

Models of care for severe asthma: the role of primary care

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Asthma control has improved globally in recent decades but, despite the availability of effective therapies, it still remains suboptimal.^{1,2} While milder forms of asthma can be treated adequately in primary care with appropriate use of inhaled corticosteroids (ICS) and bronchodilators as directed by guidelines,³ severe asthma represents a diagnostic and therapeutic challenge, and is associated with a disproportionate economic burden to the community and health care system.⁴⁻⁶

Severe asthma is heterogeneous; it is defined as treatment-refractory disease with persistent symptoms or frequent exacerbations despite optimised standard treatments.⁷ It includes patients with “difficult-to-treat” asthma, for whom various factors contribute to poor asthma control, and a smaller group of patients with “biologically severe” asthma, who continue to have poor control even after the exclusion of alternative diagnoses and optimisation of contributory factors. For some patients with biologically severe asthma, there are now effective, targeted biological therapies aimed at treating the underlying pathological mechanisms.⁸⁻¹⁰ However, many patients with difficult-to-treat asthma have comorbidities and risk factors which confound symptoms, and they can obtain significant improvement with careful management of these contributory factors.¹¹ Therefore, it is important to develop models of care that best deal with the complex and varied needs of individuals with severe asthma, with the greater aim of improving patient outcomes for all.¹²

Primary care providers are at the front line of asthma management, and have the crucial role of early identification and management of uncontrolled asthma. An Australian survey reported that uncontrolled asthma in the community was as high as 45%, with frequent hospital admissions and unscheduled medical visits. Yet, only half the patients had been seen by a general practitioner within the previous year, and only 10% had been reviewed by a specialist.⁶ This highlights the need for both better guidance for primary care physicians to assist in managing severe or difficult asthma and clear advice about when patients should be referred for respiratory physician review. This Narrative Review will discuss how primary care providers, with support from respiratory physicians, can assist in the broad management of patients with severe asthma.

Current model of care

Across Australia, current models of care for severe asthma are variable in different states and hospitals. Most primary care referrals for asthma will be managed in a general respiratory clinic, with selected tertiary centres providing a subspecialised severe asthma multidimensional service (Box 1). Data from Alfred Health in Melbourne suggest that 13% of patients with asthma already seen in a general respiratory clinic would further benefit from subspecialised review for difficult-to-treat asthma.¹²

A subspecialised severe asthma service offers the advantage of a structured, multidimensional approach to confirm the diagnosis, asthma severity and phenotype and manage risk factors and

