommendations into their daily practice and how they would like to communicate with their patients about these important topics. In order to disseminate this crucial information to the public, several different approaches can be taken, including posters, lectures, social media campaigns and informal conversations during counselling sessions. Advice for creating a successful public health campaign can be found in the WHO's "Effective communications participant handbook".<sup>65</sup>

#### 3.2.1 Smoking cessation

Tobacco use has been reported as the one risk factor common to NCDs, especially CRDs, cardiovascular diseases, cancer and diabetes. Worldwide, 14% of all NCD deaths of adults aged 30 years and over are attributable to tobacco.<sup>66</sup> The WHO Framework Convention on Tobacco Control including Article 14 to treat tobacco use and dependence has been included in the United Nations Sustainable Development Goal 3.<sup>67, 68</sup> Tobacco smoking is the leading cause of COPD,<sup>69</sup> and according to the US Centers for Disease Control and Prevention, eight out of ten COPD deaths in the USA are caused by smoking.<sup>70</sup>

*In-utero* exposure to maternal tobacco smoking, exposure to second-hand smoke during childhood, or smoking during teenage years all reduce lung growth and function, increasing the risk of asthma and COPD development later in life. Also, exposure to second-hand smoke can trigger an asthma attack in both children and adults.<sup>69, 70</sup> Exposure to second-hand smoke at a young age, also known as exposure to environmental tobacco, can result in respiratory symptoms such as cough and wheezing. Over time, these symptoms can lead to the development of asthma and impair lung function. The risk of development of CRDs from environmental tobacco exposure is more prominent in low-resource settings where living spaces may be crowded and nutrition is poor.<sup>71</sup> Therefore, early screening for people presenting with symptoms can trigger pharmacotherapeutic interventions and preventive measures to slow disease progression.

Smoking cessation is one of the most important interventions to reduce NCDs. The WHO has incorporated smoking cessation as one of the six MPOWER measures (i.e., offer help to quit tobacco use).<sup>72,73</sup> For the WHO, health professionals, including pharmacists, have the greatest potential of any group in society to promote the reduction of tobacco use.<sup>74</sup> So, in order to train health professionals on tobacco cessation, the WHO developed an online, self-learning course, free of charge for primary care practitioners and other health professionals all over the world. This is a valuable resource for pharmacists interested in providing cessation services as part of their routine practice,<sup>75</sup> especially for those who live in LMICs, where the percentage of tobacco users is over 80% and where smoking cessation services are limited.<sup>72</sup>

Also, in support of its position paper "Treating tobacco dependence: guidance for primary care on life-saving interventions",<sup>76</sup> the IPCRG has produced practical tools for healthcare professionals supporting patients to quit tobacco, including its <u>desktop helper no. 4</u>, using very brief advice (plus pharmacotherapy if available), and <u>filmed case studies</u>".<sup>77</sup>

Helping people quit is the most effective treatment for preventing and reducing the evolution of COPD, and improving asthma symptoms.<sup>69</sup> Pharmacists, together with their pharmacy teams, play a huge role in supporting patients in smoking cessation by raising awareness of tobacco use and working with patients who are ready to quit smoking but are unable to. Pharmacists and their teams can use different approaches to help people quit smoking, by offering individual or group-based behavioural counselling, by using digital tools for smoking cessation including text messaging, chat bots and apps, and recommending pharmacological interventions such as nicotine replacement therapy (NRT), varenicline, bupropion and cytisine .<sup>72</sup>

Pharmacists can support behaviour change by using different evidence-based behavioural tools. A key message is that tobacco dependence is a relapsing long-term condition that often begins in childhood, and therefore it is important that pharmacists consistently ask about tobacco use and offer support. The simplest model is Very Brief Advice (VBA+) or the 3As model (Ask, Advise, Act). VBA+ is an extended option if the pharmacist has the opportunity to recommend pharmacological interventions. If the pharmacist has more time, then they may prefer the WHO's 5As model (Ask, Advise, Assess, Assist, Arrange) to help people quit smoking.

Once pharmacists help people get used to the idea of quitting, they can then use the 5R model (Relevance, Risks, Rewards, Roadblocks, Repetition) to help encourage consistent motivation to quit. These models help pharmacists in all healthcare settings to be able to assess and evaluate their patients' tobacco use and develop a plan on how to help them quit in a way that is specific to them. Details on these strategies can be found in the WHO "Toolkit for delivering the 5As and 5Rs brief tobacco interventions in primary care".<sup>78 79</sup>

Pharmacists can utilise the COM-B model (Capability, Opportunity, Motivation, Behaviour) to design smoking cessation services. The COM-B model guides the design and implementation of behavioural change interventions. Specifically, using COM-B can guide pharmacists to develop and implement targeted interventions to encourage smoking cessation.<sup>80</sup> "Capability" refers to a person's capacity (in the form of knowledge and skills) to engage in the activity, in this context, quit smoking. "Opportunity" refers to external factors beyond the individual that can make behavioural change possible. "Motivation" refers to the drive to change behaviour, comprising of emotions, habits, and analytical decision-making. Collectively, capability, opportunity and motivation interact to influence and drive behavioural changes.<sup>80</sup> Furthermore, the COM-B model can also be used to elucidate factors or facilitators and barriers to adherence to nicotine replacement therapy. A systematic review published in 2020 has identified and reviewed 26 studies that incorporated the COM-B model to elucidate facilitators and barriers to NRT adherence. The findings can inform and guide development of pharmacist-led interventions to improve adherence to NRT.<sup>81</sup>

According to the study "Smoking cessation at the community pharmacy",<sup>82</sup> community pharmacists play a huge role in promoting smoking cessation. The purpose of the study was to look at pharmacists' contribution to smoking cessation and understand the determinants of success in the community pharmacy setting. The authors found that the implementation of a smoking cessation programme, where there was counselling combined with pharmacotherapy indication, helped increase tobacco control and resulted in successful smoking cessation. Results showed that 43.7% of patients enrolled in the community pharmacy smoking cessation programme had successfully quit smoking after one month, 32.6% maintained success after three months, and 20.7% maintained success after 12 months.<sup>82</sup>

Other studies describing successful pharmacy interventions in smoking cessation around the world and an overview of different tobacco cessation activities pharmacists are involved in can be found in FIP's "Establishing tobacco-free communities: A practical guide for pharmacists".<sup>83</sup>

#### 3.2.2 Exposure to allergens

Exposure to allergens is very common. With many allergen types, individuals can be exposed to indoor or outdoor allergens. Examples of indoor allergens include house dust mites, furred pets (cats and dogs), pest rodents, cockroaches and fungi. Outdoor allergens include grass pollen and grass weed. In addition, some foods and medicines are common allergens for many people. Patients who develop sensitivity to indoor or outdoor allergens are likely to develop allergic status. Persistent exposure to allergens, especially pollen, can trigger allergic reactions that include allergic rhinitis and allergic conjunctivitis, and induce or worsen asthma symptoms, leading to poor asthma control.<sup>8</sup>

Pharmacists play a role in the education for the reduction of allergen exposure as well as the treatment of allergies. Pharmacists can help patients identify what potential allergens they are reacting to, or recommend allergy testing at a physician's office for allergen identification. Allergen tests can measure their atopic status via skin prick tests or by measuring the levels of serum immunoglobulin E. A positive test and a history of developing respiratory symptoms after exposure to a specific allergen confirm allergic asthma.<sup>8</sup>

Avoiding indoor allergens is not recommended for asthma because there is no clinical benefit, even for sensitised patients.<sup>84</sup> Besides, avoidance strategies can be complicated and expensive. There is evidence, however, that correcting dampness or mould in homes can minimise asthma symptoms in adults. Also, pharmacists can recommend self-care measures for patients such as washing bedsheets weekly and vacuuming daily if they have a pet dander allergy. Outdoor allergens can be effectively avoided by remaining indoors, closing windows and doors, and using air conditioners.<sup>8</sup>

Patients with predominant allergies can benefit from allergen-specific immunotherapies. Currently, there are two approaches in immunotherapy: subcutaneous and sublingual.<sup>85, 86</sup> Before selecting either method, the healthcare professional should compare it to the pharmacological and avoidance options concerning the risk of side effects, inconvenience and cost of allergen immunotherapy.<sup>87</sup>

#### 3.2.3 Air pollution (outdoor and indoor)

Air pollution is a growing problem that has a significant impact on respiratory health. One review on the environmental and health impacts of air pollution states that particulate matter (particles of variable but very small diameter) penetrates the respiratory system via inhalation, causing respiratory and cardiovascular diseases, reproductive and central nervous system dysfunctions, and cancer.<sup>88</sup> Both indoor and outdoor pollution are considerable risk factors for asthma and COPD exacerbations.<sup>89,90</sup> Air pollution ultimately affects patients' quality of life as it impacts lives daily. According to the WHO, "almost all of the global population (99%) breathe air that exceeds WHO guideline limits and contains high levels of pollutants, with LMIC suffering from the highest exposures". Air quality is intimately related to climate change, so campaigns and policies to reduce air pollution offer a win-win strategy for both climate and health.<sup>91</sup>

The primary indoor air pollutants are nitric oxide, nitrogen oxides, carbon monoxide, carbon dioxide, sulphur dioxide, formaldehyde and endotoxins.<sup>92</sup> The primary sources of indoor air pollution are improperly vented cooking and heating devices. Common outdoor air pollutants include nitrogen oxides, acidic aerosols and particulate matter.<sup>89</sup> Several studies linked the proximity to main roads of homes and schools with increased asthma morbidity.<sup>93-95</sup>

Many patients are aware that outdoor pollutants tend to be from industrial emissions, construction, vehicle emissions and forest fires. However, not many patients are aware of the indoor pollutants that could be harming their health. These pollutants are smoking, building materials, cleaning products, air freshener products, and solid fuel use in cooking (e.g., coal, wood and animal dung). One study looked at the association between household air pollution and COPD and found that patients that were exposed to household air pollution were 41% more likely to have COPD than those without exposure.<sup>96</sup> People should use non-polluting heating and cooking devices to minimise the build-up of indoor air pollutants.

Pharmacists have a role in preventing and mitigating the risk of air pollutant consequences by providing patient education and treatment regimens in cases of respiratory diseases and infections.<sup>54</sup> Healthcare professionals should advise people living with CRDs to manage their exposure to risk factors by knowing their triggers and reducing their exposure to them. People at risk of asthma triggers may need to keep windows closed. Individuals can restrict exposure to outdoor pollutants by staying indoors and avoiding weather conditions that facilitate air pollution, such as thunderstorms.<sup>97</sup> However, people at risk of COPD may need to reduce exposure to sources of indoor air pollution by increasing ventilation. This may include opening windows, using chimneys, banning indoor smoking, or, if these are not possible, ensuring that children are kept away from polluted spaces. Reduction of outdoor air pollutants requires national and local government policies. FIP's global survey about mitigating the impact of air pollution on health can found <u>here</u>. Examples of campaigns advising on the reduction of air pollution exposure can be found <u>here</u>, <u>here</u> and <u>here</u>.

There has been some information on the impact of diet in preventing pollution repercussions on respiratory diseases. A review about pollution and respiratory disease looked at the role of diet in the prevention of respiratory disease due to pollution and concluded that there was evidence that carotenoids and vitamins D and E were useful in the protection of pollution damage that leads to asthma and COPD. This review also noted that vitamin C, curcumin, choline and omega-3 fatty acids have some protective role but there needs to be more data to further support that claim.<sup>98</sup> With training in this area, pharmacists can play a role in providing information to patients on foods rich in these nutrients and, if necessary, indicate a food supplement suitable for the patient's needs.

#### 3.2.4 Climate change

Climate change has a significant impact on every aspect of human life, from agriculture to infrastructure, economics and, perhaps most importantly, health. A review by Doherty and colleagues discusses the impact of climate change on human health in Europe through its effects on air quality. According to the authors, the key processes that influence air quality occur through changes in temperature, water vapour, precipitation and clouds, and meteorological transport and mixing.<sup>99</sup> These are all factors that are affected by climate change. They concluded that extreme air pollution episodes are associated with changing weather patterns, such as heat waves and stagnation episodes.<sup>99</sup> It can also be concluded that, if climate change can worsen the quality of life for patients with CRDs.

An article by Eguiluz-Gracia and colleagues, which studied the effect of air pollution and climate change on asthma and allergic rhinitis (AR), validated Doherty's argument by concluding that: (i) higher temperatures and increased frequency of heatwaves amplify the exacerbation rate, morbidity and mortality of respiratory diseases; (ii) seasonality and severity of AR and asthma are affected by the growth patterns of allergenic species, which can act synergistically with air pollutants; (iii) global warming and a changing climate may alter the growth and proliferation of allergenic species dominating distinct ecological niches; and (iv) intensive rain and flooding that may result from climate change induce dampness and fungal proliferation in affected households, which can worsen indoor air quality.<sup>100</sup>

Doherty *et al* also acknowledge that, in the near term, air quality will be dominated primarily by carbon emission changes rather than changes in climate or long-range transport, and that stronger emission controls will be needed in the future to avoid higher health risks associated with climate change-induced worsening of air quality in populated regions.<sup>99</sup> Climate change and global warming will only help to exacerbate respiratory illness. People must work to combat this health threat.

One way healthcare professionals can contribute to the fight against climate change is by changing the types of medicines they prescribe. A United Kingdom study by Starup-Hansen and colleagues explored the role of

inhaler prescribing in climate change.<sup>101</sup> The study states that around 3.5% of the UK National Health Service's (NHS) carbon footprint is derived from pressurised metered-dose inhalers (pMDIs), which are used in the management of asthma and COPD. This is because pMDIs contain a hydrofluoroalkane (HFA) propellant, which has a higher global warming potential. On the other hand, dry powder inhalers (DPIs) contain substances that can impact marine eutrophication<sup>102</sup> and fossil depletion.<sup>103</sup> By (i) incentivising prescribers to recommend inhalers without HFA propellant, such as DPIs, or to shift to pMDIs containing a HFA propellant with a low global warming potential, e.g., HFA-152a, (ii) considering inhaler recycling programmes, (iii) reducing SABA use and (iv) combining inhalers,<sup>104</sup> healthcare professionals and healthcare systems as a whole can reduce their carbon footprint, their environmental impact and their contribution to global climate change.<sup>101</sup> In addition, manufacturers have a responsibility to make inhalers more recyclable and introduce dose counters for all inhalers. "Recover and Breathe" is the first project in Europe to raise environmental awareness aimed at correctly disposing of all respiratory inhalers from all manufacturers through an organised collection in pharmacies.

#### 3.2.5 Occupational exposure

According to the American Thoracic Society and the European Respiratory Society, occupational exposure contributes largely to the number of cases of respiratory diseases in adults across the world.<sup>105</sup> Occupational exposure to sensitising agents accounts for about 5%–20% of new cases of adult-onset asthma. Persistent exposure to occupational sensitisers can precipitate or worsen existing asthma symptoms. Sometimes, however, exposure to high levels of occupational sensitisers can trigger asthma.<sup>106, 107</sup> An international prospective study of people from 13 countries demonstrated an elevated risk of asthma among people exposed to inhalation accidents involving fires, cleaning products or chemical spills.<sup>108</sup>

The management of occupational asthma involves early diagnosis and elimination of sensitising agents. The pharmacist's role in preventing and mitigating the risk of occupational exposure is to provide patient education on the consequences of occupational exposure leading to respiratory diseases or infections. They can help people understand what occupational exposure is and which occupational sensitisers they may be exposed to, and can recommend prevention strategies so workers can mitigate their exposure.<sup>106, 107</sup>

Pharmacists should refer suspected or confirmed cases of occupational asthma to specialists for expert assessment and advice. Besides removing patients from further exposure and requiring a change in occupation, some measures can successfully minimise occupational sensitisers in industrial settings. Pharmacists can encourage workers to take the necessary precautions if they are working in an area where they may inhale hazardous particles. They can also recommend workers wear masks, gloves, covered clothing and protective eye equipment to prevent any skin contact or inhalation of the particles.<sup>106</sup>

Prolonged exposure to organic and inorganic dust, chemical agents and fumes in workplaces poses a significant risk factor for COPD. A statement by the American Thoracic Society associated about 10%–20% of COPD cases with occupational exposures.<sup>109</sup> Several studies have demonstrated a link between occupational exposures and COPD symptoms.<sup>110-113</sup> So, it is essential to stop further exposure to potential irritants by advising patients to take relevant avoidance measures.

In summary, occupational exposure to sensitising agents is a significant risk factor for asthma and COPD. Pharmacists should employ early identification and prompt elimination of occupational sensitisers to prevent further exposure. It is important to note that patient education plays a critical role in advising patients on how to eradicate or reduce exposure to potential occupational irritants.

#### 3.2.6 Respiratory infections

Viral respiratory infections trigger asthma exacerbations. Many children suffer from wheezing episodes due to respiratory diseases in their early life. Later in life, these infections subside; however, some children develop asthma.<sup>114</sup> The most commonly implicated virus is the human rhinovirus (HRV). Other viruses include respiratory syncytial virus (RSV), influenza and coronaviruses.<sup>115</sup> Respiratory viral infections can severely worsen symptoms in patients with established asthma. Studies show that they cause about 80% of asthma exacerbations in children and adults.<sup>116</sup>

The main recommendation to mitigate the impact of respiratory infections in people with asthma is to adopt prevention strategies. Several respiratory hygiene measures effectively reduce the transmission of viral

respiratory infections in households, schools and other social areas. They consist of frequent handwashing, physical distancing and wearing face masks.<sup>117</sup> In 2020, Scotland and Wales reported a 36% decline in emergency admissions due to asthma, partly due to the hygiene measures instituted at the peak of the COVID-19 pandemic.<sup>118</sup> Studies also recommend general immunological strategies such as maintaining a healthy diet, having adequate exercise and having proper sleep, to improve immune function since most respiratory viral infections are self-limiting. Some common methods are adequate exercise, a healthy diet and proper sleep.<sup>119</sup>

Since there are currently no practical antiviral therapies and vaccines against HRV and RSV, the role of primary prevention against viral respiratory infections cannot be understated. There are, however, safe and effective influenza vaccines and antiviral treatments. Therefore, pharmacists should monitor and effectively manage respiratory infections in asthma patients, especially in children and pregnant women.<sup>120</sup> In the clinical setting, pharmacists should collaborate with other healthcare practitioners to:

- Identify asthma patients at high risk of contracting viral respiratory infections;
- Determine the most appropriate definitive and symptomatic treatments for the infections;
- Initiate, modify and monitor the efficacy of the selected regimen;
- Identify suitable candidates for immunoprophylaxis, with a particular emphasis on patient safety;
- Administer influenza vaccines where supported by regulations; and
- Implement policies for the management and prevention of respiratory infections.<sup>121,122</sup>

They also have a significant role in patient education concerning the importance of primary prevention measures against respiratory infections. These include the benefits of influenza vaccines, proper hygiene measures, and the adoption of immunological strategies.<sup>121, 122</sup>

Both bacterial and viral infections cause significant AECOPD, in contrast to asthma, where viral infections are the major risk factor. These infections trigger AECOPD events via airway inflammation resulting in diminished airflow and increased lung hyperinflation.<sup>123</sup> The main bacteria implicated in COPD are *Streptococcus pneumoniae*, *Haemophilus influenzae*, *Moraxella catarrhalis*, *Enterobacter*, and *Pseudomonas aeruginosa*. The viral infections of concern include influenza, rhinovirus, parainfluenza and metapneumoviruses.<sup>124</sup>

Pharmacists have a role in ensuring the rational use of antibiotics when managing bacterial infections in COPD cases. When dispensing, they should confirm that antibiotic regimens are in accord with individual patient factors such as type of infection, comorbidities and risk factors. Therapeutic care should also incorporate routine monitoring of the treatment regimen for efficacy and adverse effects.<sup>125</sup> The same principles apply when dispensing the appropriate antivirals to manage viral infections in COPD cases. Influenza vaccination is also beneficial in preventing the incidence of AECOPD, as well as in asthma.

There are documented practical examples of managing bacterial and viral infections in patients living with COPD. A multicentre clinical trial in Spain found that a course of amoxicillin/clavulanate had a 74.1% success rate in treating cases of mild-to-moderate COPD and significantly decreased the rates of AECOPD events.<sup>126</sup> Another study conducted in Greece illustrated the efficacy of levofloxacin/imipenem or colistin for treating multidrug-resistant bacterial infections.<sup>127</sup> A clinical trial in Belgium showed that a three-month regimen of low-dose azithromycin prevents treatment failure among patients admitted with infectious AECOPD.<sup>128</sup>

#### 3.2.7 Physical activity

Physical activity can trigger asthma symptoms in young children and many patients. Asthma due to physical activity often indicates poor symptom control. Exercise-induced bronchoconstriction (EIB) can be managed effectively and should not stop people with asthma participating in physical activity, including competitive sport. The management of EIB involves the following strategies:<sup>129</sup>

- Administration of ICS as regular controller treatment for asthma symptoms;
- Administration of SABAs before exercising;
- Advising athletes to warm up adequately before training;
- Advising athletes to avoid training in extreme cold weather conditions; and
- Assessing asthma patients' inhaler technique and adherence to their controller medication.

