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Severe asthma care and treatment

Indicators and data for performance management across ten countries

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Abbreviations

CAD	Canadian dollars
CIHI	Canadian Institute for Health Information
COPD	Chronic obstructive pulmonary disease
ER	Emergency room
GINA	Global Initiative for Asthma
GP	General practitioner
ICD	International Classification of Diseases
ISAR	International Severe Asthma Registry
LOS	Length of stay
MDT	Multi-disciplinary team
mOCS	Maintenance oral corticosteroids
OCS	Oral corticosteroids
PY	Patient Years
SA	Severe asthma
SUA	Severe uncontrolled asthma
UK	United Kingdom
USD	United States dollars
WHO	World Health Organization

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Abstract

OBJECTIVES: This paper outlines the rationale and need for a conceptual framework comprising a standard set of necessary indicators to assess performance in severe asthma (SA) care and practice, together with an analysis of the current availability of statistical data on this topic across ten countries in order to understand the quality of evidence on performance in SA care and practice.

METHODS: An expert panel contributed to the creation of the framework and performance indicators, based on what is relevant and clinically meaningful for SA as an indication; the framework consists of four components: diagnosis of SA, treatment of SA, care provision for SA, and the socio-economic impact of SA. Study countries included were Australia, Brazil, Canada, France, Germany, Italy, Japan, Spain, Sweden, and the United Kingdom, all representing different approaches to health care financing, organisation and delivery, and geographic regions. Publicly available data from national and international sources was reviewed against the framework along with research to identify statistical sources and assess the availability of data on SA in each study country.

RESULTS: SA is a complex diagnosis and condition, and performance indicators need to be designed to reflect SA care and practice holistically and accurately. 44 indicators were identified across six themes: prevalence, policy structures and organisation, diagnosis, treatment, care delivery, and socio-economic impact. Clear gaps in the statistical evidence for performance in SA care exist across the study countries, as little public national or international data was identified for these indicators. Where available, data is limited to general data on healthcare resource use and drug reimbursement and often exists only for asthma diagnoses, not SA in particular.

CONCLUSION: SA remains an area of significant unmet need. There is clear imperative to improve data collection and reporting across all dimensions of SA care to ensure appropriate interventions are designed and implemented to reduce avoidable morbidity and mortality and improve quality of care. Both clinician and patient perspectives should be recognised when considering country-level performance in SA care and practice.

1. Background & Objectives

Severe asthma (SA) is a complex diagnosis given when asthma symptoms do not improve over a period of time, even where usual treatments are administered correctly and observed symptoms are not attributable to other external factors. Several subtypes of SA exist: allergic asthma, eosinophilic asthma, and non-eosinophilic asthma.

1.1. Severe asthma: prevalence and unmet need

Definition & diagnosis of severe asthma

Severe asthma was introduced into the International Classification of Diseases (ICD) in the 2016 update, with the addition of a new code (J45.5) on severe persistent asthma. Prior to this stage, the ICD covered only allergic, non-allergic, mixed, or unspecified types of asthma.

The remit of diagnostic parameters has experienced a recent shift as well: where previously asthma severity was defined by lung function, it is now predominantly based on an evaluation of the degree of control over asthma symptoms (Lommatzsch and Virchow, 2014).

Prevalence rates for SA vary per country, source, and subtype. Rates are difficult to ascertain as a lack of consensus on the definition associated with the condition and reliance on 'control' as the primary diagnostic parameter results in difficulty in the tracking and monitoring of the actual number of individuals suffering from SA in a specific country. The World Health Organization (WHO) estimates that 339 million people live with asthma worldwide (WHO, 2020). Based on estimates that 5 to 10% of the total asthma population have SA (Chung et al., 2014), between 17 to 34 million people suffer from SA in the world today.