Summary

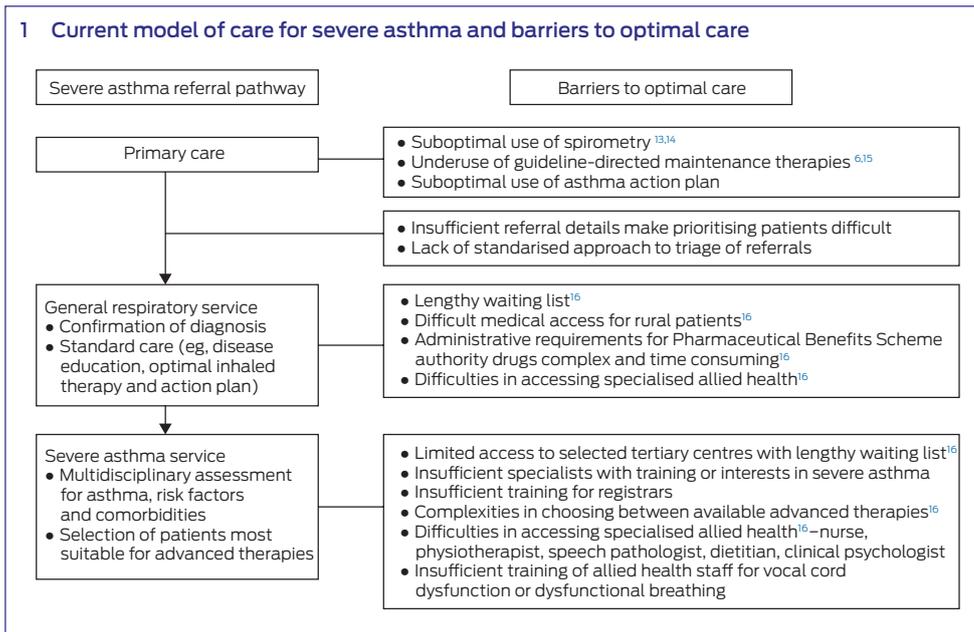
- Severe asthma encompasses treatment-refractory asthma and difficult-to-treat asthma.
- There are a number of barriers in primary, secondary and tertiary settings which compromise optimal care for severe asthma in Australia.
- Guidelines recommend a multidimensional assessment of severe asthma, which includes confirming the diagnosis, severity and phenotype and identifying and treating comorbidities and risk factors. This approach has been found to improve severe asthma symptoms and quality of life and reduce exacerbations.
- Primary care providers can contribute significantly to the multidimensional approach for severe asthma by performing spirometry, optimising therapy and addressing risk factors such as non-adherence and smoking before referring the patient to a respiratory physician for review.
- Primary care practitioners are encouraged to remain engaged with the management of a patient with severe asthma following specialist review by assisting with community-based allied health referrals, managing general medical comorbidities and administering prescribed biological therapies.
- Specialists can support primary care by providing advice to individuals with indeterminate diagnosis, streamlining investigation and management of unrecognised risk factors and complex comorbidities, optimising treatment for severe or difficult asthma including assessment of suitability for and, if appropriate, initiating advanced therapies such as biological therapies.
- When discharging patients back to primary care, specialists should provide clear recommendations regarding ongoing management and should specify the indications requiring further specialist review, ideally offering a streamlined referral pathway.

comorbidities (Box 2).^{17,18} This multidimensional approach often involves a team of respiratory physicians, nurses and allied health professionals, including physiotherapists, speech therapists, dietitians and clinical psychologists, in secondary or tertiary settings. These health care providers offer physician review, lung function testing, blood tests for peripheral eosinophilia and atopy, optimisation of inhaler use and general disease education, in addition to assessment and management for common comorbidities. It allows further scope for education and self-management skills and access to advanced biological therapies. International guidelines recommend such a multidimensional approach⁷ based on prospective observational studies showing positive results on asthma symptom control, quality of life and reduced exacerbations.¹⁹⁻²¹

Barriers to delivery of optimal care

In the current climate, there are numerous barriers to achieving optimal care in Australia (Box 1).¹⁶ The asthma care for patients

1 Current model of care for severe asthma and barriers to optimal care



with milder disease in the primary care setting could be improved by increased use of spirometry, increased adherence to guideline-recommended maintenance therapy, and increased utilisation of asthma care plans; the referral process for those with severe or difficult asthma could also be streamlined by providing a detailed referral letter. For patients with asthma who live in rural or remote areas, access to hospital-based clinics may be difficult or impossible. Even within tertiary hospital settings, funding and resource limitations make it challenging to deliver the recommended multidimensional approach, often resulting in prolonged referral waiting times. It is therefore likely that a flexible approach based on effective communication and collaboration between specialists and GPs and between hospital- and community-based resources may be required.

Primary care contribution to the multidimensional assessment and management of severe asthma

A multidimensional approach to severe asthma is not necessarily complex and provides a structured framework for assessment and management – it is equally applicable to the management of milder forms of asthma. As such, some core elements of this approach could be delivered through primary care with help from available community or online resources (Box 3).

Is it asthma?

Multidimensional assessment starts with the diagnosis of asthma based on compatible history and spirometric evidence of variable airflow limitation. Accurate diagnosis helps to avoid unnecessary costs and adverse effects from inappropriate use of pharmacotherapy for presumed severe asthma.