Despite the potential of physical activity to cause asthma exacerbations, moderate exercise still benefits asthma control and lung function.<sup>130</sup> As a non-pharmacological intervention, regular physical activity should be recommended by pharmacists to people with asthma. For children with asthma, swimming improves lung function and cardiopulmonary fitness.<sup>131</sup>

Physical inactivity is both a cause and consequence of COPD exacerbations. COPD patients often have multiple extrapulmonary manifestations and comorbidities, resulting in more sedentary time and less physical activity.<sup>132</sup> Patients living with COPD engage in fewer physical activities due to disease severity, comorbidities, fear of exacerbations, behavioural changes and breathlessness on exertion.<sup>133·135</sup> Several studies demonstrated an inverse relationship between levels of physical activity and lung function or the incidence of COPD.<sup>136, 137</sup> These findings are corroborated by a study that established physical inactivity as one key predictor of COPD outcomes. Lower activity levels predisposed patients to a high risk of exacerbations and all-cause mortality.<sup>138</sup> Due to the established benefits of regular physical activities on the risk of COPD.<sup>139</sup> the GOLD strategy recommends that all COPD patients should incorporate regular physical activities in their action plans.<sup>132</sup> In the <u>COPD Magazine</u>, an online magazine published by the IPCRG for people with COPD to support them to self-manage their breathing and physical activity, there are suggestions of different physical activities that decrease sedentary time and improve patients' breathing and well-being.

#### 3.2.8 Diet and nutrition

In the context of asthma, nutritional factors play a role in the control of symptoms. For instance, asthma is more challenging to manage in obese patients.<sup>140</sup> Dietary restriction is one strategy employed to induce weight reduction in obesity. Diets rich in fruits and vegetables are also recommended for asthma patients due to their antioxidant properties.<sup>141</sup> Scientists reason that the antioxidant properties of healthy diets, such as plant-based diets, can mitigate the inflammatory processes characteristic of asthma.<sup>142, 143</sup>

Allergies to food contents and chemicals pose significant risk factors for asthma-related mortality.<sup>144</sup> Sulphites are the most commonly identified causes of severe asthma exacerbations among sensitive patients. Sulphites typically occur in processed potatoes, shrimp, dried fruits, beer and wine.<sup>145</sup> Avoidance of specific foods and chemicals is justified in case of confirmed food allergies or food chemical sensitivities.

COPD patients are at high risk of malnutrition.<sup>146</sup> Some causes of malnutrition include:<sup>147</sup>

- Disease effects (e.g., breathlessness, anorexia, inflammation);
- Psychological factors such as depression;
- Social isolation;
- Poor living conditions;
- Increased nutritional requirements of the body; and
- Adverse effects of medicines such as changes in taste and dry mouth due to inhaled therapy and oxygen therapy.

Malnutrition is associated with increased rates of mortality among patients living with COPD.<sup>147</sup> Pharmacists are therefore advised to carry out routine nutritional screening of all COPD patients using validated screening tools such as the <u>Malnutrition Screening Tool</u>, the <u>Malnutrition Universal Screening Tool (MUST)</u>, and the <u>Subjective Global Assessment</u>. Patients identified with malnutrition should be managed using the principles of recording risks, setting nutritional goals and monitoring progress. Pharmacists should offer dietary advice to patients to ensure they meet daily requirements for essential nutrients. Where applicable, oral nutritional supplementation should be initiated.<sup>147</sup> A practical guide to "Managing malnutrition in COPD" can be found <u>here</u>.

#### 3.2.9 Stress

Stress is a significant risk factor for developing asthma or triggering asthma exacerbations in children and adults due to changes in the airways that trigger an inflammatory response.<sup>148</sup> <sup>149</sup> Features of emotional stress, such as anger, fear or crying, may cause hyperventilation, narrowing the airways.<sup>150, 151</sup> Panic attacks also result

in hyperventilation and decreased pulmonary function.<sup>152</sup> Mothers experiencing emotional stress during pregnancy predispose their children to develop asthma.<sup>153, 154</sup>

Stress associated with life events negatively impacts the mental health of individuals. It can then lead to behavioural changes such as frequent smoking, inadequate sleep and physical inactivity, increasing the risk of COPD.<sup>155</sup> Stress can trigger inflammatory processes in the body, potentially leading to COPD exacerbations.<sup>156</sup> The sources of stress in COPD patients include fear of the illness, breathing difficulties, heightened emotions and limited physical activity.<sup>157</sup> In some instances, work-related stress can induce COPD exacerbations.<sup>156</sup> An observational cohort study found that one in four people with COPD has anxiety and depressive symptoms.<sup>158</sup> Depressive symptoms worsen pulmonary rehabilitation. Stressed individuals will likely have poor symptom control of asthma and COPD due to non-compliance with their medication.<sup>158</sup>

Pharmacists should evaluate asthma and COPD patients for stress, anxiety or depression signs using brief evidence-based tools such as <u>Patient Health Questionnaire 4 (PHQ-4)</u>.<sup>159</sup> Any identified cases should be referred to the GP for further mental assessment and treatment.<sup>160</sup> Effective management of stressed patients involves engaging them to identify their triggers and prepare goals and strategies for coping with stress. Other identified measures for managing stress include recommending relaxation strategies and breathing exercises. The evidence is laid out <u>here</u> for COPD and mental health.

#### 3.2.10 Medicines-induced asthma

Non-steroidal anti-inflammatory drugs (NSAIDs), especially aspirin, ibuprofen, diclofenac and naproxen, can cause severe asthma exacerbations.<sup>161</sup> Aspirin-exacerbated respiratory disease (AERD) often occurs among cases of medicines-induced asthma, with a prevalence of 7% in general adult asthma and 15% in severe asthma cases.<sup>162, 163</sup> It presents as an acute asthma attack shortly after taking NSAIDs.

Pharmacists can identify patients at risk of medicines-induced asthma by asking about their medication history. This includes a record of their current medicines as well as previous incidences of reactions. The diagnosis of AERD consists of a history of asthma exacerbations after taking aspirin or other NSAIDs.<sup>164</sup> It is then confirmed via an aspirin challenge test, which should be carried out in a specialised centre with adequate resuscitation capabilities.<sup>165</sup>

Pharmacists should advise patients to avoid medicines that can worsen their asthma symptoms and recommend suitable alternatives. For instance, pharmacists should advise AERD patients to avoid NSAID containing products and other cyclooxygenase-1 (COX-1) inhibitors. In conditions where NSAIDs are necessary, suitable options include paracetamol and COX-2 inhibitors, in countries that allow this latter option.<sup>166</sup> The recommended treatment for asthma in AERD is inhaled corticosteroids.<sup>167</sup> Sometimes, aspirin desensitisation may be considered.<sup>168</sup>

Beta-blockers, including ophthalmic preparations, may cause bronchospasm. However, these medicines have proven to be beneficial in acute coronary events. Asthma is not an absolute contraindication to beta-blockers, but the relative risks and benefits should be considered, and treatment must be initiated under close medical supervision by a specialist.<sup>8</sup>

## 3.3 The role of vaccination in the prevention and management of CRD complications

Influenza is an acute viral respiratory illness that can be severe and, in some high-risk groups, result in death. The risk of influenza infection can be reduced by annual vaccination. Annual immunisation is thus currently recommended by many national and international organisations, such as the WHO,<sup>169</sup> the US Centers for Disease Control and Prevention (CDC),<sup>170</sup> and the European Centres for Disease Prevention and Control.<sup>171</sup> However, many countries are well below the target immunisation rates for individuals with high-risk conditions, including respiratory diseases. This low coverage may be due to complex and multifactorial reasons, but the lack of confidence in the effectiveness and safety of vaccines is a major factor.<sup>172</sup> Respiratory viruses, including influenza, rhinovirus, respiratory syncytial virus and coronaviruses, have been shown to increase the risk of asthma exacerbations.<sup>173</sup> A few studies have shown a significant reduction in exacerbations in vaccinated subjects compared with those that received a placebo.<sup>174</sup> A recent systematic review and meta-analysis study that included a wide range of observational studies with various study designs showed a reduction in the risk of asthma exacerbations.<sup>172</sup> Therefore, the GINA guidelines advise that patients with moderate to severe asthma receive an influenza vaccination every year or at least when vaccination of the general population is recommended.<sup>8</sup>

According to the COPD GOLD guidelines, the influenza vaccination reduces severe illness and death in patients with COPD.<sup>9</sup> In addition, a population-based study suggested that patients with COPD have a decreased risk for ischaemic heart disease when vaccinated for influenza over a period of time.<sup>175</sup> Vaccines that are either killed or live inactivated viruses are recommended since these are most effective in the elderly population with COPD.<sup>9</sup>

Pneumococcal disease is a group of illnesses caused by *Streptococcus pneumoniae*. There are two vaccine types available globally: pneumococcal conjugate vaccines (PCV13, PCV15, and PCV20) and pneumococcal polysaccharide vaccine (PPSV23).<sup>173, 176</sup> The COPD GOLD guidelines recommend that all patients aged 65 years or over should receive PCV13 and PPSV23. Also according to the CDC, patients aged 65 years or over should receive the PPSV23 vaccine. Administering a single dose of PPSV23 at least one year after a patient received PCV13 completes the pneumococcal vaccination series.<sup>177</sup> Based upon a randomised control trial, PPSV23 has been shown to reduce the incidence of community-acquired pneumonia in patients with COPD aged 65 years or over with an FEV1 of less than 40% or other comorbidities.<sup>178</sup>

According to a Cochrane database systematic review conducted in 2016, injectable polyvalent pneumococcal vaccination provides significant protection against community-acquired pneumonia. Overall, vaccination reduced the risk of COPD exacerbations.<sup>179</sup>

GINA 2022 and GOLD 2022 guidelines recommend that individuals with asthma and COPD, respectively, should be up to date with the COVID-19 vaccine, including booster doses, dependent on national recommendations.<sup>8,</sup> <sup>9</sup> The CDC and GOLD guidelines also recommend the Tdap (tetanus, diphtheria and acellular pertussis) vaccine in patients with COPD or asthma who have not been vaccinated in adolescence.<sup>9, 180</sup> Lastly, the zoster vaccine is recommended in adults with COPD aged 50 years or over to protect against shingles.<sup>9</sup>

Overall, vaccines can positively impact health, cognitive development and productivity, leading to healthier lives, less severe forms of diseases, fewer limitations in terms of family and social interactions, and better functional ability.<sup>181, 182</sup>

## 4 Screening tests for CRDs

Community pharmacists are uniquely positioned as the first point of contact with healthcare systems. Therefore, they are also ideally placed to conduct screening tests for CRDs. Not only are they capable of detecting patients who do know that they could be living with a chronic respiratory condition, but they can also refer to a physician those people who are at risk of having flare-ups of their condition. The role of pharmacists in screening and subsequent management of CRDs was cited in a systematic review, in which the authors concluded that community pharmacists play an effective role in screening people with poorly controlled asthma and undiagnosed COPD and providing them with the necessary disease management interventions.<sup>183</sup>

## 4.1 Screening of undiagnosed patients with asthma

Population-based studies in children, adults and the elderly worldwide suggest that from 20%–70% of people with asthma in the community could remain undiagnosed.<sup>184</sup> Community pharmacists can help detect those undiagnosed patients, especially in the case of adolescents and adults without suspicion of asthmatic disease in childhood. It is vital to seize the opportunity when they visit the pharmacy in search of relief for those signs or symptoms that they believe are minor and not part of a more complex chronic disease.

Pharmacists should be attentive to people who present a continuous history of signs or symptoms such as wheezing, shortness of breath, chest tightness or dry cough, in addition to having a history of atopy, or other allergic conditions such as rhinitis or hives.<sup>8</sup> Also, they should be attentive to patients who are continuously demanding antitussives, and those that use SABAs without a medical diagnosis, or patients with uncontrolled chronic rhinitis. A pharmacist's intervention in these cases should be to refer such individuals to their physicians in order to confirm, or rule out, an asthma diagnosis.<sup>61</sup>

## 4.2 Screening of undiagnosed patients with COPD

Globally, there is a large variation in the prevalence of COPD, with 10%–95% under-diagnosis due to differences in the definition of diagnosis used, and the unavailability of spirometry.<sup>185</sup>

Due to the progressive and irreversible nature of COPD, a delay in diagnosis leads to higher morbidity, as well as higher healthcare costs. According to the WHO, early diagnosis and treatment, including smoking cessation support, is needed to slow the progression of symptoms and reduce flare-ups of COPD. Thus, early diagnosis is essential.<sup>7</sup> Furthermore, national and global guidelines such as GOLD, recommend mechanisms to detect those patients at the early stages of the disease, given the importance of early treatment for clinical and cost-effectiveness reasons.<sup>9</sup> Given the unfeasibility of mass screening, the most efficient alternative is to select populations at high risk and use screening or diagnostic support tests that meet minimum sensitivity requirements, reproducibility and validation.<sup>186</sup>

COPD should be considered in all individuals over 35 years of age who present potential risk factors, such as tobacco smoking, long-term exposure to other lung irritants (such as second-hand smoke, air pollution or chemical fumes), and dust from the environment or workplace, and presenting chronic symptoms compatible with the disease such as cough, expectoration and exertional dyspnoea.<sup>9</sup>

In order to screen people at risk, pharmacists may use validated questionnaires such as COPD Population Screener, COPD Diagnostic Questionnaire and Initial Screening Questionnaire to identify high-risk patients and refer them to a physician for medical assessment.<sup>9, 186-188</sup> See Table 9 for details and links for further information.

Lung function tests have been presented as an opportunity for pharmacists to improve evidence-based practice for screening CRDs.<sup>189</sup> The efficacy of COPD screening in community pharmacies has been reported in several studies, either using small portable devices, such as COPD6-Vitalograph and PiKo-6, or using more sophisticated devices such as the EasyOne Air.<sup>34, 190</sup> Portable microspirometers measure the forced expiratory

volume in the first second (FEV1) and the volume at six seconds (FEV6) and simultaneously provide the calculation of the FEV1/FEV6 ratio as a measure of obstruction. GOLD experts have defined the disease based on spirometric criteria by using the FEV1/FVC (forced vital capacity) ratio <70%. Additionally, GOLD experts advise spirometry as the gold standard to diagnose COPD due to its accurate and repeatable measurement of lung function.<sup>9</sup>

Lung function tests via validated portable devices, which measure some significant indicators such as FEV1, FEV6, and FEV1/FEV6, are already being used by pharmacists in some settings.<sup>187</sup> Findings from a meta-analysis of 11 studies that compared the diagnostic accuracy of FEV1/FEV6 with FEV1/FVC have shown FEV1/FEV6 to have high sensitivity and specificity for detection of COPD in adult populations.<sup>191</sup>

However, microspirometers do not measure the FVC value. FVC is the volume of air expelled during the forced expiratory manoeuvre (being an indicator of lung capacity expressed in litres). It is a parameter that can only be determined using diagnostic spirometers.

The reason why it is suitable to claim that results obtained on microspirometers can be useful in the diagnosis of COPD is that FEV6 is an acceptable surrogate for FVC in the diagnosis of airway obstruction in adults. Furthermore, it is easier to perform than conventional spirometry and has acceptable sensitivity and specificity values.<sup>192</sup>

However, the use of the FEV1/FEV6 cut-off value of <0.75 as the best correlation with the FEV1/FVC ratio,<sup>34</sup> has been questioned and eventually it appears that the most accurate cut-off value depends on which microspirometer has been used.<sup>193, 194</sup> Nevertheless, all of them have been shown to be useful for screening for chronic airflow obstruction. Therefore, microspirometers can be a valuable means to detect airway obstruction, also giving information on the classification of the patient's possible COPD according to the GOLD scale, based on FEV1.<sup>9, 193-195</sup>

It should be noted that the performance of these tests by pharmacists is not being proposed with the goal of establishing a final diagnosis but to describe interventions that have been implemented by pharmacists and assessed as described in the cited literature. The objective of these interventions is to identify patients at risk of having COPD. They must be referred to a physician for further clinical evaluation, conventional spirometry and eventual treatment.<sup>9</sup>

## 4.3 Monitoring and referring patients with CRDs

#### 4.3.1 Asthma

In order to assess the current control of patients with asthma, various validated questionnaires have been developed that are simple and easy for patients to complete. Those that have been more extensively validated and culturally adapted are the Asthma Control Test (ACT),<sup>196</sup> the Asthma Control Questionnaire,<sup>197</sup> and the Control of Allergic Rhinitis and Asthma Test (CARAT) which is the only one that also assesses allergic rhinitis.<sup>198</sup> See Table 9 for details and links for further information.

Several studies have demonstrated that the ACT questionnaire could be a useful tool to assess the degree of control of patients with asthma in a community pharmacy.<sup>55, 199</sup> By using these questionnaires, pharmacists can identify partially or poorly controlled patients, who should be referred to a general practitioner, but not before conducting a review of their treatment, since sometimes pharmacist-led interventions are sufficient to improve a patient's symptoms and achieve the necessary control of the disease.<sup>200</sup> Research has shown that patients who receive specific asthma self-management services from community pharmacists increased their quality of life, decreased their symptoms and increased adherence to their maintenance treatments in comparison with those who do not.<sup>31, 200</sup>

Peak expiratory flow (PEF) assessment by using a peak flow meter (PFM) is another system which has been used in order to assess asthma control in community pharmacies.<sup>201, 202</sup> A PFM is a hand-held, inexpensive and easy-to-use device that measures how fast someone can breathe out forcefully. It is a measure of the amount of narrowing of the airways. The personal best value (personal peak flow number) for a given person should be recorded and, ideally, it should be kept at this level. Peak flow normally goes down a little with age, and

normal rates for every person will depend on gender, race and height. The PEF varies widely during the day: it is usually at its lowest rate in the early morning and at its highest rate in the afternoon. In a person who does not have asthma, it can range between 10% and 15%. In a person with poorly controlled asthma, it can change significantly by more than 20%. Due to the fact that asthma is a variable condition, PEF should be measured several times daily and for two weeks in order to get the most benefit from its use. PEF meters can be used both to support the diagnosis of asthma, and for monitoring purposes.<sup>203</sup> Long-term PEF monitoring is generally only recommended for patients with severe asthma, or for those with impaired perception of airflow limitation.<sup>8</sup>

The fractional exhaled nitric oxide (FeNO) test is another way that has been used in primary care for asthma management. The FeNO test measures the level of NO in the exhaled breath and provides an indication of eosinophilic inflammation in the lungs. Alongside a detailed clinical history and other fundamental tests to assess variability (peak flow meter, spirometer), it is used to support the diagnosis of asthma and for monitoring purposes. However, its use has been anecdotal in community pharmacy settings so far. Moreover, robust evidence of its cost-effectiveness has not been reported yet.<sup>204</sup>

#### 4.3.2 COPD

With regard to assessing COPD control in community pharmacies, pharmacists may use some simple tests such as the COPD Assessment Test (CAT)<sup>205</sup>, the Clinical COPD Questionnaire (CCQ),<sup>206</sup> and the Modified Medical Research Council (mMRC) dyspnoea scale.<sup>207</sup> See Table 9 for details and links for further information.