Greater severity and/or greater numbers of asthma exacerbations for people living with SA are accompanied by significant decreases in asthma-related quality of life (Hossny et al., 2017; Lloyd et al., 2007). Frequent exacerbations and hospital admissions may affect individuals' quality of life through isolation and loneliness, frequent oral steroid use, general fear and/or anxiety, and not being able to work (Asthma UK, 2020c). People living with SA are also more likely to suffer from comorbidities (such as inter alia, obesity, sleep apnoea, and anxiety/depression) when compared to those with mild or moderate asthma; the presence of comorbidities may be linked to worse outcomes for people living with asthma (University of Newcastle, Australia, 2019). Oral corticosteroid (OCS) treatments, a widespread treatment option for those with SA, have been linked to the development of OCS-related comorbidities and complications and increased risk of fatal outcomes, creating an additional disease burden (Chung et al., 2019).

SA is associated with substantial morbidity (Trevor and Chipps, 2018; Asthma UK, 2020c), and asthma-related deaths still occur in many settings, disproportionally affecting those with SA or improperly diagnosed asthma (Royal College of Physicians, 2015). A review of asthma deaths in the UK found asthma deaths are often avoidable, in the sense that they should 'not occur in the presence of effective and timely healthcare' (Nolte and McKee, 2004; RCP, 2015; Asthma UK, 2017). A 20-year observational study in the US suggested mortality rates were particularly high for people living with SA who were treated with OCS (Bourdin et al., 2017). These substantial mortality rates are accompanied by recent reports that improvements in asthma mortality have stagnated over recent years (Jenkins, 2017).

People living with SA are also thought to have increased levels of healthcare resource use, and it is estimated to account for a larger portion of direct and indirect asthma costs compared to mild/moderate asthma despite being less prevalent (FitzGerald et al., 2017; Trevor and Chipps, 2018; Ivanova et al., 2012; Antonicelli et al., 2004). OCS treatment, and the resulting side effects, have also been linked to a significant increase in healthcare resource utilisation and hospital visits (Volmer et al., 2018; Chung et al., 2019).

1.2. Unlocking improvements through performance assessment

Evidence suggests that avoidable deaths for asthma remain high. Mortality for people living with SA who are treated with OCS may be higher than for those who are not, and people living with SA suffer from extensive morbidity and decreases in quality of life. These findings indicate there are recurrent issues in the care, treatment, and management of people living with asthma and SA. These issues can be addressed by changes to ensure more effective care, treatment and management of people living with SA: more effective management of SA could result in noticeably reduced mortality and improve the management of exacerbations, while treatment of comorbidities may, in turn, improve asthma outcomes (University of Newcastle, Australia, 2019; RCP, 2015). Control of asthma and related issues is one of the factors associated with improvements in quality of life (Hossny et al., 2017).

To understand *why* these issues remain and *how* they may be minimised or eradicated, healthcare systems should build an understanding of, and measurement systems for, the assessment of quality of care. Performance measurement and appropriate data collection are considered essential elements to improving overall performance and ensuring health system accountability (Smith et al., 2008; Smith et al., 2009). These are especially relevant for conditions where there is a direct link between disease management and overall mortality. Ensuring appropriate and thorough data is collected for SA will allow countries to conduct improved performance reviews, to identify key bottlenecks, and to feed back to practicing clinicians. This, in turn, will allow decision-makers to ensure appropriate interventions are in place to reduce avoidable mortality and improve quality of care.

1.3. Objectives

High prevalence figures and high avoidable mortality for individuals with SA, as well as extreme unmet needs for those living with SA (Menzies Gow et al., 2018), highlight the need to understand deficits in SA treatment and care. Additionally, there is an added need for governments and healthcare providers to improve understanding of SA care and practices at national and inter-country level in the current context of COVID-19. Most countries have implemented quarantine and isolation guidelines over the course of the pandemic, and many people living with chronic conditions, such as asthma and SA, were asked to safeguard and adapt to changes in access to, and delivery of, their healthcare. The pandemic and threat of novel viruses has brought the unmet need in the management of respiratory conditions to the forefront.

In this context, the objective of this study is to understand current capabilities and means of assessing performance in SA care and practice across the possible performance indicators identified and provide recommendations for next steps and considerations for system-level adjustments for performance assessment and metrics.

Report aims

1. Outline the rationale and need for a standard set of indicators to assess performance in SA.
2. Create a framework of indicators to measure performance in SA care and practice, while considering the complexity of the indication.
3. Map the availability of and assess existing publicly available data from ten countries against indicators to understand the quality of evidence on performance in SA care and practice.