Worldwide, spirometry with or without bronchodilator response is underperformed in primary care for the diagnosis of asthma.^{13,14} Misdiagnosis of asthma can be as high as 50% due to the suboptimal use of relevant diagnostic testing among patients referred for management of severe asthma in a specialist tertiary setting.^{22,23} Time constraints, staff training, equipment requirements,

suboptimal remuneration and concerns about correct interpretation are common barriers to the routine use of spirometry in primary care. To assist with this problem, there are a variety of resources available in person or online for spirometry training and interpretation (Box 3). Spirometry results with confirmed variable or persistent airflow obstruction will help facilitate triaging and earlier review by specialists when included with the referral.

Is it severe asthma?

Severe asthma is defined as asthma that requires treatment with high dose ICS and one or more other maintenance medication (eg, long-acting β -agonist [LABA], long-acting muscarinic antagonists, leukotriene modifier or theophylline) or oral corticosteroids for more than half the

previous year to prevent asthma from becoming uncontrolled, or disease that remains uncontrolled despite this therapy.⁷ Patients with uncontrolled or severe asthma should be referred for respiratory specialist review.

Is the asthma controlled?

Assessment of asthma control is essential for the initiation and subsequent titration of maintenance inhaled therapy and should be completed at every opportunity. In a multinational survey, 90% of patients self-rated their asthma as well controlled, but of these only 18% were indeed controlled based on the definition in the Global Initiative for Asthma guideline.² As per these guidelines, a patient with well controlled asthma should have no limitation of activities; no nocturnal, early morning or daytime symptoms; and minimal use of reliever therapy (less than twice per week). It is therefore important to ask direct and specific details of symptom frequency and severity, exacerbation episodes, oral corticosteroid use and emergency department visits. The Asthma Control Questionnaires (www.qoltech.co.uk/acq.html)³ and Asthma Control Test (QualityMetric/GlaxoSmithKline)³ are validated questionnaires that are accessible and easy for patients to complete. They provide a valuable objective framework that can be used to assess response to treatment over time.

Is inhaled therapy optimised?

Guideline-recommended maintenance therapy

Best practice management of severe asthma starts in primary care with guideline-based therapies, including appropriate use of inhalers. In the United Kingdom, in the national review of asthma deaths that occurred between February 2012 and January 2013, expert panels identified multiple factors that could have contributed to these deaths.¹ Suboptimal implementation of guidelines was observed in 46% of deaths; there was excessive prescription of short-acting β -agonist, and, most importantly, there was underprescription of

2 Checklist for the systematic assessment of severe asthma

Clinical question	Assessment
Is it asthma?	<ul style="list-style-type: none"> • Compatible history and objective evidence of variability in symptoms and lung function over time, either spontaneously, with treatment, or following bronchial provocation testing
Is it severe?	<ul style="list-style-type: none"> • Demonstrations of: <ul style="list-style-type: none"> ▶ poor control ▶ airflow obstruction ▶ frequent exacerbations ▶ life-threatening episodes
Is treatment optimal?	<ul style="list-style-type: none"> • Treatment with high dose inhaled corticosteroids and long-acting β-agonists or other controller
Are self-management skills optimal?	<ul style="list-style-type: none"> • Inhaler device technique • Adherence • Self-monitoring • Disease knowledge • Written action plan
Are trigger factors identified and managed?	<ul style="list-style-type: none"> • Examples: <ul style="list-style-type: none"> ▶ allergens ▶ cigarette smoke ▶ sinus infection ▶ emotional stress ▶ mould or dampness ▶ other patient-reported precipitants
Is comorbidity identified and managed?	<ul style="list-style-type: none"> • Examples: <ul style="list-style-type: none"> ▶ sinonasal disease ▶ dysfunctional breathing ▶ vocal cord dysfunction ▶ obstructive sleep apnoea ▶ anxiety and/or depression ▶ gastro-oesophageal reflux ▶ obesity
What is the pattern of airway inflammation?	<ul style="list-style-type: none"> • Eosinophilic (sputum assessment, FeNO, blood eosinophils) • Non-Eosinophilic (sputum assessment)
What is the optimal individualised management plan?	<ul style="list-style-type: none"> • Developed with evidence-based interventions that target clinical issues identified during a systematic and multidimensional assessment, in partnership with patients and clinicians, considering patient preferences

FeNO = fractional exhaled nitric oxide. Source: developed within the National Health Medical Research Council Centre of Excellence in Severe Asthma, reproduced with permission.¹⁸

maintenance therapy — 80% patients were prescribed less than the recommended maintenance inhaler therapy in the previous year. There was also evidence of inappropriate prescription of LABA as monotherapy.