The mMRC scale is widely used to measure breathlessness because of its brevity and simplicity. It is easy to administer as it allows the patient to indicate how their breathlessness affects their mobility. The CAT score is a multidimensional method, which also assesses other symptoms and health status. CAT is a standardised and simple health-related quality of life (HRQoL) questionnaire for routine clinical practice. It is structured into eight clinical questions about clinical characteristics, activities, self-confidence, sleep and sense of strength, with a weighting for each of these between zero (lowest) and five (highest). The obtained score correlates closely with quality of life. The questionnaire has good validity and reliability, as well as excellent internal consistency. The test can be self-administered and is very sensitive to identify changes in case of exacerbations.<sup>208</sup> Therefore, not only is CAT a reliable HRQoL questionnaire, it is also a relevant tool to predict and detect exacerbations. Although the use of CAT in community pharmacies is not yet widely implemented,<sup>202</sup> it has been reported as a significant tool for identifying patients at high risk of exacerbations.<sup>209</sup>

Community pharmacists may also use microspirometers to assess COPD control and detect exacerbations due to the fact that they can measure the FEV1 value with acceptable sensitivity and specificity.<sup>194</sup>

Table 9 outlines the main tools and point-of-care tests to support pharmacists' role in CRDs.

| CRD  | Screening technique                | Type of tool/<br>device | Aim   | Required<br>investment | More<br>information |
|------|------------------------------------|-------------------------|---|------------------------|---------------------|
| COPD | COPD Population<br>Screener        | Questionnaire           | <ul> <li>Detecting high-risk<br/>patients for spirometry<br/>testing</li> </ul> | None                   | <u>Click here</u>   |
| COPD | COPD Diagnostic<br>Questionnaire   | Questionnaire           | <ul> <li>Detecting high-risk<br/>patients for spirometry<br/>testing</li> </ul> | None                   | <u>Click here</u>   |
| COPD | Initial Screening<br>Questionnaire | Questionnaire           | <ul> <li>Detecting high-risk<br/>patients for spirometry<br/>testing</li> </ul> | None                   | <u>Click here</u>   |

#### Table 9. Tools and point-of-care tests to support pharmacists' role in chronic respiratory diseases

| CRD    | Screening technique   | Type of tool/<br>device | Aim  | Required<br>investment | More<br>information                 |
|--------|---|-------------------------|--|------------------------|-------------------------------------|
| COPD   | Portable<br>microspirometers (e.g.,<br>COPD6-Vitalograph and<br>PiKo-6) | Device                  | <ul> <li>Evaluating lung function</li> <li>Detecting airway<br/>obstruction for<br/>spirometry testing</li> <li>Assessing COPD control<br/>and detecting<br/>exacerbations</li> <li>Measuring FEV1, FEV6,<br/>FEV1/FEV6 ratio</li> </ul> | Medium                 | <u>Click here</u>                   |
| COPD   | Sophisticated<br>spirometers (e.g.,<br>EasyOne Air)                     | Device                  | <ul> <li>Diagnostic spirometry<br/>testing</li> <li>Measuring lung function</li> </ul>   | Medium-<br>high        | <u>Click here</u>                   |
| COPD   | COPD Assessment<br>Test <sup>205</sup>                                  | Questionnaire           | <ul> <li>Assessing COPD control</li> <li>Assessing not only<br/>dyspnoea but also other<br/>symptoms and health<br/>status (health-related<br/>quality of life)</li> <li>Also used to predict and<br/>detect exacerbations</li> </ul>    | None                   | <u>Click here</u> or<br><u>here</u> |
| COPD   | Clinical COPD<br>Questionnaire <sup>206</sup>                           | Questionnaire           | <ul> <li>Assessing COPD control</li> <li>Health-related quality of<br/>life questionnaire (HRQoL)<br/>with good psychometric<br/>properties</li> </ul>   | None                   | <u>Click here</u>                   |
| COPD   | Modified Medical<br>Research Council<br>dyspnoea scale <sup>207</sup>   | Questionnaire           | Measuring breathlessness   | None                   | <u>Click here</u>                   |
| Asthma | Asthma Control Test <sup>196</sup>                                      | Questionnaire           | <ul> <li>Assessing asthma control</li> <li>A patient self-<br/>administered tool for<br/>identifying those with<br/>poorly controlled asthma</li> </ul>  | None                   | <u>Click here</u>                   |
| Asthma | Asthma Control<br>Questionnaire <sup>197</sup>                          | Questionnaire           | Assessing asthma control   | None                   | <u>Click here</u><br>or <u>here</u> |
| Asthma | Control of Allergic<br>Rhinitis and Asthma<br>Test <sup>198</sup>       | Questionnaire           | • Assessing asthma and rhinitis control  | None                   | <u>Click here</u> or<br><u>here</u> |
| Asthma | Primary Care Asthma<br>Control Screening<br>Tool <sup>210</sup>         | Questionnaire           | Assessing asthma control   | None                   | Click here                          |
| Asthma | Peak flow meter   | Device                  | <ul> <li>Measuring the peak<br/>expiratory flow (PEF) over<br/>time</li> </ul>   | Small                  | <u>Click here</u> or<br><u>here</u> |
| Asthma | Fractional exhaled<br>nitric oxide test                                 | Device                  | <ul> <li>Assessing airways<br/>inflammation and<br/>supporting the diagnosis</li> <li>Measuring the level of NO<br/>in the exhaled breath</li> </ul>   | High                   | <u>Click here</u> or<br><u>here</u> |
#### 4.3.3 Leveraging mobile applications to monitor CRDs

With the rise in mobile health (mHealth) solutions, there has been an increasing utilisation of mobile applications, coupled with gamification, to assist patients and healthcare professionals in monitoring the progress and control of CRDs. Applications are commonly designed to facilitate self-management and enhance patients' autonomy in managing their diseases. As CRDs require long-term care, many of these applications can adapt to patient's changing needs and disease control. Such interactive mHealth devices have shown to enhance patients' awareness of their condition and their confidence in self-managing and improving disease control. Such mobile applications also enhance engagement with healthcare providers and allow them to monitor their patients' symptom and disease progress and control.<sup>211</sup> From a health system perspective, these mobile applications have been found to be cost-effective.<sup>212</sup>

Pharmacists can leverage mobile applications to guide people living with CRDs in identifying triggers, monitoring their symptoms and enhancing other self-management aspects. One example of such technology that has been explored and evaluated is the Adolescent Adherence Patient Tool (ADAPT). ADAPT was introduced to adolescents living with asthma and community pharmacies in the Netherlands. ADAPT allows patients and pharmacists to monitor symptoms. It also supports medication adherence, and allows pharmacists to share educational resources (such as inhaler techniques), and includes a chat function to tall to the pharmacist. Patients and pharmacists who adopted ADAPT were generally positive and satisfied to use the mobile application.<sup>211</sup> One of the key facilitators to the uptake of ADAPT by pharmacists is the increased contact time with patients, and key facilitators to the uptake of ADAPT by patients include convenience and ease of use. However, lack of reimbursement and time constraints were significant barriers for pharmacists to use ADAPT for caring for patients living with asthma. This example illustrates the feasibility and possibility of pharmacists and pharmacy teams to use mHealth to improve care quality for people living with CRDs.<sup>211</sup>

More examples of mHealth applications, wearables and devices to manage CRDs have been reported in the <u>study</u> by Himes and colleagues.<sup>213</sup>

## 5 Referral and interprofessional collaboration to support people with CRDs

CRD treatment and management means symptom control and prevention from future risks. Thus, it is important to have smooth traceability between healthcare providers in different healthcare settings.<sup>8, 9</sup> Effective disease management requires the development of a partnership between the patient and healthcare providers, as this would enable people with asthma or COPD to gain the knowledge and skills to assume a bigger role in the management of their disease.<sup>8, 9</sup>

Pharmacists, together with other healthcare providers responsible for treating and following patients with CRDs, should encourage their patients to participate in decisions about their treatment and give them the opportunity to express their expectations and concerns. This is also known as shared decision-making, an essential element of people-centred care for the management of CRDs. This people-centred element has been advocated in the United Kingdom as "<u>no decision about me</u>, without me" — a vision of the National Health Service. This partnership needs to be dependent on each patient's case and situation. A person's willingness and ability to engage in self-management may vary depending on factors such as health literacy, and beliefs about CRDs and medicines.<sup>183, 214</sup>

Asthma and COPD are respiratory diseases that require the input of multiple care providers who need to work closely together. Well-organised care is important, and the use of a formal structured programme that determines how each component is delivered should make care more efficient and effective. Pharmacists have a major role to play in referring patients to other members of the healthcare team not only for clinical assessment and diagnosis, but also to receive additional guidance on how to make and sustain disease management and lifestyle changes in a safe and effective manner. Patients can be referred to a pneumologist, a general practitioner or family physician, a respiratory therapist, or even to structured group programmes that support individuals living with CRDs. Once these patients are referred, pharmacists can play an important role in following up with them frequently and providing encouragement and support to sustain any lifestyle changes they may have made.<sup>44</sup>

Pharmacists can provide education to patients and increase patient adherence to their medication (see Section 8.2). This is because they have frequent contact with patients, providing them with knowledge about which medication regimens have been effective or ineffective in certain patients.<sup>215</sup> Pharmacists are also likely to have current knowledge about novel medicine therapies.<sup>215</sup> With their knowledge of pharmacology, medicine interactions and evidence-based care, pharmacists can manage therapy and establish therapeutic goals with other healthcare providers such as pneumologists and respiratory therapists. They can consider individual patient factors and assess which medicines would be best suited for that individual patient to meet their therapeutic goals. Where appropriate, pharmacists can also make recommendations to other healthcare providers to initiate, modify or discontinue certain medicines as well as recommend dosing adjustments. They can also take steps to prevent adverse effects, medicine interactions and medication non-adherence, among other things.<sup>44, 183, 214</sup>

In relation to NCDs, such as CRDs, a pharmacist's referral is a relevant and valuable health resource.<sup>31</sup> Pharmacists should play a proactive role in the detection and management of CRDs in the community.<sup>216</sup> Pharmacists, especially community pharmacists, are well positioned to identity patients with uncontrolled asthma and poor COPD management and refer them for assessment by their general practitioner.<sup>31, 32</sup> Studies have shown that pharmacist-delivered asthma care programmes improve asthma control.<sup>31, 32</sup>

In order to refer patients to other healthcare professionals, pharmacists need to be available to and approachable by patients.<sup>215</sup> This includes being both knowledgeable in the physical assessment of patients and having competent communication skills in both listening to and speaking with patients. Pharmacists should also be able to access patients' health records, and have a good understanding of patients' lifestyles and socioeconomic status as these may affect the evolution of their condition and their treatment.

Pharmacists should also endeavour to establish effective collaboration with patients' physicians. In a study by Manasse and colleagues, it was stated that referrals are most effective when pharmacists and physicians have already established a working relationship.<sup>215</sup> Manasse *et al* further explain that developing working

relationships with physicians could include shadowing opportunities in which physicians and pharmacists can experience each other's working environments. This would build more trust and understanding in this interprofessional relationship.

# 6 Non-pharmacological management of CRDs

Non-pharmacological management of CRDs typically involves patients making changes to improve their habits and avoiding triggers, often with the goal of improving symptom control and reducing future risk. Making these lifestyle changes is an important component of asthma and COPD control as it supports patients in achieving their therapeutic goals. As already mentioned in Section 3.2, pharmacists can play an important role in promoting these health behaviour changes to their patients and educating them on the importance of good communication between patients and healthcare providers in order to manage disease exacerbations.<sup>217</sup>

In addition to pharmacological treatment and patient counselling based on medicine knowledge and disease management, pharmacists should always follow up on patients' daily attitudes and lifestyle behaviours. For example, pharmacists should:

- Ask asthma and COPD patients about medicines that may make asthma worse (e.g., beta-blocker medicines, and aspirin and other NSAIDs) in order to give counselling and referrals based on the individual patient's circumstances;<sup>8</sup>
- Advise asthma and COPD patients and support the management of occupational asthma, by early identification and avoidance of allergen exposure as early as possible;<sup>8</sup> and
- Inform patients about trigger avoidance.

### 6.1 Smoking cessation (treating tobacco dependence)

Smoking has multiple harmful effects on people with established asthma, and it is known as the largest risk factor contributing to the development of COPD.<sup>218</sup> Therefore, smoking cessation is very important in halting the progression of lung function decline. Smoking cessation has been shown to be more effective than all pharmacological treatments for improving COPD outcomes and reducing COPD-related mortality.<sup>218</sup> While quitting smoking cannot reverse the damage caused by COPD, smoking cessation is the only established intervention for slowing respiratory function decline (FEV1) associated with COPD.<sup>218</sup>

As such, smoking cessation is a key intervention, and pharmacists should strongly encourage those who smoke to quit and to avoid environmental smoke exposure as soon as a diagnosis is made, particularly when COPD is diagnosed in the early stages.<sup>8,9</sup>

The 5As model (Ask, Advise, Assess, Assist, Arrange) can be used to guide smoking cessation services. First, ask the patient about their current smoking status, and advise smokers to quit through pharmacotherapeutic interventions and lifestyle support. Subsequently, assess the smoker for his or her readiness to quit smoking. For people who are ready to quit smoking, assist them by drawing up smoking cessation plans and methods of quitting, as well as resources and self-help support for their cessation journey. Arrange for follow-up to monitor and motivate patients to eventually quit smoking.<sup>78</sup>

Here are some tips for quitting tobacco:77

- The first step when a patient is willing to quit is for them to have motivation (acceptance and readiness) and emotional support (from family and friends). The use of scaling questions can help ascertain the motivation (e.g., "On a scale from 1 to 10, how motivated are you to stop smoking right now?").
- When using first-line smoking cessation medicines, it is recommended to use them in combination with behavioural support from a trained professional. If the support is not available or the person is unwilling to see a specialist, then offering non-prescription medicines and pharmacy advice on how to use the treatments is more effective than doing nothing.
- Patients should list their smoking triggers and try to have a plan to avoid them.

### 6.2 Physical activity

Physical activity is often known to be a common trigger for asthma and COPD, as it can provoke symptoms of both respiratory diseases, reflecting an insufficient control of symptoms. Thus, asthma and COPD patients may often intuitively or purposefully avoid exercise and adopt a sedentary lifestyle. However, the development of a wide range of potent medicines and effective delivery devices has led to a new understanding and a change of the perception of physical activity by asthma and COPD patients. The ultimate goals of disease management is based on the minimisation of symptoms so that patients can maintain normal levels of activity and achieve good quality of life. GINA recommends that people with asthma engage in regular physical activity in order to improve their general health.<sup>8, 9, 217</sup>

Uncontrolled asthma is often associated with obesity and physical inactivity. Therefore, maintaining physical activity is important for every patient living with asthma or COPD, improving the management of CRDs. Higher adherence to physical activity is associated with positive clinical outcomes such as improved lung function and asthma control, fewer exacerbations and less use of healthcare facilities.<sup>219</sup> It also has a significant effect on reducing cardiovascular risk and in improving quality of life.<sup>9</sup>

Patients living with CRDs should be encouraged to find activities they enjoy doing, and they should try to incorporate them into their daily life at their own pace. Activities such as walking, Pilates, Tai-Chi, Qigong or yoga, are relaxing activities that combine mind and body exercise, i.e., they combine different postures, breathing techniques, meditation, concentration and gentle movements. Breathing techniques such as diaphragmatic breathing strengthen respiratory muscles and improve lung capacity.<sup>220</sup> More examples of physical activities and how healthcare professionals can encourage patients to practise them can be found in the <u>COPD Magazine</u> of the IPCRG.

### 6.3 Nutritional support

While primarily trained to address CRDs from a pharmacological perspective, pharmacists can also play a role in promoting healthy dietary approaches to their patients. Considering their clinical status (stable or exacerbation) and disease severity, asthma and COPD patients should be assessed individually when proposing nutritional support.<sup>221</sup>

Weight management and diets emphasising the consumption of plant-based foods, and avoiding the consumption of animal products at the expense of fruits, vegetables, whole grains and legumes, have been associated with reduced asthma risk and better asthma control.<sup>222</sup> Antioxidants, fibre and vitamin D protect against COPD and asthma development by strengthening the immune system and improving asthma symptoms through their effects on systemic inflammation.<sup>222</sup>

### 6.4 Pulmonary rehabilitation

The GOLD 2022 report recommends that patients with COPD should be encouraged to take part in a formal rehabilitation programme based on self-management education that includes setting patient goals, designed and delivered in a structured manner and suiting individuals' preferences and objectives, in order to gain benefits from the programme.<sup>9, 223</sup>

Physical activity can be achieved through enrolment in an exercise-based programme, such as pulmonary rehabilitation, which is designed based on a strict and specific frequency, intensity, and modality (following a list of restrictions such as smoking cessation and nutritional needs support). This intervention (programme of education about living with the condition, tailored exercise and advice on breathing techniques) is monitored by a personal programme by healthcare professionals and experts (physical and respiratory therapists, exercise specialists, and dietitians) to reduce breathlessness, control symptoms, reduce exacerbations optimising functional status and healthcare costs, and improving the quality of life for patients with COPD.<sup>223, 224</sup> More information about pulmonary rehabilitation can be found <u>here</u>.

For patients living in rural or remote areas, healthcare professionals may recommend home-based training using a stationary bicycle or a walking programme, as an alternative to the rehabilitation training programmes.<sup>9</sup>

### 6.5 Non-pharmacological management of breathlessness

Chronic breathlessness is the most common symptom in patients living with COPD and can be difficult to manage. Chronic breathlessness impacts all aspects of a patient's life, impairing quality of life. While this symptom is commonly caused by chronic lung conditions, there are many other underlying contributing factors such as obesity, heart disease, infections and vocal cord dysfunction, among others. Breathlessness also can be connected to a patient's responses to their sensations, as thoughts affect and are affected by breathing and physical activity. Patients with CRDs should address all negative thoughts in relation to breathlessness and try to manage symptoms of anxiety and low mood, as this has a great potential to improve adherence to treatment.<sup>159, 225</sup> More information about chronic breathlessness can be found <u>here</u>.

Smoking cessation and pharmacological treatment are the most effective approach when it comes to managing breathlessness. For individuals whose activity has been limited by their breathlessness, pulmonary rehabilitation could be a hugely beneficial step, with major positive outcomes for individuals and the community, since it has proved its effectiveness in relieving breathlessness, reducing tiredness, preventing deconditioning and disability, and Improving the patient's mood and sense of control over their condition.<sup>8, 224, 225</sup>

Relaxation techniques, pursed lip breathing, facial cooling with a hand-held fan or cool flannel, cognitive behavioural therapy, mindful breathing, acupuncture and positive psychology can all be effective in managing breathlessness.<sup>159</sup> These techniques fall under holistic care, which gives a sense of control and confidence to the COPD patient, reduces anxiety and depression, leading to improvement in self-efficacy.<sup>159</sup> With the aim of helping patients improve their breathing literacy, the IPCRG has developed a video: <u>How we breathe</u>.

# 7 Pharmacological management of CRDs

There are many medicines available to treat CRDs; however, their availability and affordability vary around the world. The management of asthma and COPD involves the use of inhaled corticosteroids (ICS) and bronchodilators. In asthma, long-acting beta-2-agonists (LABAs) and long-acting muscarinic antagonists (LAMAs) should never be used without Inhaled corticosteroids (ICS); in patients with COPD, the treatment is initiated with LABAs and/or LAMAs without ICS.<sup>226</sup> Chapter 7 provides an overview of the main medicines used to treat asthma and COPD.

### 7.1 Pharmacological treatment of asthma

When selecting a pharmacological treatment for asthma, the following principles must be considered:<sup>227</sup>

- Asthma medicines can be classified into two types: long-term controllers that are used for long-term control of the disease, and reliever medicines that are used for immediate rescue and are aimed at treating asthma exacerbations (acute therapy).<sup>8, 228</sup>
- The use of inhaler devices is of particular importance, as they deliver the medicine locally to the airways, and are effective at lower doses, act faster and have fewer adverse effects than systemic dosage forms.
- The choice of an inhaler device should take into account the characteristics of the patient and also their preferences. Education on the correct use of inhaler devices should always be provided in order to reduce the risk of non-adherence and increase the likelihood of therapeutic success.
- Asthma in adults and adolescents should not be treated with a short-acting beta-2-agonist (SABA) alone, because of the risks of SABA-only treatment and SABA overuse and over-reliance.<sup>8</sup>
- Treatment of persistent asthma consists of long-term maintenance treatment with an anti-inflammatory medicine (inhaled corticosteroids) and symptomatic treatment with a long-acting beta-2-agonist (LABA).
- The combination of inhaled anti-inflammatory medicines and bronchodilators is adjusted according to asthma control.
- The dose at which treatments are started depends on the severity of asthma. Initially, it should be maximal to achieve rapid symptom control. As symptoms are controlled, it can be reduced.
- Treatment should start at the earliest stages of the disease; this treatment should be staged according to the severity of the disease and should be reviewed every three to six months.<sup>8</sup>
- Treatment can be stepped down at three-month intervals when symptoms are well-controlled. ICS doses should be stepped down by 25%– 50% at each interval, until the lowest ICS dose to maintain control of asthma is achieved.<sup>8</sup>
- Patients often incorrectly assume that being diagnosed with mild asthma means that they are not at risk and do not need controller treatment. Therefore, GINA recommends avoiding the term "mild asthma" and, if it is used, to stress that patients with infrequent symptoms can still have severe or fatal exacerbations and that this risk is substantially reduced with ICS-containing treatments.<sup>8</sup>

More information on the main options for pharmacological therapy for asthma can be found in Figure 4 and Table 10.

#### Figure 4. Pharmacological therapy for asthma



#### Table 10. Therapeutic categories used in asthma

| Therapeutic category                               | Most common<br>medicines   | Main characteristics   | Main adverse<br>effects  | Pharmacist interventions/<br>considerations   | Combination therapy   |
|--|--|--|--|---|---|
| Inhaled<br>corticosteroids (ICS)                   | Beclometasone,<br>budesonide,<br>fluticasone,<br>ciclesonide,<br>mometasone and<br>flunisolide | Initial controller<br>treatment  | Most common<br>side effects<br>include<br>oropharyngeal<br>candidiasis,<br>dysphonia or<br>throat irritation. <sup>8,</sup><br><sup>43</sup> | To prevent oral side effects,<br>pharmacists should suggest that the<br>patient rinse their mouth with water<br>after using an ICS. Pharmacists also<br>should advise asthma patients on<br>smoking cessation as it reduces the<br>effects of ICS, and impairs respiratory<br>function. <sup>43</sup> | Increasing the ICS dose helps in<br>alleviating severe acute<br>exacerbations. However, if the<br>dosage exceeds the high dose,<br>further effects proportional to the<br>dose cannot be achieved, and the<br>risk of adverse effects increases.<br>Thus, it is recommended to add one<br>or more agents other than ICSs,<br>rather than simply increasing the<br>dose of an ICS. <sup>43</sup> |
| Inhaled short-acting<br>beta-2-agonists<br>(SABAs) | Salbutamol,<br>levalbuterol and<br>terbutaline   | SABAs act by causing small<br>muscles relaxation;<br>binding to the beta-2<br>receptors. They are fast-<br>acting bronchodilators<br>commonly used as a<br>reliever in an exacerbation<br>situation. <sup>43</sup> | Most common<br>side effects<br>include tremors,<br>palpitations and<br>tachycardia.43  | The risk of severe exacerbations and<br>mortality increases incrementally with<br>higher SABA use. <sup>8</sup><br>See Section 8.3.3  | In patients who only experience<br>symptoms infrequently, lasting for<br>short periods, SABAs are the only<br>recommended therapy. <sup>226</sup>   |
| Inhaled long-acting<br>beta-2-agonists<br>(LABAs)  | Formoterol,<br>salmeterol and<br>vilanterol  | LABAs act by causing small<br>muscles relaxation;<br>binding to the beta-2<br>receptors. They are the<br>first choice of<br>bronchodilators in older<br>persons. <sup>43</sup>                                     | Most common<br>side effects<br>include tremors,<br>palpitations and<br>tachycardia.43  | LABAs should be used more carefully in<br>patients with ischaemic heart disease,<br>hyperthyroidism or diabetes mellitus. <sup>43</sup>   | GINA recommends that LABAs are<br>added on to regular ICS when the<br>desired outcomes are not achieved<br>with low-dose ICS alone. <sup>8</sup><br>The combined inhalation of ICS and<br>LABAs are more effective than<br>using them separately. <sup>8</sup>  |
| Short-acting<br>muscarinic<br>antagonists (SAMAs)  | Ipratropium<br>bromide   | SAMAs mainly act by<br>blocking the<br>bronchoconstrictor<br>effects of acetylcholine.<br>Their duration of action is<br>6 to 8 hours. <sup>9</sup>  | Side effects<br>include dry<br>mouth,<br>constipation and<br>cough. <sup>229</sup>   |   |   |

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| Therapeutic category                                | Most common<br>medicines  | Main characteristics   | Main adverse<br>effects   | Pharmacist interventions/<br>considerations  | Combination therapy   |
|---|---|--|---|--|---|
| Long-acting<br>muscarinic<br>antagonists (LAMAs)    | Tiotropium<br>bromide,<br>umeclidinium<br>bromide and<br>aclidinium | LAMAs are used in adult<br>patients with a history of<br>exacerbations; however,<br>the evidence supporting<br>this use is not robust. <sup>226</sup><br>Mainly used in COPD.  | Most common<br>side effects<br>include tremors,<br>palpitations and<br>tachycardia.<br>Patients may also<br>experience<br>nausea, difficulty<br>swallowing and<br>difficulty<br>urinating. <sup>230</sup>   | Careful administration is required in<br>patients with severe heart disease.<br>LAMAs are contraindicated in patients<br>with angle-closure glaucoma or benign<br>prostatic hyperplasia with dysuria. <sup>43</sup>  | The combined inhalation of ICS and<br>LAMAs is essential for LAMAs to be<br>effective. LAMA monotherapy is not<br>safe in asthma patients. There is an<br>increased risk of severe<br>exacerbations in patients receiving<br>LAMAs separately. <sup>8</sup> |
| Oral theophylline                                   | Theophylline  | Theophylline is not<br>recommended for regular<br>use. Sustained-release<br>theophylline has only<br>weak efficacy in asthma<br>and adverse effects are<br>common and may be life-<br>threatening at higher<br>doses. It is only<br>recommended if other<br>treatments are<br>inadequate for adult<br>patients. <sup>8</sup> | Side effects<br>include<br>gastroesophageal<br>reflux disease,<br>nausea and<br>vomiting,<br>diarrhoea,<br>palpitations,<br>tachycardia and<br>arrhythmia.<br>Patients may also<br>experience<br>convulsions,<br>headaches and<br>sleep problems. <sup>8,</sup><br><sup>230</sup> | Theophylline has a high potential for<br>medicine interactions. There is also<br>significant interaction with smoking,<br>so regular monitoring is needed if a<br>person stops or starts smoking.  |   |
| Oral corticosteroids<br>(OCS)                       | Prednisolone and prednisone   | Oral corticosteroids may<br>be used in adults with<br>severe asthma who have<br>failed to achieve control<br>on inhaled controller/<br>preventer initial<br>treatment. <sup>8, 226</sup>   | Frequent side<br>effects include<br>sleep<br>disturbance,<br>reflux, increased<br>appetite and<br>mood changes. <sup>8</sup>  | OCS advised to be intermittently<br>administered for short periods, and a<br>high-dose ICS is subsequently used.<br>Caution should be observed when<br>switching from long-term<br>administration of an OCS to a high-<br>dose ICS because of possible adrenal<br>insufficiency. <sup>43</sup> | They are used as long-term<br>management agents to<br>complement ICS. <sup>43</sup>   |
| Oral leukotriene<br>receptor antagonists<br>(LTRAs) | Montelukast,<br>zafirlukast and<br>zileuton                         | LTRAs facilitate<br>bronchodilation and<br>inhibit airway  | LTRAs are<br>generally safe,<br>but possible side   | Pharmacists should focus on safety, as<br>post-marketing surveillance reports<br>have mentioned suicidality.   | The effect of LTRAs is inferior to that of ICS. LTRAs are mainly used concomitantly with ICS or   |

| Therapeutic category                               | Most common<br>medicines   | Main characteristics  | Main adverse<br>effects   | Pharmacist interventions/<br>considerations | Combination therapy  |
|--|--|---|---|---|--|
|  |  | inflammation. They act by<br>blocking the action of<br>leukotrienes that play a<br>role in the inflammatory<br>response in the airways.   | effects include<br>gastrointestinal<br>and sleeping<br>problems. <sup>43</sup>                          |   | ICS/LABAs to achieve and maintain<br>asthma control. <sup>226</sup> LTRAs can be<br>used in isolation in patients<br>unwilling or unable to use ICS. <sup>43</sup> |
| Chromes  | Nedocromil sodium<br>and sodium<br>cromoglycate  | Chromes have a low<br>efficacy and have been<br>discontinued in some<br>countries, e.g., Australia. <sup>226</sup>  |   |   |  |
| Anti-immunoglobulin<br>E (anti-IgE)                | Omalizumab   | Biologic agent that<br>controls IgE-mediated<br>reactions and suppresses<br>asthma symptoms. <sup>43</sup><br>Omalizumab is indicated<br>for patients with severe<br>allergic uncontrolled<br>asthma.   | Most common<br>side effects<br>include injection<br>site reactions,<br>headaches and<br>irritability.43 |   |  |
| Anti-interleukins:<br>Anti-IL-5R and Anti-<br>IL4R | Anti-IL-5R:<br>mepolizumab,<br>benralizumab and<br>reslizumab<br>Anti-IL4R:<br>Dupilumab | Anti-IL-5R is a biologic<br>agent that suppresses the<br>proliferation,<br>differentiation, invasion,<br>activation and survival of<br>eosinophils and,<br>ultimately, the<br>development of asthma<br>symptoms. Subcutaneous<br>mepolizumab or<br>intravenous reslizumab is<br>indicated for patients with<br>severe uncontrolled<br>eosinophilic asthma. <sup>226</sup><br>Anti-IL4R is a biologic<br>agent that suppresses IL-<br>4/IL-13-mediated asthma<br>symptoms. | The major<br>adverse effects<br>are pain and<br>swelling at the<br>injection site. <sup>43</sup>        |   |  |

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| Therapeutic category                              | Most common<br>medicines | Main characteristics   | Main adverse<br>effects | Pharmacist interventions/<br>considerations | Combination therapy |
|---|--------------------------|--|-------------------------|---|---------------------|
| Thymic stromal<br>lymphopoietin (TSLP)<br>blocker | Tezepelumab              | This new TSLP blocker is a<br>human monoclonal<br>antibody. It blocks the<br>action of TSLP, an<br>epithelial cytokine that<br>has been suggested to<br>have an important role in<br>the initiation and<br>persistence of airway<br>inflammation associated<br>with severe asthma. |                         |   |                     |

### 7.2 Pharmacological treatment of COPD

Pharmacological treatment aims to reduce symptoms, frequency and severity of exacerbations, as well as promoting better exercise tolerance and improving overall health. When selecting a pharmacological treatment for COPD, the following principles must be considered:

For initiation of pharmacotherapy:9, 226

- Initiation of pharmacotherapy should be based on assessment of airflow limitation and symptoms. For initial pharmacotherapy, determine the predominant treatable trait dyspnoea or exacerbations.
- Rescue short-acting bronchodilators should be given to relieve symptoms.
- Inhaler devices should be individually tailored, prescribed and dispensed depending on the patient's preferences.
- The importance of proper inhaler technique should be emphasised.<sup>9</sup>
- Risks and benefits of ICS should be weighed before initiation.

For follow-up pharmacotherapeutic management:9

- Symptoms and exacerbation risk should be reviewed.
- Optimising inhaler choices and assessment of techniques are essential before reaching conclusion about treatment insufficiency.
- Adherence to inhaler use should be assessed.
- Escalation or de-escalation of pharmacotherapy should be considered after assessing symptoms and inhaler adherence and technique.
- The IPCRG <u>COPD Right Care</u> wheel is a quick helper for prescribing choices. Side A of this tool supports healthcare prescribers who know that people with COPD need inhaled medicine(s) but are unsure which option to choose (see Figure 5).

#### Figure 5. COPD Right Care wheel, side A



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Where dyspnoea is the major symptom (persistent breathlessness or exercise limitation):

- Patients on long-acting bronchodilator monotherapy can be recommended to switch to two bronchodilators.<sup>9</sup>
- Patients on LABA/ICS treatment can be recommended to add a LAMA, escalating to triple therapy.
- ICS are indicated for patients with COPD who experience exacerbations despite treatment with LABAs and LAMAs.<sup>9, 231</sup>

The main therapeutic options used in COPD are presented in Table 11.

#### Table 11. Therapeutic categories used in COPD

| Therapeutic category                            | Most common medicines   | Main characteristics   | Main adverse<br>effects   | Pharmacist interventions/<br>considerations   | Combination  |
|---|---|--|---|---|--|
| Inhaled short-acting<br>beta-2-agonists (SABAs) | Salbutamol and levalbuterol                                       | Fast-acting. SABAs mainly<br>act by relaxing airway<br>smooth muscle,<br>stimulating beta-2-<br>adrenergic receptors.<br>Their duration of action is<br>4 to 6 hours. <sup>9</sup>   | Resting sinus<br>tachycardia.<br>Higher doses of beta-<br>2-agonists may cause<br>exaggerated somatic<br>tremor. <sup>9</sup> | Increasing the dose of beta-2-<br>agonist when given by a<br>nebuliser provides benefit in<br>acute episodes, but not in<br>stable COPD. <sup>9</sup> | Combining different<br>bronchodilators may<br>increase the degree of<br>action with a lower<br>risk of side effects<br>compared with<br>increasing the dose of<br>a single<br>bronchodilator. <sup>9</sup> |
| Inhaled long-acting beta-<br>2-agonists (LABAs) | Formoterol, indacaterol, salmeterol,<br>olodaterol and vilanterol | LABAs mainly act by<br>relaxing airway smooth<br>muscle, stimulating beta-<br>2- adrenergic receptors.<br>Their effect usually wears<br>off within 12 to 24 hours.<br>Formoterol and<br>salmeterol are twice-daily<br>LABAs. Indacaterol,<br>olodaterol and vilanterol<br>are once-daily LABAs. <sup>9</sup> | Resting sinus<br>tachycardia.<br>Higher doses of beta-<br>2-agonists may cause<br>exaggerated somatic<br>tremor. <sup>9</sup> | Increasing the dose of beta-2-<br>agonist when given by a<br>nebuliser provides benefit in<br>acute episodes, but not in<br>stable COPD. <sup>9</sup> | Combining different<br>bronchodilators may<br>increase the degree of<br>action with a lower<br>risk of side effects<br>compared to<br>increasing the dose of<br>a single<br>bronchodilator. <sup>9</sup>   |
| Short-acting muscarinic<br>antagonists (SAMAs)  | Ipratropium bromide   | SAMAs mainly act by<br>blocking the<br>bronchoconstrictor<br>effects of acetylcholine.<br>Their duration of action is<br>6 to 8 hours. <sup>9</sup>  | Side effects include<br>dry mouth,<br>constipation, and<br>cough. <sup>229</sup>  |   |  |

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| Therapeutic category                          | Most common medicines  | Main characteristics  | Main adverse<br>effects  | Pharmacist interventions/<br>considerations   | Combination  |
|---|--|---|--|---|--|
| Long-acting muscarinic<br>antagonists (LAMAs) | Aclidinium bromide,<br>glycopyrronium bromide,<br>tiotropium bromide and<br>umeclidinium bromide | LAMAs mainly act by<br>blocking the<br>bronchoconstrictor<br>effects of acetylcholine.<br>Their effect usually wears<br>off within 12 to 24 hours. <sup>9</sup>   | Mouth dryness.9  |   |  |
| Inhaled corticosteroids<br>(ICS)              | Beclometasone, budesonide,<br>fluticasone and ciclesonide  | The use of ICS in COPD is<br>mostly in those with<br>frequent exacerbations<br>and eosinophilic<br>inflammation (e.g.,<br>indicated by raised blood<br>eosinophils). Their use<br>needs to be balanced<br>against the risks<br>involved. <sup>226</sup> | Most common<br>side effects include<br>oropharyngeal<br>candidiasis,<br>dysphonia, or throat<br>irritation. <sup>9</sup><br>Pneumonia is a less<br>frequent but more<br>serious side effect.           | To prevent oral side effects,<br>pharmacists should suggest<br>patients rinse their mouth<br>with water after using an ICS.<br>Pharmacists also should<br>advise COPD patients on<br>smoking cessation as<br>smoking reduces the effects<br>of ICS and impairs<br>respiratory function. <sup>43</sup> | The use of ICS in<br>monotherapy is not<br>recommended.<br>But there are some<br>advantages in using<br>ICS in combination<br>with LABAs and<br>LAMAs.<br>Triple therapy of<br>ICS/LAMA/ LABA has<br>been found to improve<br>lung function,<br>symptoms and<br>exacerbations when<br>compared with either<br>LAMA alone or the<br>ICS/LABA<br>combination. <sup>226</sup> |
| Phosphodiesterase 4<br>(PDE4) inhibitors      | Roflumilast and cilomilast   | PDE4 inhibitors reduce<br>exacerbations in patients<br>who have chronic<br>bronchitis, severe to very<br>severe COPD and a<br>history of<br>exacerbations. <sup>226</sup>   | Wide range of side<br>effects compared<br>with other COPD<br>medicines: diarrhoea,<br>nausea, reduced<br>appetite, weight loss,<br>abdominal pain,<br>sleep disturbance,<br>and headache. <sup>9</sup> | Pharmacists should stress<br>and advise on weight<br>monitoring while treating<br>with PDE4 inhibitors<br>(avoiding roflumilast in<br>underweight patients).9   | The addition of PDE4<br>inhibitors to long-<br>acting<br>bronchodilators<br>improves lung<br>function <sup>9</sup>   |

| Therapeutic category | Most common medicines                               | Main characteristics  | Main adverse<br>effects   | Pharmacist interventions/<br>considerations   | Combination   |
|----------------------|---|---|---|---|---|
| Methylxanthines      | Aminophylline (solution) and<br>theophylline (oral) | Both aminophylline<br>(solution) and<br>theophylline (oral) have a<br>duration of action of up<br>to 24 hours. Minor<br>bronchodilators, they act<br>as non-selective PDE<br>inhibitors. The use of<br>methylxanthines remains<br>controversial because of<br>concerns about their<br>exact effects. <sup>9</sup> | Toxic effects,<br>because the<br>therapeutic ratio of<br>methylxanthine is<br>small and most of<br>the benefit occurs<br>only when near-toxic<br>doses are given.<br>Headache, insomnia,<br>nausea, heartburn<br>and palpitations<br>caused by atrial and<br>ventricular<br>arrhythmias 9 | Pharmacists should pay<br>attention to the significant<br>interactions with commonly<br>used medicines such as<br>erythromycin, certain<br>quinolone antibiotics<br>(ciprofloxacin), allopurinol,<br>cimetidine, serotonin uptake<br>inhibitors (fluvoxamine) and<br>the 5-lipoxygenase inhibitor<br>zileuton. <sup>9</sup><br>Theophylline has a high<br>potential for drug<br>interactions. Also significant<br>interaction with smoking, so<br>a regular monitoring is<br>needed if a person stops or<br>starts smoking. | The addition of<br>theophylline to LABAs<br>specifically<br>salmeterol, produces<br>greater improvement<br>in breathlessness that<br>salmeterol alone. <sup>9</sup> |

#### 7.2.1 Antibiotics, mucolytics and antioxidant agents

In addition to the therapeutic categories mentioned in Table 11, antibiotics, mucolytics and antioxidant agents may reduce exacerbations in patients with COPD and improve health status. According to the GOLD report, the use of macrolides azithromycin or erythromycin is useful in reducing exacerbations over a one-year period. But there are no data showing the efficacy or safety of these antibiotics to prevent COPD exacerbations beyond one year of treatment.<sup>9</sup>

The treatment with mucolytic and antioxidant agents such as carbocysteine and N-acetylcysteine may reduce exacerbations and modestly improve health status. In contrast, erdosteine may have a significant effect on mild exacerbations.<sup>9</sup>

#### 7.2.2 Oxygen therapy

Oxygen is used to alleviate hypoxaemia. COPD patients who receive oxygen therapy often see improvement, mainly in hypoxaemia and its sequelae, exercise capacity, reduction of dyspnoea, and quality of life.<sup>232, 233</sup> The long-term administration of oxygen (for more than 15 hours per day) to patients with chronic respiratory failure has been shown to improve mortality or morbidity in patients with severe resting hypoxaemia. However, oxygen has not been shown to increase survival for people who are breathless but not hypoxic.<sup>9, 225</sup> Oxygen therapy should not be routinely prescribed to people with stable COPD or resting- or exercise-induced moderate desaturation.<sup>225</sup>

# 8 Optimising medicines use

### 8.1 Medication management for people living with CRDs

#### 8.1.1 Importance of optimal medication management

Optimal management of medicines for people living with CRDs is vital for controlling symptoms and reducing the risk of exacerbations. Medication management refers to the process of monitoring the use of medicines to ensure that patients are taking medicines as directed (adherence) to achieve the intended therapeutic outcomes (efficacy) and reduce any potential harms and side effects (safety).<sup>234</sup> Medicines used for the management and long-term control of asthma and COPD are mainly inhaler formulations, such as inhaled corticosteroids — the cornerstone of asthma treatment —and muscarinic antagonists for COPD management. Therefore, correct inhaler technique remains key to optimising therapeutic outcomes in CRDs. In addition to correct inhaler technique, medicines adherence coupled with affordability are also important to consider while managing medicines used in CRDs.

Fundamentally, medication management should reduce errors and harm by ensuring the five "rights" are achieved: right patient, right medicine, right dose, right route and right time.<sup>235</sup> The iterative medication management process includes medicines reconciliation (which accounts for all medicines, review of medical conditions and comorbidities), and optimising the medication regimen.<sup>234</sup>

#### 8.1.2 Roles of pharmacists in medication management

Pharmacists are well-positioned to play a collaborative role as part of a person-centred healthcare team in managing medicines for people living with CRDs. Having clinical expertise in pharmacotherapy, pharmacists can educate patients on the correct and appropriate medicine administration techniques, optimise medicines use, promote adherence, address and resolve medicine-related problems and minimise occurrence of adverse events. Specifically, community pharmacists can play a critical role in supporting people with CRDs in the community, not only dispensing prescription medicines but also providing medicine-related education and be directly involved in medication management. For example, the INspira cluster randomised controlled trial conducted in Portugal, which involved a community pharmacist-led educational intervention on inhaler technique, adherence to medicines and therapeutic goals, resulted in a significantly greater proportion of people living with asthma or COPD using their inhalers correctly.<sup>236</sup> Furthermore, community pharmacists are readily accessible and often the first port-of-call for people living with CRDs.<sup>237</sup> This provides an opportunity for community pharmacists to build rapport and to review and recommend individualised treatment, provide education on proper inhaler and medicines use, encourage medication adherence and follow through with written action plans.<sup>55</sup>

Correct and appropriate use of inhalers remains pivotal in maintaining control of CRDs and reducing the risk of exacerbations. While pharmacists do not have prescribing rights in many jurisdictions, they are able to engage in education and behavioural change activities to improve the use of medicines and adherence to medication. In a pharmacist-pulmonologist collaborative care clinic of a tertiary hospital in Japan, pharmacists collaborated with physicians to recommend inhaler choice and subsequently provided counselling for people living with COPD.<sup>238</sup> Over the 26-week period of this cohort study, there was a significant improvement in mean trough FEV1 of 0.39 litres (95% confidence interval: 0.26–0.49, p<0.001).<sup>238</sup> A meta-analysis of 12 studies on pharmacist-led medication management interventions found significant improvement in medicines adherence (RR 1.34, 95% confidence interval: 1.18–1.53) and inhaler technique (RR 1.85, 95% confidence interval: 1.57–2.17).<sup>57</sup> Evidently, pharmacists can play a collaborative role with physicians and the primary healthcare team to manage medicines for people living with CRDs.

#### 8.1.3 Medication management for children living with asthma

Asthma is the most common chronic disease among children, with rising prevalence especially in low- and middle-income countries (LMICs), resulting in significant morbidity.<sup>239</sup> Appropriate medication management, ensuring medication adherence, and hence optimal asthma control are vital in reducing morbidity and mortality. However, ensuring adherence to treatment regimens in children is challenging.<sup>240</sup> Family and caregivers should be educated and empowered on asthma and inhaler technique to ensure optimal medicines

use in children. A family empowerment education intervention evaluated through a randomised controlled trial of 82 families in Tunisia found that the intervention led to a significant improvement in asthma symptom control and inhaler technique.<sup>241</sup> Technology can also be leveraged to help pharmacists monitor inhaler use in children. This includes using smartphone applications to track inhaler use, incentives and reminders to reinforce adherence.<sup>242</sup>

#### 8.1.4 Medication management for people living with COPD

People, especially the elderly, living with COPD are often afflicted with other chronic conditions such as cardiovascular diseases.<sup>243</sup> Living with multiple comorbidities can mean a high medication burden and possibly polypharmacy, which necessitates appropriate and optimal management of medicines use. Polypharmacy, commonly defined as the concomitant use of five or more medicines, is associated with a high risk of adverse events, which can lead to an increased number of hospitalisations, worsened quality of life, and mortality.<sup>244, 245</sup> Lack of medicines knowledge, poor health literacy, misperceptions and financial difficulties are some of the established barriers to the adequate management of polypharmacy.<sup>246</sup> Pharmacists can play a role in addressing polypharmacy and enhancing clinical and health outcomes.