Australian studies have similarly revealed suboptimal use of asthma medications and poor asthma control in the primary care setting, and highlighted the importance of regular, ongoing education for patients and their GPs.^{6,15} The Australian guidelines³ have been applauded for their well rounded collaborative approach, with involvement from major stakeholders including subspecialty physicians, primary care providers, pharmacists and asthma foundations.²⁴ Maintenance therapy using low dose ICS followed by addition of LABA should be considered for any patient who experiences daytime or night-time symptoms or who uses reliever therapy more than twice per week. Appropriate knowledge and implementation of national guidelines with

improved ICS use can reduce unscheduled primary care or ED visits.^{25,26}

Managing non-adherence and poor inhaler technique

Appropriate use of inhaler therapy is fundamental to the treatment of asthma. A significant proportion of patients referred for severe asthma assessments have poor adherence,^{20,27} which can and should be managed in primary care. In some Australian reports, only 10% of patients were able to use their inhaler device correctly.³ Critical mistakes are common for all inhaler devices, ranging from 12% for metered dose inhalers, 35% for Diskus (GlaxoSmithKline) and HandiHaler (Boehringer Ingelheim), and 44% for Turbuhalers (AstraZeneca).²⁸ Poor inhaler technique is associated with increased risk of hospitalisation and increased exacerbations requiring oral corticosteroids.²⁸

3 The role of primary care in the multidimensional model of care for asthma

Assessment of airway pathology

- Is it asthma?
- Confirm history is compatible
 - Obtain spirometry for evidence of variable airflow limitation:
 - ▶ training available through asthma foundations, NAC Australia, ALF; online resources also available*
 - ▶ consider external referral for spirometry
- Is it severe asthma?
- Definition:
 - ▶ high dose ICS plus one other maintenance therapy, or oral corticosteroid for > 50% of the previous year required to keep asthma under control; or
 - ▶ uncontrolled asthma despite such therapies
 - If severe, respiratory physician referral recommended
- Is the asthma controlled?
- Definition:
 - ▶ no nocturnal or early morning symptoms
 - ▶ no limitation of activities
 - ▶ daytime symptoms \leq 2 days per week
 - ▶ need for reliever \leq 2 days per week
 - More than two exacerbations per year
 - Assess at every opportunity with specific questioning
 - Consider use of validated questionnaires (eg, ACQ or ACT)[†]
 - If not controlled, review and escalate therapy, as below, followed by referral to respiratory physician

Management

- Is inhaled therapy optimised?
- Escalate maintenance therapy as required in stepwise manner according to guideline recommendation:³
 - ▶ low dose ICS
 - ▶ low dose ICS/LABA
 - ▶ medium /high dose ICS/LABA
 - Assess adherence and inhaler technique, and address as required. Ask:
 - ▶ how often the patient is actually taking their maintenance therapy
 - ▶ what makes it difficult to take
 - ▶ what makes it easier to take
 - Consider use of trained practice nurse, pharmacists, asthma educator from asthma foundations, online resource such as videos and patient resource from NAC Australia
- Asthma action plan³
- Should explain:
 - ▶ what patient should do when well
 - ▶ how to recognise worsening symptoms
 - ▶ what patient should do when symptoms worsen
- Smoking cessation advice
- Provide advice and support for smoking cessation (eg, through motivational interviewing, opportunistic counselling, pharmacotherapy, QUIT line)