### 8.2 Improving medication acceptance and adherence

#### 8.2.1 Prevalence and impact of non-adherence

Once the availability of medicines for people with CRDs is secured, all efforts should be made to help patients make the most of their medicines, which is a key responsibility of pharmacists. The pharmacist is the last person interacting with the patient before their pharmacological treatment is initiated. Guiding the patient and ensuring medication acceptance and adherence is essential for the medicines to work optimally. Indeed, while clinical trials have shown the efficacy of asthma/COPD medicines in controlled settings and selected populations, real-world effectiveness during medicines use in daily practice may differ.<sup>247</sup>

Notably, non-adherence to respiratory medication is highly prevalent and therefore requires ongoing attention during medicines dispensing. The WHO estimated that globally around 50% of patients on chronic treatments do not take their medicines or do not take them correctly.<sup>248</sup> Due to the complexity of the inhaled route of administration, frequent comorbidities and variable symptoms, adherence rates in asthma/COPD may be even lower. Adherence rates to oral and biologic medication are generally higher than for inhaled medication, yet also have room for improvement.<sup>249, 250</sup> For patients with asthma or COPD, non-adherence has been associated with poor symptom control, more hospital admissions, lower work productivity, higher economic burden and higher mortality.<sup>251-253</sup>

Factors associated with non-adherence can be related to the patient (e.g., comorbidities, beliefs, socioeconomic situation), the medication (e.g., side effects, type of medicine administration, intake regimen) or the healthcare system (e.g., relationship with healthcare professional, receiving instructions, reimbursement and continuity of care).<sup>254</sup> As such, managing non-adherence cannot be based on a one-size-fits-all approach. In fact, it is a challenging process and requires proper insight into the patient's actual adherence, possible reasons for non-adherence and provision of patient-tailored interventions.

#### 8.2.2 Measuring adherence

Various options to measure and characterise patients' adherence are available, each with their advantages and limitations. The most commonly used method to measure medication adherence in daily practice is by self-reported surveys or questions. This is an inexpensive, fast and easy method, but is subjective as it is often prone to socially desirable answers and underreporting of non-adherence due to recall bias.<sup>255</sup> However, it provides insights into reasons for non-adherence and could pick up signals that allow further in-depth assessment.

Pharmacists making use of electronic dispensing records and data have an additional option available by reviewing frequency of dispensing as a marker for patients' adherence. Through the use of dispensing records, a patient's medication possession ratio or the proportion of days covered can be determined. This is an objective measure of adherence but it is not particularly detailed and does not guarantee actual (correct) intake.<sup>256</sup>

More invasive options include the use of bioanalytical assessment of medicines exposure in body fluids or tissues such as blood, urine or hair.<sup>257, 258</sup> These types of measurements provide a more accurate assessment of medicines intake and are the most objective. However, except for the latter, these measures only provide a snapshot of adherence in the past one to two days and are prone to "white coat" adherence where patients know they are going to be measured. Indirectly, adherence to inhaled corticosteroids might be monitored by measuring the fractional exhaled nitric oxide.<sup>259</sup> These bioanalytical measures can, however, be seen as invasive and not at all patient-friendly. Besides, all measures require laboratory equipment that is often not available or affordable at the community pharmacy level.

An emerging objective measurement option is the use of digital inhalers. While some are only used in clinical trial settings, digital inhalers are becoming increasingly available in daily practice. Digital inhalers can measure the exact moment of inhaler effect over time and most are connected to a smartphone application that allows for an overview of adherence patterns, sometimes linked to trigger exposure and symptom burden. Some of the more advanced devices can also measure inhaler technique and send reminders when doses are about to be missed.<sup>260</sup> With a plethora of digital inhalers and apps being developed, data integration, privacy and reimbursement remain issues to be addressed before they can become available at a wider global scale.<sup>261</sup> Finally, these digital methods are the gold standard to identify and monitor adherence, but need to be combined with more qualitative methods to also identify the reasons for non-adherence.

#### 8.2.3 Reasons for non-adherence

Reasons for non-adherence are diverse and can be either intentional or non-intentional or a combination of both. The WHO distinguishes three behavioural types of non-adherence, namely, erratic, intelligent and unwitting non-adherence.<sup>248</sup> Erratic non-adherence is non-intentional, and underlying reasons are forgetfulness and missing doses due to a busy or hectic lifestyle. Intelligent non-adherence is an intentional form of non-adherence and is due to a conscious or reasoned decision of the patient to alter their dose or not take their medicines at all. Reasons include the experience or fear of side effects, not feeling the necessity to take medicines (e.g., not being or feeling sick), mistrust in their healthcare professional or a financial reason. Finally, unwitting non-adherence is an unintentional form of non-adherence with patients being unaware that they are non-adherent. Examples of this type of non-adherence are taking the medicine more or less often than prescribed, using the wrong medicine or inhaler or taking it incorrectly (e.g., with suboptimal inhaler technique).

Reasons for non-adherence can be structurally reviewed during a clinical consultation at the pharmacy with several validated questionnaires that are available to assist in this process. General widely used medicines adherence questionnaires include the Medication Adherence Rating Scale and the Beliefs about Medicines Questionnaire.<sup>262</sup> Furthermore, a respiratory specific questionnaire is the Test of Adherence to Inhalers (freely available in multiple languages from <u>www.taitest.com</u>).<sup>263</sup> Of note, the latter questionnaire consists of 10 questions for the patient and two for the healthcare professional and includes the three WHO classes of non-adherence. The accompanying TAI Toolkit can be used to select matching evidence-based adherence enhancing interventions based on the individual responses on the TAI.<sup>264</sup> Pharmacists have been shown to effectively enhance adherence, asthma control and lung function by using the TAI questionnaire in patients with asthma.<sup>265</sup>

#### 8.2.4 Adherence-enhancing interventions

Given the multitude of reasons for non-adherence, enhancing adherence requires patient-tailored interventions. While no single trial has applied this fully personalised approach, many elements have been studied. Theoretically, for patients with erratic non-adherence, reminders and linking medicines intake with daily habits seems to be the most appropriate strategy.<sup>248, 264</sup> Indeed, reminders have been shown to be effective in improving adherence and lowering rescue medicines use in children with asthma.<sup>266</sup> A recent study showed that digital interventions, such as the use of electronic monitoring devices and short message services, were likely to improve adherence to maintenance medication in asthma.<sup>267</sup> Patients with intelligent non-adherence may benefit more from behavioural change strategies such as shared decision making and motivational interviewing.<sup>268</sup> Finally, patients with unwitting non-adherent behaviour require educational and self-management interventions, including structured training on how to use their inhalers (see Section 8.4.1).

While these single strategies may help for subgroups of patients, pharmacist intervention programmes have often taken a more complex and comprehensive approach, including multiple elements. One of the largest community pharmacy-based clinical trials is the PHARMACOP study involving over 700 COPD patients in Belgium. This programme included two visits to a pharmacy with structured COPD disease education, smoking cessation, feedback on medication adherence and provision of inhaler instructions. After three months, not only did adherence improve by around 10%, there was also a significant drop in hospital admissions, making this an effective and a cost-effective approach.<sup>269, 270</sup> Novel adherence-enhancing strategies include the use of digital inhalers to characterise patients' day-to-day inhaler use and provide tailored feedback based on individual usage patterns. In Ireland, pharmacists have successfully applied this strategy with significant improvement in asthma and COPD patients' adherence and quality of life.<sup>271</sup> The beneficial effects of pharmacist interventions focusing on improving adherence in patients with asthma have been summarised and confirmed in a meta-analysis of 11 studies.<sup>272</sup>

### 8.3 Evaluating and resolving medicines-related problems

A medicines-related problem, is defined as an "event or circumstance arising from usage of a medicine that has or can affect the optimal outcome of medical care" and this includes both efficacy and safety.<sup>273</sup> Apart from detrimental effects on clinical outcomes and health, medicines-related problems have been associated with increased utilisation of healthcare services and hospitalisations, which translates to a significant economic burden on people living with CRDs.<sup>274</sup> Therefore, early identification and resolution of medicines-related problems are pivotal in ensuring efficacious therapy and safe medicines use.

Pharmacists play a central role in addressing medicines-related problems, such as medicine interactions, inappropriate regimens and side effects. Addressing medicines-related problems should be coupled with education on medicines use and communication with the patient's primary physician. This should be achieved through interprofessional collaboration, in which care is centred around the patient and anchored on shared decision-making between the patient and the healthcare team.

Pharmacist-led collaborative interventions have shown promising outcomes in resolving medicines-related problems and optimising clinical outcomes.<sup>275</sup> For example, medicines reconciliation that included review of medicines-related problems, potential medicine interactions, and potentially inappropriate medicines use in elderly individuals living with cardiovascular diseases performed by clinical pharmacists led to a reduction in adverse events and improvement in treatment adherence.<sup>276</sup> A pharmacist-led clinic that focused on asthma knowledge and inhaler use and adherence for people living with asthma led to a significant improvement in medication adherence.<sup>277</sup> Another study conducted in the Netherlands that involved collaboration between clinical pharmacists and general practitioners in addressing medicines-related problems resulted in fewer medicines-related hospitalisations.<sup>278</sup> Taken together, these studies show that pharmacists are vital as part of a collaborative care team in evaluating and resolving medicines-related problems. However, any changes to medicines or treatment regimens should be clearly documented and communicated to all stakeholders in the healthcare team, including patients.

Community pharmacists are often the first port-of-call for individuals living with CRDs for medicines- and disease-related advice. Community pharmacists are also well-positioned to establish rapport and build relationships with people living with CRDs, who may need regular advice on using their medicines and on inhaler technique. However, reimbursement for such direct patient care activities is not available in many countries.

#### 8.3.1 Medicine interactions and side effects

Medicine interactions and adverse effects can lead to medicines-related problems, including non-adherence, reducing the safety of treatments.<sup>226</sup> The main interactions for medicines used in CRDs and examples of side effects are presented in Table 12.

| Medicine class                                       | Examples   | Indications     | Medicine interactions   | Side effects  |
|--|--|-----------------|---|---|
|  | -Manife to -   |                 |   |   |
| Short-acting<br>beta-2-agonists<br>(SABAs)           | Salbutamol,<br>terbutaline and<br>levalbuterol                                 | Asthma,<br>COPD | Beta-blockers   | Tremors and tachycardia,<br>usually associated with<br>overuse of inhaler   |
| Long-acting<br>beta-2-agonists<br>(LABAs)            | Formoterol,<br>salmeterol,<br>vilanterol and<br>indacaterol                    | Asthma,<br>COPD | Beta-blockers   | Tremors, tachycardia,<br>palpitations, headache   |
| Short-acting<br>muscarinic<br>antagonists<br>(SAMAs) | Ipratropium  | COPD            | Beta-blockers   | Xerostomia, bitter taste  |
| Long-acting<br>muscarinic<br>antagonists<br>(LAMAs)  | Aclidinium,<br>tiotropium,<br>glycopyrronium and<br>umeclidinium               | COPD            | Beta-blockers   | Xerostomia, constipation<br>and urinary retention   |
| Inhaled<br>corticosteroids<br>(ICS)                  | Budesonide,<br>beclometasone,<br>fluticasone,<br>ciclesonide and<br>mometasone | Asthma,<br>COPD | Beta-blockers   | Oropharyngeal candidiasis,<br>dysphonia, hoarseness   |
| Oral<br>corticosteroids                              | Prednisolone,<br>methylprednisolone<br>and hydrocortisone                      | Asthma,<br>COPD | Fluoroquinolones, azoles,<br>NSAIDs   | Osteoporosis, cataract,<br>glaucoma, hypertension,<br>hypothalamic-pituitary-<br>adrenal axis suppression,<br>skin thinning, diabetes,<br>weight gain, insomnia |
| Anti-IgE   | Omalizumab   | Asthma          |   | Injection site reactions,<br>urticaria, pruritis  |
| IL-5 receptor<br>antagonists                         | Mepolizumab,<br>benralizumab and<br>reslizumab                                 | Asthma          |   | Injection site reactions,<br>myalgia, headache  |
| IL-4 receptor<br>antagonist                          | Dupilumab  | Asthma          |   | Injection site reactions,<br>transient blood eosinophilia   |
| Leukotriene<br>modifier                              | Montelukast  | Asthma          | Phenytoin, warfarin,<br>carbamazepine   | Headache, cold-like<br>symptoms, ear infection,<br>fatigue  |
| Methylxanthines                                      | Theophylline   | Asthma,<br>COPD | Rifampin, phenytoin,<br>carbamazepine,<br>phenobarbital, macrolides,<br>quinolones, linezolid. Also<br>significant interaction with<br>smoking, so a regular<br>monitoring is needed if a<br>person stops or starts<br>smoking. | Nausea, vomiting, headache,<br>anorexia, diarrhoea, seizure   |
| PDE-4 inhibitor                                      | Roflumilast  | COPD            | Rifampicin, phenytoin,<br>clarithromycin  | Diarrhoea, nausea, reduced<br>appetite, weight loss,<br>abdominal pain, sleep<br>disturbance, headache  |
| Chromes  | Sodium<br>cromoglycate and<br>nedocromil sodium                                | Asthma,<br>COPD |   | Cough, throat irritation,<br>headache, nausea   |

#### Table 12. Medicine interactions and side effects of medicines used in the management of CRDs

#### 8.3.2 Therapeutic medicines monitoring

Therapeutic medicines monitoring (TMM) allows medicine doses to be adjusted for optimisation of treatment outcomes based on medicine blood concentrations.<sup>279</sup> TMM can be used to personalise treatment not only to optimise clinical outcomes but also to assess adherence to medication.<sup>279</sup> TMM has been applied in assessing

adherence to theophylline, and inhaled and oral corticosteroid medication.<sup>280</sup> More recently, using TMM to personalise omalizumab treatment for severe asthma has been proposed.<sup>279</sup>

TMM should be conducted for medicines with narrow therapeutic ranges, and theophylline is one such example. Oral theophylline takes around five days to reach steady state and sampling should be taken four to six hours after each dose initially and then at intervals of three days after each dose change. The target range for theophylline in serum is 10 to 20µg/l in most individuals but lower levels of 5 to 15µg/l may be effective for some patients. Lower doses might be considered for some patients, including elderly patients, individuals with hepatic impairment and patients with heart failure.<sup>281</sup>

#### 8.3.3 Over-reliance on inhaled short-acting beta-2-agonists

Overuse and hence over-reliance on inhaled short-acting beta-2-agonists (SABAs) is associated with increased risk of exacerbations and mortality.<sup>282</sup> Over-reliance on inhaled SABAs also implies poor asthma control and poor health outcomes.<sup>282</sup> SABAs do not address the underlying inflammatory pathology of asthma and over-reliance on SABAs may be associated with poor adherence to ICS.<sup>282</sup> GINA emphasises the importance of using inhaled corticosteroid treatments for mild asthma, specifically to initiate ICS-formoterol as controller and reliever at step 1, instead of SABA only. Notably, receiving three or more canisters of a SABA per year has been found to be associated with increased risk of emergency department visits while receiving 12 or more canisters of SABA per year was associated with increased risk of death.<sup>8</sup> For example, higher SABA usage was found to be associated with incrementally increased mortality risk among people living with asthma in Sweden (three to five canisters per year: hazard ratio [HR] 1.26 [95% confidence interval 1.14–1.39); 11 or more canisters per year: HR 2.35 (95% confidence interval 2.02–2.72]).<sup>282</sup> In addition, over-reliance on SABAs resulted in significant economic burden. SABA over-reliance was associated with higher healthcare costs among people living with asthma in Spain (SABA recommended use, EUR 1,916 vs SABA overuse, EUR 5,702, p<0.001).<sup>283</sup>

Over-reliance on SABA implies poor asthma control, which may stem from poor adherence or underuse of ICS maintenance therapy.<sup>284</sup> One significant barrier to ICS adherence is the psychological reluctance to use chronic medicines when one is not experiencing any symptoms.<sup>284</sup> Misperceptions of corticosteroids and believing that ICS should only be used when symptoms worsen are other barriers to ICS adherence.<sup>284</sup> Poor adherence to ICS could lead to poor asthma control and the need to use SABAs for symptom relief.<sup>284</sup> Coupling the efficacy of SABAs in relieving symptoms quickly and maintaining the ability to carry on with daily activities, patients have developed reliance and emotional attachment to their SABA inhaler.<sup>284</sup> In low-resource settings, the underuse of ICS may also be attributed to the high out-of-pocket payment for ICS, lack of training and competency of prescribers, and unavailability of ICS in public hospitals. Many people in low-resource settings living with asthma have a lower socio-economic status and they visit public hospitals where the treatment is free or low cost. However, in public hospitals, ICS is not available and prescribers tend to prescribe oral medicines.<sup>285</sup> Pharmacists should proactively educate patients on the importance of adherence to ICS therapy and the problems associated with underuse of ICS, and explain the implications and risks of over-reliance on SABAs alone.

The IPCRG has piloted the <u>Asthma Right Care</u> social movement to improve the management of asthma, specifically to eliminate the overuse or underuse of effective interventions in asthma management.<sup>286</sup> Asthma Right Care aims to advocate improvements in asthma management through reviewing clinical practices and aligning practice to guidelines as well as to drive changes at the policy level. Right care, social movement, creating large scale changes, and followership are the underpinning principles of Asthma Right Care.<sup>286</sup> One of the key priority problems is over-reliance on SABAs, and it aims to address this through engaging and convincing relevant stakeholders (patients, prescribers, pharmacists) that over-reliance is a problem.

Right care is guided by evidence with benefits and risks weighed, and it is patient-centred.<sup>287</sup> In the context of over-reliance on SABAs, pharmacists could actively identify those with frequent SABA use (e.g., by assessing their electronic or paper dispensing records). Subsequently, they could initiate conversations with patients first to understand their beliefs and knowledge on using SABAs (as well as ICS). In addition, pharmacists should educate patients on the appropriate use of SABAs and the consequences of over-reliance. Pharmacists can use the Asthma Right Care slide rule (see Figure 6) and question and challenge cards (see Figure 7) to engage patients in conversations about their use of SABAs as a reliever. (See <u>here</u> how to use Asthma Right Care slide rule and the question and challenge cards in a pharmacy setting.) The Asthma Right Care slide rule associates the frequency of SABA use with severity of symptoms and disease control.<sup>288</sup> Pharmacists can also use the

<u>Reliever Reliance Test</u>, which is a self-test designed to help patients and healthcare professionals understand what the patient knows about their SABAs for asthma and whether the patient might be relying on it too much.<sup>289</sup> The IPCRG has developed an implementation pack to guide the Asthma Right Care movement.<sup>290</sup> Pharmacists can take the lead in this movement and engage all relevant stakeholders, from patients to prescribers, to do the right things in the right way for the right people at the right time in the right place.<sup>286</sup>

#### Figure 6. Asthma Right Care slide rule



#### ASTHMA SLIDE RULE

#### 1. Questions for prescriber/dispenser to ask themselves and a person with asthma

Using this slide rule, how much short-acting beta<sub>2</sub> agonist (SABA) also known as reliever/rescue/ salbutamol/albuterol inhaler would you think was acceptable for a person with asthma to take in a year, week or day before you thought a review was necessary? What made you choose that?

|                                     | Increa | asing SA | BA use* |     |      |      |      |      |      |      |      |      |
|-------------------------------------|--------|----------|---------|-----|------|------|------|------|------|------|------|------|
| Number of SABA inhalers Rx per year | 1      | 2        | 3       | - 4 | 5    | 6    | 7    | 8    | 9    | 10   | 11   | 12   |
| Puffs of SABA used per year         | 200    | 400      | 600     | 800 | 1000 | 1200 | 1400 | 1600 | 1800 | 2000 | 2200 | 2400 |
| Puffs of SABA used per week         | 4      | 8        | 12      | 15  | 19   | 23   | 27   | 31   | 35   | 39   | 42   | 46   |
| Puffs of SABA used per day          | <1     | 1        |         | 2   |      | >3   | 4    | >4   | 5    | 6    | >6   | 7    |
|                                     | Symp   | toms     |         |     |      |      |      |      |      |      |      |      |

\*Some devices do not contain 200 puffs. Check the number in the devices you prescribe/dispense or use, and modify these messages accordingly

Suggestion: Try asking a person with asthma question 1 after asking the ACT<sup>™</sup> question: (www.nhp.org/provider/asthma/Survey\_ACT\_adult\_EN.pdf) During the past 4 weeks, how often have you used your rescue inhaler or nebulizer medication (such as albuterol): 3 or more times per day / 1 or 2 times per day / 2 or 3 times per week / Once a week or less / Not at all

Asthma Right Care Guidance Notes available at www.iprcg.org/asthmarightcare

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#### Figure 7. Questions and challenge cards (Asthma Right Care)



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# 8.4 Pharmacists' interventions on the use of inhaler devices

#### 8.4.1 Recommendations and guidance on the correct use of inhalers

The correct use of inhalers is pivotal in ensuring optimal control of asthma and COPD. Choosing an appropriate inhaler also plays a significant role in determining the efficacy and safety of treatment. A patient-centred approach should be adopted in choosing an appropriate inhaler, accounting for the patient's beliefs, values, needs, preferences and lifestyle. Together, a patient-centred approach in choosing an inhaler device and educating the person on its correct use are associated with increased adherence to treatment as well as improved quality of life.<sup>236, 291</sup>

Pharmacists can play an important role in ensuring patients are treated effectively with appropriate medicines and can assist patients with inhaler use and adherence. They are also helpful in referring patients when their current treatment regimens are inadequate for disease control. A systematic review of 39 studies that assessed the impact of pharmacist-led inhaler technique interventions has been published.<sup>292</sup> One study assessed the impact of pharmacist intervention on appropriate inhaler technique and found that it significantly improved with pharmacist help.<sup>56</sup> Evidently, pharmacists play a central role in selecting an appropriate inhaler and ensuring correct use and adherence.

There are many factors that can affect the selection and use of inhalers, including patient, medication and healthcare provider factors. Patient factors include personal preference, disease severity, ability to use the inhaler correctly, comorbidities and concomitant medicines, as well as socioeconomic status.<sup>293</sup> Medication factors include cost, portability, medicine interactions and contraindications, mechanisms of medicine delivery such as particle size and velocity, inhaler design and environmental considerations. Healthcare provider factors include familiarity with inhaler, competency in counselling, and competency in assessing patient's inhaler techniques.<sup>293</sup>

When an individual presents with poor control of asthma or COPD, the first step is to check the inhaler technique and adherence to inhaler use. The prevalence of incorrect inhaler technique, involving at least one critical error, was reported to be as high as 80% in several studies.<sup>294-298</sup> Determinants of poor or incorrect inhaler techniques include usage of multiple inhalers, age, cognitive status, dexterity, and coordination between inhaler actuation and inhalation.<sup>298, 299</sup> While incorrect inhaler techniques are associated with overall poor disease control, they are also associated with respiratory symptoms such as cough and breathlessness, which can limit patients' daily activities and affect overall quality of life.<sup>300</sup> Furthermore, poor adherence and poor disease control can lead to over-reliance on reliever medicines (see Section 8.3.3). Therefore, pharmacists must keep up to date on inhalers available in the market, support self-management and ensure correct inhaler technique for people living with CRDs.

Inhalers can generally be categorised as dry-powder inhalers (DPIs), pressurised metered-dose inhalers (pMDIs), and soft mist inhalers (SMIs) (see Table 13).

DPIs are compact and consist of two types: multidose and single-dose inhalers. The medicine in DPIs is deaggregated from its carrier molecules by the inspiratory flow and airflow generated by the patient. Therefore, DPIs are not suitable for patients with insufficient inspiratory flow who are not able to perform a quick deep voluntary inhalation. This also implies that DPIs are not suitable for use during exacerbations.

pMDIs contain a metered dose and are suitable for patients who are severely breathless. However, pMDIs produce a high-velocity spray and therefore require adequate hand-lung coordination to minimise deposition of the drug in mouth or throat. It is advisable to use pMDIs with a spacer (see Section 8.4.2). Breath-actuated pMDIs automatically actuate at low inspiratory flow, hence overcoming the limitation of poor hand-lung coordination. Another concern about pMDIs is the use of propellants that have negative environmental effects.

SMIs atomise the medicine to produce fine particles that come out slowly, yet do not use a propellant. Therefore, SMIs do not rely much on inspiratory flow and are able to deposit large amounts of medicine in the lung at slow velocity.

Cataldo and colleagues proposed a treatment algorithm to guide the selection of inhalers based on patient's characteristics. An appropriate inhaler device can be selected by asking the following questions:<sup>293</sup>

- Is a deep quick voluntary inhalation possible?
- Can sufficient inspiratory flow be obtained?
- Does the patient have sufficient hand-lung coordination?

Based on the answers to these questions an appropriate device can be selected based on the following colour code (see Figure 8)<sup>293</sup>:

- Green device option possible;
- Red device option not recommended;
- Yellow consider a device requiring low inspiratory flow; and
- Orange only in combination with a spacer.

#### Figure 8. Treatment algorithm to select appropriate inhaler

#### Selecting dry powder inhalers (DPIs):

|                               |     | Is a deep quick voluntary inhalation possible?           |              |              |              |  |  |  |
|-------------------------------|-----|--|--------------|--------------|--------------|--|--|--|
|                               |     | Pos  | sible        | Not possible |              |  |  |  |
| Can sufficient<br>inspiratory | Yes |  |              |              |              |  |  |  |
| flow be<br>obtained?          | No  |  |              |              |              |  |  |  |
|                               |     | Sufficient   | Insufficient | Sufficient   | Insufficient |  |  |  |
|                               |     | Does the patient have sufficient hand-lung coordination? |              |              |              |  |  |  |

#### Selecting pressurised metered-dose inhalers (pMDIs):

|                               |     | Is a deep quick voluntary inhalation possible? |  |              |              |  |  |  |  |
|-------------------------------|-----|--|--|--------------|--------------|--|--|--|--|
|                               |     | Pos  | sible  | Not possible |              |  |  |  |  |
| Can sufficient<br>inspiratory | Yes |  | With spacer  |              | With spacer  |  |  |  |  |
| flow be<br>obtained?          | No  |  | With spacer  |              | With spacer  |  |  |  |  |
|                               |     | Sufficient                                     | Insufficient   | Sufficient   | Insufficient |  |  |  |  |
|                               |     | Does the pat                                   | Does the patient have sufficient hand-lung coordination? |              |              |  |  |  |  |

#### Selecting soft mist inhalers (SMIs):

|                               |     | Is a deep quick voluntary inhalation possible? |  |              |              |  |  |  |  |
|-------------------------------|-----|--|--|--------------|--------------|--|--|--|--|
|                               |     | Pos  | sible  | Not possible |              |  |  |  |  |
| Can sufficient<br>inspiratory | Yes |  |  |              |              |  |  |  |  |
| flow be<br>obtained?          | No  |  |  |              |              |  |  |  |  |
|                               |     | Sufficient                                     | Insufficient   | Sufficient   | Insufficient |  |  |  |  |
|                               |     | Does the pat                                   | Does the patient have sufficient hand-lung coordination? |              |              |  |  |  |  |

Adapted from: Cataldo D, Hanon S, Peche RV et al. How to Choose the Right Inhaler Using a Patient-Centric Approach? Adv Ther. 2022; 39:1149–1163. [accessed: 18 June 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/35080761. Table 13 lists examples of the different types of inhaler devices and their advantages and limitations. FIP does not endorse the use of any particular brand in the examples mentioned below. The information included here is for educational purposes only.

#### Table 13. Types of inhalers: advantages and limitations

| Type of inhaler                         | Examples of inhaler devices  | Advantages  | Limitations  |
|---|--|---|--|
| Dry-powder<br>inhalers (single<br>dose) | Aerolizer® Breezehaler® Handihaler®                                | <ul> <li>Compact<br/>and<br/>portable</li> <li>Do not<br/>contain<br/>propellant<br/>gas</li> </ul> | <ul> <li>Require sufficiently<br/>high inspiratory<br/>flow</li> <li>Require good hand-<br/>lung coordination</li> </ul> |
|   | Zonda <sup>®</sup> MRX003-T10 <sup>®</sup> Neumohaler <sup>®</sup> |   |  |
| Dry-powder<br>inhalers<br>(multidose)   | Spiromax <sup>®</sup> Ellipta <sup>®</sup> Easyhaler <sup>®</sup>  |   |  |
|   | Turbuhaler®  |   |  |
|   | Novolizer <sup>®</sup> Nexthaler <sup>®</sup>                      |   |  |
|   | Clickhaler® Genuair®   |   |  |

| Type of inhaler                         | Examples of inhaler devices | Advantages   | Limitations   |
|---|-----------------------------|--|---|
| Pressurised<br>metered dose<br>inhalers | pMDI                        | <ul> <li>Compact<br/>and<br/>portable</li> <li>Can be<br/>used in<br/>very<br/>breathless<br/>patients</li> </ul>  | <ul> <li>Require good hand-<br/>lung coordination</li> <li>Use of<br/>hydrofluorocarbon-<br/>containing<br/>propellant gas.<br/>Most use HFA<br/>currently that is<br/>less polluting but<br/>still impacts the<br/>environment. In<br/>2025, the more eco<br/>friendly HFA-152a<br/>will enter the<br/>market<sup>104</sup></li> <li>Need to clean<br/>regularly (e.g.,</li> </ul> |
| Soft mist<br>inhalers                   | Respimat®                   | <ul> <li>Compact<br/>and<br/>portable</li> <li>Do not<br/>need to<br/>account<br/>for<br/>inspiratory<br/>flow</li> <li>Good lung<br/>deposition</li> <li>Do not<br/>contain<br/>propellant<br/>gas</li> </ul> | <ul> <li>Only one SMI<br/>device is available<br/>in the market</li> <li>Limited range of<br/>medicine<br/>compatibility</li> </ul>   |

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Amato, C; Garcia Pardo, M; Gorreto, L; Llort, M; Moranta, F; Aguilera, A. Todo lo que debes saber antes de prescribir un inhalador.

#### 8.4.1.1 Guidance on inhaler technique

Pharmacists can refer to <u>RightBreathe</u> for guidance on a comprehensive list of inhaler devices and their inhaling techniques. Table 14 presents an overview of the main types of inhalers with video links on the correct administration technique for each of them, which pharmacists can use for patient education. FIP does not endorse the use of any particular brand in the examples mentioned below. The information included here is for educational purposes only.

Each inhaler device has its own particularities. However there are basic steps for the correct use of all devices in general. The seven steps to using an inhaler device are:<sup>301</sup>

- 1. Prepare the inhaler device
- 2. Prepare or load the dose
- 3. Breathe out, fully and gently, but not into the inhaler
- 4. Tilt the chin up slightly and place the inhaler mouthpiece in the mouth, sealing the lips around the mouthpiece
- 5. Breathe in:
  - a. Aerosol e.g., pMDI: slow and steady
  - b. SMI: slow and steady
  - c. DPI: quick and deep
- 6. Remove inhaler from the mouth and hold the breath for up to 10 seconds
- 7. Wait for a few seconds then repeat as necessary

| Type of inhaler                         | Inhaler device      | Administration technique <sup>302</sup>   | Demonstration video      |
|---|---------------------|---|--------------------------|
| Dry-powder<br>inhaler (single-<br>dose) | <b>Breezehaler®</b> | <ol> <li>Remove the cover to expose<br/>the mouthpiece.</li> <li>Peel the foil of the blister<br/>strip to get one capsule.</li> <li>Place the capsule in the<br/>capsule chamber.</li> <li>Close the mouthpiece firmly<br/>until a click sound is heard.</li> <li>Hold the device upright and<br/>press both side buttons<br/>completely once to pierce<br/>the capsule.</li> <li>Sit upright and breathe out<br/>gently.</li> <li>Firmly seal the lips around<br/>the mouthpiece of the<br/>inhaler.</li> <li>Breathe in rapidly and<br/>deeply.</li> <li>Hold breath for as long as it<br/>is comfortable and then<br/>breathe out gently through<br/>the nose.</li> <li>Open the mouthpiece and<br/>remove the used capsule<br/>before closing the<br/>mouthpiece and lid.</li> </ol>   | How to use a Breezhaler? |
| Dry-powder<br>inhaler (single-<br>dose) | Handihaler®         | <ol> <li>Peel the foil of the blister<br/>strip to get one capsule.</li> <li>Open the device cover and<br/>mouthpiece and place the<br/>capsule in the centre<br/>chamber.</li> <li>Close the mouthpiece firmly<br/>until a click sound is heard.</li> <li>Hold the device upright and<br/>press the green button<br/>completely once to pierce<br/>the capsule.</li> <li>Sit upright and breathe out<br/>gently.</li> <li>Firmly seal the lips around<br/>the mouthpiece of the<br/>inhaler.</li> <li>Breathe in slowly and<br/>deeply.</li> <li>Hold breath for as long as it<br/>is comfortable and then<br/>breathe out gently through<br/>the nose.</li> <li>Ensure that no powder<br/>remains in the capsule. If<br/>there are powder left in the<br/>capsule, repeat steps 5 to 8<br/>until all powder is taken up.</li> <li>Open the mouthpiece and<br/>remove the used capsule<br/>before closing the</li> </ol> | How to use a Handihaler? |

#### Table 14. Administration techniques of the different types of inhalers

| Type of inhaler                      | Inhaler device | Administration technique <sup>302</sup>  | Demonstration video             |
|--------------------------------------|----------------|--|---------------------------------|
|                                      |                | mouthpiece and protective<br>cover.  |                                 |
| Dry-powder<br>inhaler<br>(multidose) | Accuhaler®     | <ol> <li>Hold the outer case and<br/>slide the cover open as far<br/>as it will go using the thumb<br/>grip.</li> <li>Face the mouthpiece<br/>towards the user.</li> <li>Push the lever away from<br/>the mouthpiece until a click<br/>sound is heard.</li> <li>Sit upright and breathe out<br/>gently.</li> <li>Firmly seal the lips around<br/>the mouthpiece of the<br/>inhaler.</li> <li>Breathe in deeply.</li> <li>Hold breath for as long as it<br/>is comfortable and then<br/>breathe out gently through<br/>the nose.</li> <li>Slide the thumb grip back<br/>over the mouthpiece.</li> </ol> | How to use an Accuhaler?        |
| Dry-powder<br>inhaler<br>(multidose) | Ellipta®       | <ol> <li>Pull the mouthpiece cover<br/>back until a click sound is<br/>heard.</li> <li>Hold the inhaler upright.</li> <li>Sit upright and breathe out<br/>gently.</li> <li>Firmly seal the lips around<br/>the mouthpiece of the<br/>inhaler without covering<br/>the air vents.</li> <li>Breathe in deeply and<br/>slowly.</li> <li>Hold breath for as long as it<br/>is comfortable and then<br/>breathe out gently through<br/>the nose.</li> <li>Close the mouthpiece cover.</li> </ol>  | <u>How to use Ellipta?</u>      |
| Dry-powder<br>inhaler<br>(multidose) | Turbuhaler®    | <ol> <li>Unscrew the cap to remove<br/>it.</li> <li>Hold the inhaler upright.</li> <li>Turn the grip as far as it will<br/>go and then back to the<br/>original position until a<br/>click sound is heard.</li> <li>Sit upright and breathe out<br/>gently.</li> <li>Firmly seal the lips around<br/>the mouthpiece of the<br/>inhaler.</li> <li>Breathe in deeply.</li> <li>Remove the inhaler from<br/>the mouth and breathe out<br/>gently through the nose.</li> <li>Replace the cap.</li> </ol>   | <u>How to use a Turbuhaler?</u> |

| Type of inhaler                        | Inhaler device | Administration technique <sup>302</sup>   | Demonstration video  |
|--|----------------|---|--|
| Pressurised<br>metered dose<br>inhaler | pMDI           | <ol> <li>Remove the cap and ensure<br/>that the inhaler is upright.</li> <li>Shake the inhaler well.</li> <li>Sit upright and breathe out<br/>gently.</li> <li>Firmly seal the lips around<br/>the mouthpiece of the<br/>inhaler.</li> <li>Press on the canister while<br/>taking a slow deep breath<br/>(breathe in fully through the<br/>inhaler).</li> <li>Hold breath for as long as it<br/>is comfortable and then<br/>breathe out gently through<br/>the nose.</li> </ol>   | <u>How to use a pMDI?</u><br><u>How to use a pMDI with spacer?</u> |
| Soft mist<br>inhaler                   | Respimat®      | <ol> <li>Load the dose by turning<br/>the base in the direction of<br/>the arrow until a click sound<br/>is heard.</li> <li>Sit upright and breathe out<br/>gently.</li> <li>Firmly seal the lips around<br/>the mouthpiece of the<br/>inhaler without covering<br/>the air vents.</li> <li>Breathe in slowly and<br/>deeply.</li> <li>Press the dose release<br/>button and continue to<br/>breathe in.</li> <li>Hold breath for as long as it<br/>is comfortable and then<br/>breathe out gently through<br/>the nose.</li> </ol> | <u>How to use Respimat?</u>  |

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Amato, C; Garcia Pardo, M; Gorreto, L; Llort, M; Moranta, F; Aguilera, A. Todo lo que debes saber antes de prescribir un inhalador.

Ensuring correct inhaler technique and being available to provide training and feedback for people using inhalers are key to optimising clinical outcomes. Common errors in administration technique include:<sup>296</sup>

- Failure to exhale completely before inhaling;
- Exhaling into the mouthpiece (especially for DPIs and pMDIs);
- Inhaling through the nose instead of the mouth when using the inhaler;
- Not ensuring lips are fully sealed around the mouthpiece of the inhaler;
- Not holding breath after inhalation from the inhaler;
- Not checking if capsule is empty after inhalation (for DPIs);
- Not shaking the inhaler well (for pMDIs);
- Tilting the head down instead of slightly backwards when using pMDIs;
- Covering the air vents (for Ellipta and Respimat); and
- Piercing the capsule more than once (for DPIs).

#### 8.4.2 Recommendations and guidance on the use of spacers

A spacer is a hollow tube that connects an inhaler at one end and a mouthpiece at the other end, which slows the flow of medicine and facilitates uptake into the lungs while reducing deposition in the mouth and throat. A spacer is recommended for use with pMDIs.

The mechanism of pMDIs involves the aerosolisation of the drug through a high-velocity spray and this high velocity means that accurate inhalation-actuation coordination is critical to delivering the medicine to the lungs.<sup>303</sup> A spacer should be used with pMDIs, which allows the medicine to be contained within the hollow tube after actuation, slowing down the velocity and allowing the patient to inhale the medicine slowly and adequately. Spacers with masks can help young children inhale the medicine adequately. Spacers should also be used in adult or elderly patients who may have dexterity and coordination difficulties. However, spacers are generally not as portable as the inhaler alone and they may contribute to additional costs for the patient or health system.

Steps to use spacers with a pMDI are:302

- 1. Remove the cap of the inhaler and shake the inhaler well.
- 2. Fit the inhaler into the spacer.
- 3. Seal the lips around the mouthpiece of the spacer tightly and press the canister of the inhaler once.
- 4. Breathe in and out slowly four to six times.
- 5. Remove the spacer and cap the inhaler.
- 6. Wash the spacer once or twice a week with warm water and soap. Air-dry the spacer; do not rinse so as not to build up electrostatic charges. Electrostatic charges can cause the medicine to stick to the side of the spacer.

A demonstration video on how to use a spacer with a pMDI can be accessed <u>here</u>.

There are several types of spacers (see Figure 9). More examples of spacers and videos showing their use can be found <u>here</u>. When choosing a spacer, it is important to consider the following factors: size, valve, material (e.g., antistatic or not), interface with the patient, feedback mechanisms and inhaler compatibility.<sup>304</sup> Note that spacers have different properties that can result in different medicine deposition in the lungs.<sup>305</sup> Therefore, in stable patients, switching between spacers needs careful consideration.<sup>306</sup> Recent developments include digital spacers that support assessment of a patient's inhaler technique and may allow personalised inhaler usage education.<sup>307</sup>

#### Figure 9. Example of different types of spacers



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Amato, C; Garcia Pardo, M; Gorreto, L; Llort, M; Moranta, F; Aguilera, A. Todo lo que debes saber antes de prescribir un inhalador.

#### 8.4.3 Guidance on the production of home-made spacers in low-resource settings

A sealed cold-drink bottle can be used as spacer and these have been found to be as effective as conventional spacers in a study conducted in South Africa.<sup>308</sup> One limitation of using spacers is the additional financial burden. However, spacers are important in ensuring adequate medicine deposition into the lungs as stated in the Section 8.4.2. A cost-effective homemade spacer can be produced easily using a plastic bottle.

#### Materials needed to produce home-made spacers:309

- Plastic bottle (500 mL or 16 oz)
- Cotton
- Medical tape
- A knife or scissors

#### Steps to produce homemade spacers:309

- 1. Wash the bottle with water and soap and cut off the bottom of the bottle.
- 2. Dry the bottle and cover the edge with the cotton.
- 3. Tape the cotton securely and ensure no cotton is exposed.
- 4. Cut a hole at the top of the bottle (near the cap) and ensure that the size can fit the inhaler.
- 5. Remove the cap of the inhaler and insert into the cut hole facing the bottom of the bottle.
- 6. Secure the inhaler by taping it tightly to the bottle.

A detailed guide to producing a home-made spacer can be found here.<sup>309</sup>

A pragmatic randomised controlled trial conducted among people who used a home-made spacer with a beclometasone dipropionate pMDI and another group of people who used a valved commercial spacer found no significant differences in asthma control between the groups after 60 days.<sup>310</sup> A cost-effectiveness analysis conducted in Colombia on home-made spacers versus commercial valved spacers in a paediatric sample found that home-made spacers resulted in significantly lower treatment costs per patient (USD 126.75 for home-made spacers versus USD 128.59 for commercial valved spacers).<sup>311</sup> In addition, home-made spacers were found to be as efficacious as commercial valved spacers in delivering salbutamol for young children with acute exacerbations of asthma.<sup>312</sup> Therefore, home-made spacers provide an economically viable option for people using inhalers, especially in low- and middle-income countries.

### 8.5 Developing treatment and monitoring plans

For many years patients living with asthma were treated according to asthma-specific guidelines, and patients with COPD were treated according to COPD-specific guidelines. This had a great improvement in health outcomes. However, the reality is that patients continue to suffer from these diseases and continue to have acute attacks, and quality of life impairment. Thus, it is necessary to adopt new approaches to managing these diseases to optimise outcomes for people living with CRDs.