Ongoing coordinated care

- Comorbidities
- Review and manage common contributory comorbidities (eg, GORD, obesity, anxiety and depression, allergic rhinitis)
 - Consider specialist referral and coordinate care for assessment and management of complex comorbidities (eg, vocal cord dysfunction, dysfunctional breathing, OSA and bronchiectasis)
 - Coordinate community allied health professional involvement as required (eg, dietitian, clinical psychologist)
- Targeted therapies
- Assist with ongoing administration of biological therapies once patient is stabilised by respiratory physician
 - ▶ appropriate GP training and support can be provided by treating respiratory physician or Centre of Excellence in Severe Asthma
- Collaboration between primary and specialist care
- Refer back to treating respiratory physician in event of:
 - ▶ deterioration in asthma symptom control after a period of stability
 - ▶ frequent exacerbations
 - ▶ deteriorating lung function
 - ▶ intolerance or adverse effects to therapies
 - Respiratory physician may support GPs by providing streamlined re-referral pathways
 - Communication between primary and specialist care may be improved by increased use of eHealth records

ACQ = Asthma Control Questionnaire. ACT = Asthma Control Test. ALF = Australian Lung Foundation. GORD = gastroesophageal reflux disease. ICS = inhaled corticosteroid. LABA = long-acting β -agonist. NAC = National Asthma Council. OSA = obstructive sleep apnoea. * For example, www.toolkit.severeasthma.org.au. † See www.astmahandbook.org.au/resources/tools/control-questionnaires (Sources: ACT, QualityMetric and GlaxoSmithKline. ACQ, Juniper EF, O'Byrne PM, Guyatt GH, et al. Development and validation of a questionnaire to measure asthma control. *Eur Respir J* 1999; 14: 902-907).

4 Referral for respiratory physician review

When to refer	<ul style="list-style-type: none"> • Diagnostic clarification: <ul style="list-style-type: none"> ▶ difficulty in confirming the diagnosis of asthma ▶ symptoms suggest an alternative or coexisting cause • Management of uncontrolled asthma or at-risk patients: <ul style="list-style-type: none"> ▶ persistent uncontrolled asthma despite good adherence and inhaler technique on moderate or high dose ICS/LABA. That is, persistent asthma symptoms, and/or frequent exacerbations (≥ 2 courses of oral corticosteroid per year) • Persistent low lung function after 3 months trial of high dose ICS • Frequent asthma-related health care use • History of life-threatening asthma
Details to include in referral letter (to enable appropriate triage of patients)	<ul style="list-style-type: none"> • Asthma symptom severity • Past and current treatments • Frequency of exacerbations • Relevant comorbidities • Spirometry results

ICS = inhaled corticosteroids. LABA = long-acting β -agonist.

GPs face considerable challenges in managing adherence, inhaler technique and the provision of asthma action plans. Barriers include time and financial constraints as well as patient behaviour, such as presenting only when unwell and poor insight and prioritisation of their medical needs.²⁹ However, a study showed that a group of Australian GPs were receptive to training in motivational interview-based adherence counselling using the five As framework (ie, ask, assess, advice, assist and arrange) and classic techniques such as OARS (ie, open questions, affirmation, reflective listening and summary reflections).³⁰ Although implementation can be challenging, 96% of the participating GPs rated the training as very or extremely useful, and were able to incorporate the skills in their usual practice with confidence.

For any inhaler device prescribed, patients should be provided with clear instruction, including physical demonstration, and should have their technique checked regularly. Trained practice nurses, educators at asthma foundations or pharmacists may also be helpful in this regard.

Asthma action plan and prompt interventions of exacerbations

Asthma action plans are highly recommended as they can be useful in educating patients about early recognition of exacerbation, and guide appropriate intervention strategies to prevent further deterioration.^{3,18} The Australian Asthma Handbook provides guidance as to how these action plans should be completed, including specific recommendations for escalation of therapy based on their usual maintenance regime.³ There are increasing data showing that early treatment using temporary escalation of ICS may ameliorate the need for oral prednisolone in the event of an exacerbation.