The <u>Treatable Traits</u> initiative is a new model of care designed to address the heterogeneity of CRDs, allowing healthcare professionals to provide personalised management of asthma and COPD. This approach recognises that all patients are different, and everyone exhibits a different number and types of traits. <u>Traits are grouped into three domains</u>: pulmonary domain, extrapulmonary domain, and behavioural risk factors (lifestyle factors). So, the Treatable Traits strategy allows healthcare professionals not only to look at pulmonary traits but also at the individual in terms of comorbidities, behaviours and risk factors, thereby providing personalised care. In short, Treatable Traits is a personalised approach to the assessment and treatment of asthma and COPD.<sup>17, 313-316</sup> The treatment is aligned with the underlying disease in each individual, not only the traditional diagnostic labels.<sup>17, 313, 316</sup> Using a <u>multidimensional assessment</u>, this approach identifies the traits underlying a patient's disease that allow the development of a personalised management plan and inform target treatment decisions.<sup>17, 313-316</sup>

Personalised care is a form of person-centred and tailored care approach that accounts for an individual's values, beliefs, perceptions, needs, preferences and capabilities to self-manage CRDs and other comorbidities.<sup>317</sup> Personalised care should centre around patients and revolve around shared decision-making between patients and the healthcare team, in which treatment plans should be developed in alignment with an individual's values, beliefs, perceptions and needs. Monitoring plans should be systematic, and education should be provided to ensure adherence to the treatment plan. Supporting people living with CRDs with health knowledge and self-management skills, hence enhancing self-efficacy, are vital in achieving optimal disease control and health outcomes.

Personalised care implies the development of action plans, such as the <u>Personalised Asthma Action Plan</u> (PAAP). A written PAAP tells patient which medicines they should take every day to prevent symptoms and cut their risk of an asthma attack, what are the signs that the asthma is getting worse and what to do in the event of an asthma attack. In general, the aim of a PAAP is to help patients take early action to prevent or reduce the severity of asthma attack symptoms.<sup>318</sup> The Asthma Action Plan card implemented in Australia could also guide and support healthcare professionals to optimising asthma therapy.<sup>319</sup> A child asthma action plan can be found <u>here</u>.

Personalised care in developing treatment plans should account for an individual's priorities and preferences, collectively setting treatment goals. This person-centred development of treatment plans and setting of goals can enhance adherence to treatment. Optimal pharmacotherapy remains the cornerstone in ensuring control of CRDs, and therefore, pharmaceutical care is an essential component of the monitoring plan. Pharmacists should focus on ensuring medication adherence, providing health education on appropriate medicines use, and supporting self-management. A multidimensional pharmaceutical care intervention that included education, demonstration of inhaler administration techniques, follow-up and monitoring resulted in significant improvements of asthma control test and COPD assessment test scores.<sup>320</sup> In addition, this study also found improvements in quality of life and patient satisfaction.<sup>320</sup> Another pharmaceutical care intervention that involved medication counselling and education on inhaler techniques conducted in Vietnam also resulted in significant improvements in medication adherence and quality of life among people living with COPD.<sup>291</sup>

The Turkish Pharmacists' Association implemented a nationwide pharmaceutical care practice for community pharmacists to manage asthma, COPD, diabetes and hypertension.<sup>321</sup> This nationwide practice illustrated the concept of person-centred care in which the pharmacist collected demographic, disease-related and medication-related information during the first visit.<sup>321</sup> At every visit, the pharmacist assessed asthma and COPD control, addressed medicines-related problems, provided education on inhaler techniques and medicines, and provided smoking cessation and lifestyle counselling.<sup>321</sup> This pharmaceutical care practice resulted in significant improvements in peak flow rates, inhaler technique scores, weekly need for reliever, and asthma control test scores for people living with asthma.<sup>321</sup> Similar improvements were also observed among people living with COPD.<sup>321</sup> This first nationwide practice showed us that community pharmacists can help improve the health outcomes of patients with CRDs through the provision of pharmaceutical care services. New strategies should be developed with the involvement of all stakeholders to make this practice sustainable and eventually efficient.

According to Cordina, the care model of pharmaceutical care fits perfectly with the needs and management model for asthma and COPD.<sup>226</sup> See Figure 10 for an overview of a pharmaceutical care programme for asthma and COPD.


#### Figure 10. Pharmaceutical care programme for asthma and COPD

Adapted from: Cordina M. Pharmaceutical care in asthma and chronic obstructive pulmonary disease In: Alves da Costa F, van Mil JWF, Alvarez-Risco A, editors. The Pharmacist Guide to Implementing Pharmaceutical Care. Cham: Springer International Publishing; 2019. pp 311–31.

The pharmacist should initiate an asthma/COPD pharmaceutical care programme by establishing a professional relationship with the patient and obtaining informed consent. After confirming the diagnosis of asthma/COPD with the physician, the pharmacist can collect data on the patient, their medication and comorbidities. During the assessment phase, a review of the medication should be performed, and understanding should be sought on whether the symptoms are under control, if the patient adheres to the treatment and how they perform the inhaler technique. The pharmacist should also determine the impact of other comorbidities on the patient's health, and if they are willing to adhere to the action plan.

Next, the pharmacist should identify if there is any medicines-related problem and, if so, they may design a therapeutic and monitoring plan.<sup>226</sup> Then the pharmacist should discuss with the patient the proposed intervention and decide on the proper action to take, referring to the physician, or to another member of the healthcare team. Appropriate pharmaceutical interventions should be performed according to the monitoring plan designed for the patient, and the results of these interventions should be monitored over time. The most common pharmaceutical interventions that are generally included in a treatment and monitoring pharmaceutical care plan are:<sup>226</sup>

- Providing adherence-aiding strategies;
- Educating on inhaler technique;
- Highlighting the need to always carry a reliever inhaler device;
- Reducing inhaler polypharmacy;
- Advising smokers on smoking cessation programmes;
- Counselling on healthy lifestyle, nutrition and diet;
- Advising patient to take appropriate vaccines;
- Educating on self-management;
- Addressing beliefs, concerns and fears;
- Providing support for necessary self-management skills;
- Advising on domiciliary oxygen, in COPD; and
- Referring to pulmonary rehabilitation, in COPD.

Specifically, pharmacists can adopt the three As (Ask, Advise, Act) while developing treatment plans with people living with CRDs. Table 15 outlines the details and guidance of the three As.<sup>322</sup>

#### Table 15. The three As framework to develop treatment plans for people living with CRDs

|        | Description   |
|--------|---|
| Ask    | Effect of asthma/COPD on daily life and how patient would like to change that   |
|        | Envision asthma/COPD control in the next six months   |
|        | Types of activities that the patient would like to be able to do  |
|        | • Patient-relevant factors for inhaler (e.g., portable, financially affordable, easily accessible, simple dosing regimen) |
|        | • Drivers of and barriers to medication adherence (e.g., cost)  |
|        | Smoking habits and routine  |
| Advise | • Explain the different types of inhalers and guide patients to select the appropriate one                                |
|        | • Educate the patient on the need for and use of spacers  |
|        | Review and revise inhaler techniques  |
|        | • Educate patients on potential triggers for asthma (e.g., allergens, exercise, environment)                              |
| Act    | • Demonstrate inhaler techniques using props and educational materials (e.g., brochures, videos)                          |
|        | Identify potential triggers with the patient  |
|        | • Tailor treatment plan to the patient's lifestyle, values, beliefs, preferences and needs                                |
|        | • Develop an asthma action plan and explain what to do and when to seek help  |
|        | Guide and help smokers to quit smoking  |
|        | • Summarise the treatment plan and what has been agreed to reinforce understanding  |

Adapted from: International Primary Care Respiratory Group. Providing personalised care to adults with asthma: a learning resource for primary care professionals. [Powerpoint presentation]. Resources. [updated 2018; accessed 23 June 2022]. Available from <u>https://www.ipcrg.org/resources/search-resources/providing-personalised-care-to-adults-with-asthma</u>)

Pharmacists play an important role as part of the healthcare team in providing pharmaceutical care. As the concept of personalised care centres around the patient as one of the key stakeholders in shared decisionmaking, it is also important to account for patient perspectives of pharmacists and pharmaceutical care. Easy to access and reach, short waiting time, empathetic and encouraging care, and confidence in pharmacists' medicines expertise were some positive patient perspectives on pharmacist-led interventions.<sup>323, 324</sup> However, lack of time and unawareness of pharmacist's roles in asthma/COPD care were some barriers to implementing pharmaceutical care (see Chapter 13).<sup>324</sup> More research should also be conducted to elucidate the drivers of and barriers to pharmacist-involved care models so as to guide real-world implementation of such care models for people living with CRDs.

## 8.6 Recommending and prescribing appropriate medicines therapy (within the scope of practice)

Pharmacists are trained in optimising pharmacotherapeutic management through practice and continuous professional development activities. Appropriate medicines use and medication management remain the cornerstone in the treatment of CRDs. This points directly to the role of pharmacists in recommending appropriate medicines, including pharmacotherapeutic choice (e.g., selecting appropriate inhalers), dosing regimen, treatment duration and monitoring of any medicines-related problems. However, pharmacists should not work in a silo; collaboration and continuous communication with the healthcare team are vital to ensure continuity of care and optimisation of health outcomes.

The paradigm for management of CRDs has shifted from a disease-centric model to one that centres around the patient in which shared decision-making is established between the healthcare team and the patient. This patient-centred paradigm is collaborative, and accounts for individual values, beliefs and preferences.<sup>317</sup> In these contemporary collaborative care models, pharmacists are often involved in providing medication-related expertise, such as recommending the prescribing of appropriate medicines. Pharmacists can play a

unique role in developing a pharmaceutical care plan, centred around medicines use and medication management, which sits predominantly within the broader treatment and monitoring plans.

A pharmacist-physician collaborative care model for the management of seven chronic diseases (heart failure, hypertension, hyperlipidaemia, diabetes, depression, asthma and COPD) resulted in positive clinical, patient-reported and healthcare utilisation outcomes.<sup>325</sup> This collaborative care model was established in six hospitals and 22 patient-centred medical homes, in which pharmacists met face-to-face with patients upon admission and discharge to monitor their medication care plan.<sup>325</sup> Subsequently, the pharmacist followed up with the patient either through face-to-face consultation or telephone contact for at least three months.<sup>325</sup> Pharmacists recommended and managed medicines, identified any medicines-related problems, performed medication reconciliation, reinforced medication adherence, provided health education and medication counselling, and empowered patients to self-manage their medicines.<sup>325</sup> Another study that evaluated the impact of pharmacist-physician collaborative care model in managing COPD reported significantly lower 30-day hospitalisations as compared with physician-centred usual care (mean difference: 0.15, 95% confidence interval: 0.04–0.27, p=0.010).<sup>326</sup>

Engaging a pharmacist to optimise prescribing plays an important role in reducing or avoiding medication errors and promoting safe medicines use. Pharmacists should discuss recommending appropriate medicines with the prescriber and, throughout this process, the patient and caregiver (especially for young children and elderly) should be engaged. The process of prescribing appropriate medicines should be person-centred and systematic.

Steps in the tripartite collaboration between prescriber, pharmacist, and patient and caregiver include:<sup>327</sup>

- 1. Detailed interview with patient or caregiver to understand sociodemographic factors, lifestyle, selfmanagement support, values and beliefs around medicines use, and preferences.
- 2. Discussion with the prescriber on the patient's disease control, and proposing pharmacotherapeutic options guided by clinical evidence and patient-related factors.
- 3. Engagement in a shared decision-making process with the patient and caregiver (and prescriber) to select appropriate medicines.
- 4. Documentation of all clinical- and patient-related rationales in the selection of medicines and incorporation of these into the pharmaceutical care plan, with specific monitoring and follow-up actions.

Community pharmacists can be engaged to provide support in monitoring of medicines-related problems, selfmanagement, lifestyle management and further optimisation of medicines after initial prescription. However, the process of recommending and prescribing medicines should be clearly documented and communicated to the community pharmacist, such as through written letters.

The optimal management of CRDs depends predominantly on the use of inhalers. Factors to consider when prescribing inhalers are summarised in Table 16.<sup>328</sup>

| Clinical factors  | Medication-related factors   | Patient-related factors   |
|---|--|---|
| Lung deposition   | Efficacy in relation to the patient's disease control                              | Age and other demographic factors                                     |
| Medication burden (e.g.,<br>polypharmacy) and regimen<br>complexity | Safety in terms of side effects and<br>potential for medicines-related<br>problems | Ability to use inhalers correctly, such as dexterity and coordination |
|   | Storage conditions and shelf-life  | Acceptability of medicines/inhalers                                   |
|   | Portability and convenience  | Financial constraints   |
|   |  | Values, beliefs and preferences                                       |
|   |  | Past experience in using particular                                   |
|   |  | inhalers/medicines  |

#### Table 16. Clinical and medication- and patient-related factors for prescribing inhalers

The role of the pharmacists in recommending medicines, dosing and treatment duration is not well recognised outside the profession. This common activity is often not well known to external health service planners and

other healthcare professionals. For example, a pharmacist identifies a medicine-related problem during a routine medication management session. They then contact the physician and share their assessment and recommendations verbally. The physician agrees with the pharmacist's assessment, suggests changes in the pharmacotherapeutic regimen and modifies the prescription. Subsequently, the pharmacist and patient work together to implement the changes in the regimen, and the pharmacist follows up with the patient to ensure appropriate use and management of medicines.

From an external perspective, the pharmacist dispensed the medicines that reflected the changes in the prescription written by the physician. There is no record, apart from their own documentation, to indicate the role of the pharmacist beyond that of dispenser. Therefore, it is vital to enhance the recognition of pharmacists' roles in the processes of prescribing and optimising medication therapy. Further research and publicity need to be explored to expand awareness the roles of pharmacists in contributing to direct patient care of people living with CRDs.

## 8.7 Stewardship of medicines supply, availability and affordability

Pharmacotherapy is critical in ensuring optimal control of CRDs and this means that barriers to supply, availability and affordability must be addressed. This is embodied within the principle of stewardship, which encompasses "responsible planning and management of resources" including health and healthcare resources, as well as environmental, economic and cultural resources, to ensure sustainable access.<sup>329</sup>

Access to medicines is a multidimensional and multifaceted problem, ranging from rising economic costs, specifically out-of-pocket expenses, to medicines shortages. In low- and middle-income countries, expenses on medicines can be up to 70% of the total healthcare expenses and this poses a significant risk to patients being able to afford medicines.<sup>330</sup>

Medicines shortages, directly affecting their supply and availability, is a long-standing problem across highincome and lower- and middle-income countries. Medicines shortages themselves are a multidimensional problem that stems from supply and demand issues to regulatory restrictions and limitations.<sup>331</sup> The issues of medicines supply, availability and affordability are directly associated with the burden of disease. Specifically, for CRDs, challenges in ensuring adequate supply, availability and affordability have resulted in high disease burden among LMICs.<sup>332</sup>

The WHO developed its Essential Medicines List to guide countries and healthcare systems to select and prioritise efficacious, safe and cost-effective medicines.<sup>333</sup> However, many of these essential medicines for CRDs remain unavailable and unaffordable in LMICs, with access to medicines for asthma being as low as 30%.<sup>334</sup> Together with financial constraints, the lack of supply and availability of medicines (especially inhalers) were found to be associated with poor adherence to inhaler use and hence poor disease control. A study conducted in Kyrgyzstan, a lower-middle income economy, among people living with COPD, revealed that only 1.0% of all people prescribed a long-acting muscarinic antagonist actually used it, mainly due to unavailability and unaffordability issues. Poor affordability was a key barrier to treatment adherence.<sup>332</sup>

Specifically, among LMICs, some medicines for asthma treatment may not be available. This means that people living with severe and uncontrolled asthma will not have access to the relevant medicines, such as higher doses of inhaled corticosteroids and bronchodilators. <u>The International Union Against Tuberculosis and Lung</u> <u>Disease</u> has established the Asthma Drug Facility to ensure procurement and quality assurance, keeping prices affordable. However, one reported challenge is the different drug reimbursement systems and healthcare financing policies across countries and territories. Healthcare providers responsible for procurement or any part of the medicines supply chain should advocate greater political motivation to develop reimbursement models for medicines used for CRDs. Pharmacists, being custodians of medicines, can play a key role in not only advocating the efficacious and safe use of medicines but also the procurement, supply, availability and affordability of medicines.

# 9 Palliative care and end-of-life care for people with CRDs

Palliative care is often provided by a specially-trained team of specialists focusing on providing relief from the symptoms along with curative treatment, with the goal of improving the quality of life for both the patient and family, regardless of the stage of disease, the patient's gender or age, or the need for other therapies.<sup>225</sup> However, every member of the multidisciplinary team can contribute to supportive and palliative care by actively assessing each symptom and offering advice on non-pharmacological or pharmacological treatments. Palliative care includes end-of-life care, which usually refers to care concerning the final stage of life and focuses on the care of the dying person and their family. The duration of end-of-life care varies according to the patient's trajectory of illness, and the most important thing is to support the person to die in their preferred place.<sup>9</sup>

Communication with patients and families about their preferences for end-of-life care should occur early in the course of a life-limiting CRD, especially for COPD, in order to facilitate high-quality palliative and end-of-life care.<sup>9, 335</sup>

Pain and difficulty in breathing are two of the most frequent symptoms experienced by patients in need of palliative care, and most patients with COPD are likely to experience moderate to severe pain at the end of their life.<sup>335</sup>

Countries around the world allocate funding for palliative care. However, palliative care services should aim to reach at least half of the patients in need. According to the WHO, 78% of people in need of palliative care live in the LMICs. Barriers to the successful implementation of palliative care services in the LMICs include lack of awareness and misconceptions among policymakers and the public, as well as the unavailability of adequate training for health professionals.<sup>335</sup>

Pharmacists can play a role in asthma and COPD patients' trajectory of illness by including palliative care in the continuum of care, linking it to prevention and treatment programmes based on a medicines policy that ensures the availability of essential medicines for managing symptoms, in particular, opioid analgesics for the relief of pain and respiratory distress.<sup>335</sup>

Pharmacists also always respond to patients' changing needs and this may include being mindful of alternative communication methods, including telephone or video calls that enable regular contact with no need for travel.<sup>225</sup>

# 10 Measuring progress: clinical and economic outcomes metrics for CRD services

Services to manage CRDs have shifted to the people-centred paradigm, in which shared decision-making and respecting patients' autonomy are key elements to the provision of efficient and quality care. This implies that the measure of progress in CRDs encompasses not only clinical outcomes but also patient-reported outcomes (PROs), patient-reported experience measures (PREMs) and economic outcomes. Fundamentally, the goals of CRD services include symptom control and improving quality of life.

Spirometry test outcomes and measures of lung function, experience of dyspnoea and other symptoms, exercise tolerance, hospitalisations or healthcare utilisation and overall disease control (assessed using questionnaires such as the Asthma Control Test or the Clinical COPD Questionnaire) were common clinical outcomes measured in randomised controlled trials and observational studies. However, the achievement of therapeutic goals is significantly associated with PROs, with medication adherence and self-efficacy (or capability to self-manage CRDs) being the most significant determinants. Therefore, measuring PROs is also essential for assessment of CRD services.<sup>336</sup>

Moving beyond the measurement of effectiveness, implementation measures are also essential to ensure success, specifically acceptance of and satisfaction with CRD services. Implementation measures to translate effective interventions into successful real-world outcomes should include PREMs such as treatment satisfaction, which assesses a patient's care journey and hence the overall quality of care. PREMs are a key feature to measure the progress of people-centred health services.

Achieving equitable access to health services is vital in ensuring universal health coverage. Measuring economic outcomes of CRD services is therefore essential in promoting access for all. CRDs such as asthma and COPD impose a significant economic burden on individuals as well as society, especially in LMICs. The economic burden of CRDs is elaborated in Section 1.2 of this handbook. While reducing direct medical costs remains key in the management of CRDs, care services should also aim to reduce indirect costs.

Table 17 summarises some clinical, economic and patient-reported outcomes for measuring the progress of CRD services.

| Clinical outcomes  | Economic outcomes  | Patient-reported<br>experience measures | Patient-reported<br>outcomes       |
|--|--|---|------------------------------------|
| Forced expiratory volume in 1 second (FEV <sub>1</sub> ) | Direct medical costs<br>(outpatient consultation<br>costs, medication costs,<br>laboratory test costs,<br>spirometry test costs) | Patient acceptance                      | Health-related quality of<br>life  |
| Forced vital capacity (FVC)                              | Indirect medical costs<br>(costs attributable to<br>absenteeism and<br>presenteeism)   | Treatment satisfaction                  | Functional and health<br>status    |
| FEV₁/FVC ratio   | Work productivity losses   | Patient perceptions and<br>perspectives | Self-efficacy                      |
| Functional residual<br>capacity                          | Healthcare utilisation costs   |   | Medicines and inhaler<br>adherence |
| Diffusing capacity of the lung for carbon monoxide       | Cost-effectiveness   |   | Treatment adherence                |
| Experience of symptoms such as dyspnoea                  |  |   |                                    |
| Frequency of exacerbations                               |  |   |                                    |

#### Table 17. Clinical, economic and patient-reported outcomes for measuring progress of CRD services<sup>337</sup>

Clinical, economic and patient-reported outcomes have been used to evaluate progress of CRD services. For example, a randomised controlled trial conducted among people aged five to 11 years living with asthma in

Jordan evaluated the clinical, humanistic and economic outcomes of a pharmacist-led telemedicine service. The trial not only evaluated clinical impact (asthma control, frequency of exacerbations, hospitalisation, usage of SABA relievers) but also economic outcomes (such as medication cost, parent absenteeism, transportation cost, and hospitalisation burdens) and humanistic outcomes (quality of life).<sup>338</sup> Another cluster randomised controlled trial conducted in Italy among people living with asthma also evaluated not only clinical outcomes but also patient-reported outcomes (such as adherence), and economic outcomes (cost-effectiveness) of a pharmacist-led medicine use review intervention.<sup>339</sup> These outcomes can guide the development and implementation of tailored, effective, efficient and quality people-centred health services.<sup>336</sup>

In a report by the European Commission on the indicators for monitoring CRDs such as COPD and asthma in the EU, the monitoring metrics for people living with asthma include monitoring for chronic symptoms, symptomatic episodes, the number of hospital visits, daily activity limitations and lung function.<sup>340</sup> According to the report by the European Commission, these metrics are the best predictors of health outcomes in people living with asthma and COPD. According to the report, minimal chronic symptoms are defined as the proportion of individuals with daytime symptoms at least once a week, and/or the proportion of individuals with reported sleep disturbances at least once a week.<sup>340</sup> People with fewer hospital visits have better health outcomes. Lung function also plays a major predictive role in health outcomes.