Optimising referral and discharge pathways

Referral to a specialist should be initiated for patients with severe or difficult asthma or suspicion of alternative or coexisting disease, including chronic obstructive pulmonary disease (Box 4). Barriers to timely respiratory physician review may include unclear reason for referral, travel distance, patient factors and

lengthy waiting lists.³¹ GPs hold an important role as advocates for their patients in securing a prioritised review at the appropriate clinic, especially in a tertiary hospital setting. The inclusion of details such as asthma symptom severity, exacerbation frequency, past and current therapies and spirometry results are important. Earlier specialist review is more likely for patients who have undergone appropriate assessments and treatments for milder asthma before referral.¹⁶

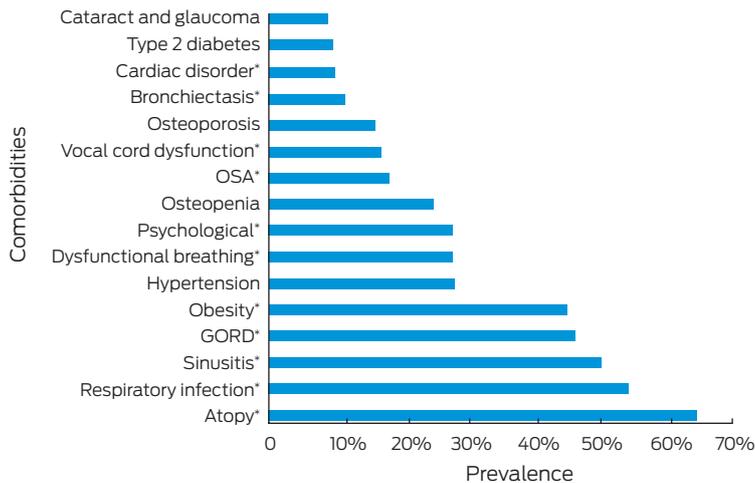
It is equally important that clear recommendations and support from specialists are in place to facilitate transfer back to primary care when severity, symptoms or lung function are stabilised. However, only a third of attendees at a round table meeting for severe asthma were either able to or comfortable with discharging patients under these circumstances. A further 11% indicated they would never refer patients back to primary care,¹⁶ which may not be sustainable in any tertiary or private specialist setting. Recommendations from the specialist about ongoing management and the indications requiring future specialist review and their urgency may be useful (Box 3).

Management of comorbidities in primary care

In patients with poorly controlled asthma, there is a high prevalence of comorbidities (Box 5) that contribute to symptoms, affect quality of life and increase the risk of exacerbations.^{23,32-34} Opinion leaders have recently proposed that many comorbidities and risk factors associated with severe asthma are considered “treatable traits” and that their treatment may lead to positive clinical outcomes.^{12,35,36}

Overall, GPs are better placed to assist in and coordinate the management of the range of comorbidities contributing to severe asthma, including corticosteroid-related morbidities.³⁷ Many of these comorbidities are chronic in nature and require regular ongoing assessments that are better facilitated in a primary care setting. Referral and access to a community-based dietitian and clinical psychologist is often invaluable and more convenient for patients when provided nearer to home. Furthermore, the concept of comorbidities and confounding illnesses are equally relevant in patients with milder asthma routinely managed in

5 Average prevalence of comorbidity conditions across different studies



GORD = gastroesophageal reflux disease. OSA = obstructive sleep apnoea. Source: Modified representation based on data from Clark and colleagues³² * Considered as "treatable traits" by opinion leaders.

primary care. Access to the various allied health services in the primary care setting could be facilitated by use of existing GP Management Plans and Team Care Arrangements or Mental Health Treatment Plans.

Some comorbidities such as vocal cord dysfunction and dysfunctional breathing, however, require input from speech pathologists and physiotherapists with more specific skills and experience, who are likely only to be accessible in a tertiary setting.