As with all CRDs, the application of preventive methods, such as vaccinations and smoking cessation, will always improve health outcomes. In the same EU report, it is stated that respiratory infections can exacerbate and potentially progress respiratory diseases.<sup>340</sup> Because of this, vaccinating patients against infections such as influenza and pneumonia will greatly improve their predicted health outcomes. The report also recommended smoking cessation as a disease reduction strategy in these same patients.<sup>340</sup>

Taken together, measuring the progress of CRD services should focus on clinical, humanistic (including PROs and PREMs) and economic outcomes. The effectiveness of preventive interventions such as vaccinations and smoking cessation should also be evaluated. Continual evaluation of CRD services should be supported by validated instruments and surveys, as well as robust research.<sup>341</sup> All in all, the measurement of progress and service quality and hence implementation of quality care involves healthcare providers such as pharmacists, healthcare administrators, policymakers and health services researchers.

# **11** Guidance for practice-based research on pharmacists' roles in CRDs

Pharmacists who intend to implement CRD services in their practice or conduct practice-based research on pharmacists' roles in CRDs should consider a variety of factors when developing their programme or research plan. Ideally, pharmacists will develop their programme in a stepwise manner, from planning to implementation to evaluation, that allows them to fully consider the needs of their community and develop a comprehensive programme implementation and evaluation plan. The key steps are described below. More detailed information regarding practice-based research and services implementation can be found in Chapter 11 of <u>Mental health care: A handbook for pharmacists</u>.

- Identifying the health issue Pharmacists should analyse local and national data related to CRDs in order to fully understand the needs of their community and guide them in identifying the focus for their programme or intervention.
- **Planning a programme** Planning is essential to ensuring the success of a programme or intervention and pharmacists should attempt to spend considerable time planning their programme. This includes: (i) reviewing the literature to identify interventions with the greatest potential to address the issue they have selected; (ii) collaborating with stakeholders and inviting patients and other healthcare providers to participate in the planning process; (iii) developing the goals and objectives that will guide the implementation of their programme; and (iv) using a planning tool (e.g., the <u>RE-AIM</u> framework).
- Implementing a programme To ensure that implementation is successful, pharmacists must consider a variety of factors, such as staff needs (e.g., additional training to provide the intervention), logistics (e.g., how will this programme fit into the daily practice), regulations (e.g., if there are any regulatory barriers to the programme implementation), budget (e.g., what is the programme or intervention cost, or if the services provided are reimbursed), resources (e.g., resources needed to implement the programme), data (e.g., how the data will be collected and managed), and documentation (e.g., who, where and when the services will be documented).
- Evaluating the programme An essential part of participating in practice-based research or implementing a new programme is determining how the programme or intervention will be evaluated. So, prior to implementation, pharmacists should develop a programme evaluation plan, and they need to determine how and when they want to analyse the data they have collected. In response to data collection, pharmacists may also wish to participate in quality improvement to refine the services they are providing.

### **12 Ethical considerations**

When caring for people living with CRDs, it is important to respect patients' autonomy. In other words, it is essential to consider a patient's beliefs, values and wishes even if they may not always be in that patient's best interest. This principle of autonomy also encompasses informed consent, privacy and confidentiality.

"Informed consent" means communicating the proposed treatment or procedure to the patient, ensuring proper understanding of those treatments or procedures by the patient, and obtaining authorisation from the patient to perform the treatments or procedures without any undue influence or coercion.<sup>342, 343</sup>

Fundamentally, the informed consent process should be patient-centred, taking into account an individual's values, beliefs, needs and preferences. The process involves shared decision-making between the pharmacist and the patient, during which the benefits of the clinical activity or treatment, associated risks and uncertainties should be clearly communicated to the patient.<sup>344</sup> Furthermore, the benefits and risks should be weighed, respecting the patient's right and autonomy to define their own goals and make decisions based on their own beliefs, values and wishes.<sup>342</sup> Patients must be allowed time to consider and then to make a decision on whether or not to receive a treatment or procedure without undue influence or coercion as well as to withdraw their consent voluntarily. The process of informed consent includes disclosure of all information to the patient, comprehension by the patient of all information disclosed, and then the patient making a voluntary decision, and authorising the decision.<sup>342</sup>

While the principle of autonomy encompasses informed consent, pharmacists and healthcare providers may need to weigh the importance of other ethical principles such as beneficence, justice and non-maleficence (Table 18).<sup>345</sup>

| Ethical principle | Definition  |
|-------------------|---|
| Autonomy          | Respect the patient's right to make decisions and determine which treatment or procedure to accept or reject. For example, presenting all inhaler options for the patient to choose one based on their needs, beliefs, preferences and capabilities to administer it correctly. |
| Beneficence       | Act in the best interest of the patient. In the context of CRDs, beneficence involves presenting all possible treatment options that maximise benefit and minimise risk to the patient based on their disease control.  |
| Justice           | Treat everyone the same. Justice comprises equitability and distributive justice — equitability refers to treatment all people similarly and distributive justice refers to distributing limited resources fairly, taken into account culture and identity.                     |
| Non-maleficence   | Avoid harming the patient or society. In other words, reduce significant risks of harm or avoid small risks of causing serious harm.  |

#### Table 18. Definitions of ethical principles in medicine

These ethical principles in real-world practice may come into conflict, giving rise to ethical dilemmas. One common scenario is the conflict between beneficence and autonomy, where the healthcare provider or pharmacist determines a treatment in the best interest of the patient (beneficence), but the patient does not agree with the benefits or has a misperception of the treatment benefit and so decides not to receive the treatment (autonomy). In CRDs, this scenario is often encountered in the recommendation of inhaled corticosteroids (ICS) for maintenance therapy in asthma/COPD, either due to misinformation on the side effects of ICS or believing that the usage of ICS is not required if symptoms are well controlled through the use (or over-reliance) of SABAs (see Section 8.3.3). Therefore, to effectively communicate the benefits and risks of a treatment, it is important for the pharmacist to establish rapport with the patient, and this means strengthening trust with the patient. Lack of trust is one of the major factors that can compromise decisional capacity, and an essential component of establishing trust is to first safeguard privacy and confidentiality.<sup>345</sup>

Privacy and confidentiality refer to the protection of a patient's personal information that the healthcare provider gathered in the course of caring for the patient. Safeguarding privacy and confidentiality is governed by the principle of autonomy and respect for persons, and it is an obligation of the healthcare provider to ensure that confidential information is securely stored based on its sensitivity.<sup>345</sup>

Pharmacists must ensure that confidential information is not shared without a patient's authorisation and if any threatening situation warrants confidential information to be shared, pharmacists should only share the most limited information necessary and required based on their professional judgement. Pharmacists must take into account ethical considerations, including obtaining informed consent and maintaining privacy and confidentiality, when caring for people living with CRDs so as to ensure highest quality and efficient care.

## 13 Barriers to providing CRD services and facilitators to help overcome them

### 13.1 Barriers

Various factors enable or hinder the delivery of pharmacist-provided CRD services in the community. To ensure that the role of pharmacists in providing care for patients with CRDs is optimised, it is important to outline the various barriers influencing pharmacists' ability to establish and provide CRD management services in the community. Pharmacists should evaluate whether these factors may be present and identify strategies to overcome them. All over the world, several studies have been published regarding the barriers to the implementation of pharmaceutical care services.<sup>346-348</sup> These barriers include, but are not limited to, factors related to the pharmacist, pharmacy, pharmacy profession, healthcare system, physician cooperation and patient awareness.<sup>347</sup> Section 13.1 will discuss the main barriers to the provision of patient-centred CRD services.

#### 13.1.1 Structural and system-level barriers

Pharmacists' involvement in providing CRD services is often hindered by many structural and systems-level barriers, including:

- **Limited time and heavy workload** Due to the busy nature of most pharmacies, pharmacists have many daily responsibilities and may not have time to engage with patients in counselling sessions or the capacity to implement new CRD services in their practice, particularly if they are short-staffed.<sup>349,</sup> <sup>350</sup> The shortage of pharmacists and associated lack of time are common factors especially in lowresource countries and in rural areas of developed countries.<sup>351</sup> As pharmacists continue to take on more and more new roles in patient care (ranging from vaccinations to point-of-care testing to enhanced roles in medication therapy management), their ability to provide specific CRD services is reduced. Community pharmacists are busy professionals, addressing myriad health concerns presented by patients, while also providing leadership and managing the day-to-day activities in the pharmacy.<sup>352-354</sup> Therefore, running a separate or additional service to manage a specific disease condition might be challenging and, therefore, serve as a demotivating factor. This challenge is exacerbated in the absence of pharmacy support staff, leaving the pharmacist to grapple with both patient care and administrative functions. This has also been identified as a barrier by patients, who view pharmacists as too busy to discuss concerns related to their CRDs.<sup>353</sup> While this is a difficult challenge to address, pharmacists can take steps to introduce initiatives that require limited time, for example sharing with patients existing CRD educational materials. If pharmacists do this, their patients still benefit from learning more about CRDs and pharmacists are not adding significant amounts of work to their existing heavy workload.
- **Remuneration** In most countries, pharmacist-provided additional services are not reimbursed or are poorly remunerated, with product-based remuneration remaining the most common remuneration model globally.<sup>355</sup> This serves as a huge barrier in the delivery of patient-centred pharmaceutical services, which in most cases present in the form of an extra service provided by pharmacists.<sup>347</sup> Several studies carried out to understand the barriers preventing the delivery of CRD services have indicated poor remuneration as an important barrier to pharmacists committing their time and resources to addressing CRDs in their community. This lack of proper remuneration, coupled with existing high job demands, makes it difficult for pharmacists to provide sustained CRD services to patients.<sup>54, 352, 354</sup> Lack of remuneration, especially in LMICs, has been reported as a barrier to the implementation of cognitive pharmacy services.<sup>356, 357</sup> Pharmacists should endeavour to work with various pharmacy and healthcare stakeholders to advocate appropriate remuneration for pharmacist-provided services, so they have a greater ability to provide services, such as CRD screenings and education campaigns to promote adherence and right use of the inhaler devices, to improve health in their community.

- Lack of access to medical records Pharmacists, particularly those who practise in a community setting, typically do not have access to a patient's medical records. This prevents pharmacists from having a clear understanding of the health status of the patient and prevents them from identifying potential areas for intervention. Thus, their ability to provide care for those with CRDs is limited.<sup>358</sup>
- Lack of a convenient space for private consultation and counselling The lack of a consulting space in the pharmacy where pharmacists can engage, interact with and counsel patients with privacy has been identified as an impediment to providing CRD services.<sup>352, 353</sup> This is because patients are more likely to share details regarding their health status and medicines in a safe and convenient environment, where privacy is guaranteed.<sup>359</sup> Hence, pharmacy premises lacking a counselling space might impede the type of services provided by the pharmacist, especially those requiring ample engagement time. In situations where there are no private spaces on the pharmacy floor, pharmacists will have to be innovative in providing alternative solutions that still allow for some privacy.<sup>359</sup> Some examples include the use of temporary structures to differentiate between the pharmacy floor and areas for consultation, and the deployment of telephone appointments for consultation.
- Lack of educational materials The lack of appropriate educational materials available to use including about inhaler devices and peak flow meters, is also referred as a barrier to providing CRD services.<sup>353</sup> This factor is especially important in LMICs. To overcome this, pharmacists can work with their national pharmacy organisations to see if there are existing CRD educational materials that could be shared with their patient population, or share some of those suggested in this handbook.
- **Models of care** There are some challenges that exist when trying to integrate pharmacists into a multidisciplinary health care team. This can be due to a variety of factors, including lack of established inter-professional collaborative pathways specially related to perceptions by physicians who are unaware of pharmaceutical care services and who, due to this lack of knowledge, fear that the pharmacist may be a professional intruder.<sup>347,354</sup> Pharmacists' have the opportunity to clarify their role and competences, and establish interprofessional collaboration with other health care professionals,<sup>360</sup> for example establishing collaborative pharmacist-physician models to improve the quality of CRD management.<sup>361</sup>

#### 13.1.2 Training

A significant barrier to increasing the availability of pharmacist-provided CRD services is the lack of specific training, which can lead to a lack of confidence in providing CRD services.<sup>54, 352</sup> If topics related to CRDs are not adequately covered in pharmacy education, pharmacists will graduate without the necessary skills to provide these services to patients. This leads to a shortage of trained pharmacists who are able to provide services to those with CRDs.<sup>352, 362</sup> One study conducted in Nepal cited that a principal barrier to the implementation of pharmaceutical services is inadequate training of pharmacists in NCD prevention and management.<sup>363</sup> In a recent study, one of the 10 recommendations for improving pharmacy practice in LMICs is to increase pharmacists' education and training in clinical skills to provide patient-oriented pharmacy services.<sup>364</sup> Despite international recommendations to educate future pharmacists focused on patient care, university curricula are still inadequate at training pharmacists on patient-centred care, maintaining a greater focus on basic sciences and a lower load of clinical sciences in pharmacy curricula.<sup>365</sup> In order to prepare pharmacy students for patient-centred practice, undergraduate pharmacy curricula should follow a competency-based model, where each competency must be perfectly aligned with the educational contents that are necessary for students to achieve it.<sup>366</sup>

#### 13.1.3 Patients' perception of pharmacists' role

How pharmacists are perceived regarding their role in patient care can serve as an impediment or facilitator to providing CRD services. Where pharmacists are regarded as dispensers of medicines, rather than providers of pharmaceutical care, it might impact the interaction and engagement level of patients with pharmacists.

Low receptivity of patients to CRD services is also reported as a barrier.<sup>354</sup> One study conducted in Malaysia about barriers to the provision of asthma services cited patients' perception that they are already well cared for by doctors and that asthma management is not part of pharmacists' roles.<sup>353</sup> A factor in this is the lack of confidence or skills of pharmacists to provide CRD services, such as asthma adherence counselling, asthma triggers factor counselling, reviewing and counselling about asthma control, asthma monitoring and asthma self-management counselling. The same study cited pharmacists' perception that providing specific asthma counselling or services is not part of their role.<sup>353</sup> This is in line with the results presented in the study "Barriers for the implementation of cognitive services in Spanish community pharmacies", which cited pharmacists' mindset as one of the barriers to the implementation of cognitive services in order to have credibility and therefore change patients' perception of the role of pharmacists in the provision of patient-centred CRD care.

#### 13.1.4 Physicians' perception of pharmacists' role

Provision of quality and cost-effective interprofessional collaborative care to manage CRDs can also be hindered by physicians' perceptions of pharmacists' role. Major barriers include physicians' lack of awareness about pharmacists' clinical roles in direct patient care and their lack of confidence in pharmacists' clinical competence, especially in aspects of care that require physical examination.<sup>367, 368</sup> Therefore, the success of pharmacist-involved services in managing CRDs relies on the advocacy of pharmacists' role and standardised robust training to enhance pharmacists' competence, thereby boosting physicians' confidence to collaborate with pharmacists.

The American College of Clinical Pharmacy has issued an opinion statement to suggest the advocacy of pharmacists' roles through standardisation of terminologies and practice standards. In addition, promotion of the success of pharmaceutical care services, such as medication therapy management, can be a primer to encouraging physicians to collaborate with pharmacists.<sup>369</sup> In addition, training to develop and enhance pharmacists' roles in direct patient care and management of CRDs can also involve physicians as the trainer. This approach will not only enhance the clinical competence of pharmacists but also increase awareness of physicians about pharmacists' roles. Furthermore, if training courses are conducted by physicians, this will also enhance their confidence towards pharmacists' capability in managing CRDs through collaborative care models or collaborative practice agreements. One example is the DIAMANTE training for community pharmacists in Singapore. This training programme encompassed both didactic teaching and experiential learning, facilitated by endocrinologists, nurses, family physicians, and advanced practice pharmacists.<sup>370</sup> These standardised and structured training programmes, coupled with consistent advocacy of pharmacists' contemporary roles in direct patient care services, can potentially serve to overcome barriers in implementing interprofessional collaborative CRD services that involve pharmacists.

### 13.2 Facilitators

Given the burden of CRDs globally, there is a need for pharmacists to increase their engagement in CRD service provision. Despite the challenges, there are steps that can be taken at both individual and system-level to overcome barriers and increase pharmacists' participation in CRD care.

#### 13.2.1 Increased accreditation and training opportunities

Training and education focused on CRDs should be integrated into pharmacy curricula globally. In order to prepare pharmacy students to engage with this patient population upon graduation, they should be educated on the topics discussed throughout this handbook and given opportunities to develop key skills in practice. Pharmacy students should have opportunities to pursue elective courses focusing on CRDs, inhaler device training and experiential rotations focused on CRD care.

Practising pharmacists should also seek continuing professional development opportunities that will allow them to further build their knowledge and skills in this area. As pharmacists continue to seek out training in these areas, their confidence in providing CRD services will continue to grow. To support this handbook, FIP has concurrently published the "FIP knowledge and skills reference guide: A companion to the chronic respiratory diseases handbook" to support pharmacists' professional development in the area. The guide

outlines the knowledge and skills for roles and interventions in CRDs by pharmacists, and is intended to be useful to pharmacists, educators and CPD providers.

Worldwide, several pharmacy faculties and pharmacist organisations offer to their members advanced training programmes and certification in CRDs. Pharmacists who are accredited in CRDs are more likely to deliver an increased number of CRD management services in their communities. Through these programmes, pharmacists acquire, for example, practice in adjusting pharmacotherapeutic asthma regimens, counselling patients on tobacco cessation, and improving inhaler device technique in order to optimise treatment regimens for patients with CRDs.<sup>371, 372</sup> This extra level of accreditation provides pharmacists with the knowledge, credibility and motivation to provide these services. Evidence consistently demonstrates a greater likelihood of pharmacists with specialised knowledge providing specialised services in disease-specific areas compared with pharmacists without expert knowledge, which emphasises the need for additional training and certification to assure pharmacists' adequate knowledge, skills and confidence.<sup>373:375</sup>

Enrolling in training activities, such as seminars, conferences, symposia and continuing professional development initiatives, prepares and equips pharmacists to provide CRD-related services. When pharmacists are trained, they become confident and willing to lead on the provision of CRD management services. Therefore, sustaining a culture of continuous learning among pharmacists can benefit pharmacists and patients in preventing and managing CRDs and their complications.

#### 13.2.2 Accessibility of pharmacists

As one of the most accessible healthcare providers, pharmacists are uniquely placed to interact with individuals with CRDs. Pharmacists can leverage this accessibility and the relationships they have with patients to provide CRD care services contributing to respiratory health in their communities. Their accessibility and knowledge of medicines and health conditions make them reliable healthcare professionals, capable of implementing a community pharmacy-based programme for patients with CRDs, improving disease control.<sup>31, 376, 377</sup> Furthermore, their proximity to patients allows them to: perform the necessary screening and follow-ups; monitor for signs, symptoms and adverse effects; offer preventive measures and support avoidance of common CRD triggers; recommend non-pharmacological measures; and educate and improve patients' adherence to treatments.<sup>54</sup>

#### 13.2.3 Policy

Policies need to capture the critical role of pharmacists in CRD service delivery in order to help facilitate the integration of pharmacists' services in CRD care. Failure to implement such policies may lead to sporadic and piecemeal involvement of pharmacists in CRD care. Further, policies should be implemented in order to ensure pharmacists are remunerated for the services they provide. Finally, pharmacy associations and groups should work to develop policies and resources to encourage pharmacists in their jurisdictions to increase their engagement in CRD care and service provision. The important role of pharmacists in CRD therapeutic education should be taken into account, and policies should be developed to highlight this important role.

## **14 Conclusions**

With the growing burden of chronic respiratory diseases worldwide, there is an urgent need for pharmacists to increase their engagement in providing people-centred pharmaceutical services in this clinical area. Due to their accessibility and expertise in all communities and across all sectors, pharmacists are ideally positioned and qualified to provide holistic CRD care to their communities.

This handbook has outlined the many ways in which pharmacists can contribute to improving respiratory wellbeing among their patients, including by acting as agents for health behaviour change (e.g., through smoking cessation programmes) and other preventive services (e.g., recommending or administering influenza and pneumococcal vaccines), asking patients to take health status questionnaires, screening for CRDs, referring patients to additional care, working as part of interprofessional teams, optimising the use of inhaler devices (e.g., inhaler technique education), improving treatment adherence, and monitoring patients for exacerbation episodes and hospitalisations.

Pharmacists should consider how they might incorporate CRD services into their approach to care and how these services might benefit their patients. Despite the barriers that exist to implementing some of these services, there are numerous opportunities for pharmacists to expand their role as public health professionals and healthcare providers by taking steps to prevent, identify and manage the treatment of people living with asthma or COPD. Pharmacies and pharmacists are fully capable of implementing these services and should be utilised more broadly to expand patient-centred care and improve patient health outcomes in CRDs.

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