Role of primary care in the administration of biological therapies for asthma

Until recently, the primary choice of therapy for recurrent exacerbations was repeated or long term use of corticosteroids. New treatments such as omalizumab (Pharmaceutical Benefits Scheme [PBS]-listed anti-IgE therapy for severe atopic asthma), mepolizumab (PBS-listed anti-interleukin [IL]-5 therapy for severe eosinophilic asthma) and benralizumab (Therapeutic Goods Administration-approved anti-IL-5 therapy for severe eosinophilic asthma) dramatically improve symptom control and reduce exacerbations and oral corticosteroid use in patients with severe refractory asthma.¹⁰

At present, according to strict PBS criteria, these therapies can only be initiated by a respiratory physician. It is possible that some patients with severe asthma requiring biological therapies could be more effectively managed by GPs or their referral physician working outside a dedicated asthma service. Both omalizumab and mepolizumab can be safely administered subcutaneously in a primary care setting after an initial period of observation at a hospital or specialist setting.¹⁸ Using omalizumab as an example, leaving aside the complexity of the approval process and drug cost, up to a third of respiratory physicians during a round table discussion also identified limited service availability or travel distance to access treatment as barriers to therapy for eligible patients.¹⁶ The exact extent of this problem is unclear without systematic collection of data, but

it is an important area to address in order to avoid disadvantaging patients with severe asthma who live in rural areas. One strategy would be to work with local primary or secondary care providers who are geographically closer to the patient. There are resources available to assist specialists and primary care providers with this transition.¹⁸ GPs' ability to assist with administration of biological therapies and surveillance for adverse events would be invaluable in reducing the burden on specialist severe asthma services, and would free up specialist capacity to offer their services to more patients. It is also advantageous for GPs to remain involved in the care of these patients, as biological therapies will be increasingly prescribed in the coming years across many disciplines of medicine.

Nursing support

Evidence for nurse-led asthma clinics in the primary care setting is inconclusive. The quality of evidence in this area is probably affected by patients' poor clinic attendance, and practice

nurses may not be adequately trained or supported to deliver the necessary self-management education.³⁸ A GP asthma clinic involving a trained specialist nurse followed by GP consultation was shown to be potentially be cost-effective in the Australian setting if it could translate to broad benefits in reducing ED presentations, unscheduled GP visits, hospitalisations and days off work.³⁹ However, this proposal was based on a small intervention trial with outdated cost estimates from 2003, and may not reflect the true costs of national implementation.

Partnership with pharmacists

There is good evidence in Australia that community pharmacists can be upskilled to take on a greater scope of practice, which includes identification and referral of patients with poorly controlled asthma who may otherwise not present to other health care providers. Trained pharmacists can improve asthma control by ascertaining and communicating to GPs the risk factors contributing to poor control, such as insufficient use of maintenance ICS/LABA therapy, poor inhaler technique and smoking.^{40,41}

Potential use of electronic records to improve asthma care

General practices are increasingly adopting software systems that allow the use of reminders and facilitate preventive care. In a randomised controlled trial in a UK primary care setting, a novel approach using an electronic asthma risk registry was found to reduce asthma hospitalisations, ED presentation and unscheduled GP visits by 50%, 26% and 21%, respectively. There was also increased prescription of recommended preventive therapies, which was considered cost-effective.⁴² The at-risk registry identified potential patients with severe or difficult-to-control asthma based on the British asthma guidelines.⁴² Electronic alerts were added to the medical records of at-risk patients at participating primary care practices. This was coupled with practice-based training about the use of alerts to improve patient access and opportunistic management of asthma at every possible contact.

The increasing use of the MyHealth electronic health record may provide another means of streamlining the care of patients with severe asthma by allowing improved communication between primary and specialist care physicians.

Conclusion

The majority of patients with asthma are managed in primary care, and GPs play a pivotal role in the diagnosis and management of the disease in its milder form and in early referral of patients with severe asthma. A model of care that offers a multidimensional approach to severe asthma may improve patient symptoms and

quality of life and reduce exacerbations. There is scope today for better collaboration between specialists and primary care providers in the management of risk factors and comorbidities, in the coordination of community access to allied health input, and in the administration of biological therapies for severe asthma. Further work is still required to streamline and standardise referral and discharge pathways for severe asthma.

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