2. Methods

The paper benefits from a two-part methodological design: 1) the creation of a set of health system performance indicators in SA care and treatment, and 2) the application of the framework to public data sources to identify the current state of health systems to measure performance in SA care and treatment. The focus of the paper is solely on SA specifically, and does not include mild or moderate asthma.

2.1. Design of performance indicators & framework

An expert panel, consisting of clinical experts, academic experts in health policy, and other stakeholders in the respiratory field, contributed to the creation of a framework of performance indicators based on issues found relevant and clinically meaningful for SA as an indication. The principles on (unmet) needs in people living with SA set out by Menzies-Gow et al. (2018; Box 1), were developed and adapted to a framework reflecting health system realities, providing meaningful, measurable, and relevant indicators for health care systems in improving care in SA.

Box 1: Principles for improved care in people living with severe asthma

Principle 1:	I deserve a timely, straightforward referral when my severe asthma cannot be managed in primary care.
Principle 2:	I deserve a timely, formal diagnosis of my severe asthma by an expert team.
Principle 3:	I deserve support to understand my type of severe asthma.
Principle 4:	I deserve care that reduces the impact of severe asthma on my daily life and improves my overall quality of care.
Principle 5:	I deserve not to be reliant on oral corticosteroids.
Principle 6:	I deserve to access consistent quality care, regardless of where I live or where I choose to access it.
Source:	Menzies-Gow et al., 2018

The panel developed a set of indicators based on a set of three considerations: the care needs of people living with SA explained in the principles in Box 1, physician information needs, and evidence or information essential for policymaking in the healthcare sector. In line with theory on performance management, the framework set out to track information across key aspects of measurement as set out in Smith et. al. (2009), including: population health measures, such as mortality; clinical quality and appropriateness of care through both process and outcome indicators; individual health outcomes; responsiveness of the health system, focusing on experience and satisfaction of people living with SA; equity; and productivity. The framework seeks to cover these issues across all aspects of the journey of people living with SA through the healthcare system, and also considers a wider system aspect to ensure the framework assesses the suitability of the policies and guidelines in place for SA. The indicators combine a system perspective with essential viewpoints from people living with SA and physicians to ensure the framework accurate reflects the needs of the multiple users and operators of the system. The panel convened over three months between November 2018 and February 2019. The final output was reviewed by members of the AstraZeneca-funded PRECISION Access Taskforce Steering Group.

Application of framework to data sources

A comprehensive data review was conducted for the systematic collection of data and statistics on the burden of disease of SA and the indicators set out in the conceptual framework to map available data on SA treatment and care. Publicly available data from national sources, such as government publications, health system documents, clinical guidelines, disease registries, and national statistical bodies, was reviewed to identify data on SA from the study countries for each indicator. Additional secondary sources, such as relevant international organisations such as the OECD and/or peer-reviewed journal articles, were also reviewed. Data was only included if it was about or relevant to SA. In addition, and where appropriate, peer-reviewed literature was consulted as well, with keyword restrictions were in place to find data on 'severe asthma'. The findings are structured following the framework produced, with emphasis on data availability in national sources. The findings are reviewed by source/institution, and for gaps in data collection.

Geographical scope

The geographic scope of the research covers Australia, Brazil, Canada, France, Germany, Italy, Japan, Spain, Sweden, and the United Kingdom. Countries were selected based on a) approaches to health care financing, organisation and delivery and b) geographical spread (see Appendix Table 1).

3. Results

3.1. Conceptual framework

The framework is made up of six sections across epidemiological data and policy structures and organisation, diagnosis of SA, treatment of SA, care delivery, and socio-economic impact covering a total of 44 indicators (Table 1). The largest sections of the framework reflect the principles essential to improving care for people living with SA enumerated by Menzies-Gow et al. (2018). Principles 1, 2, and 3 considered by Menzies et al. refer to diagnosis and early support and adequate referral and are reflected in a section on *diagnosis.* Included indicators are essential performance metrics, such as referral procedures and use of diagnostic tests, while others reflect experiences of people living with SA, such as the provision of adequate materials and inhaler training. Principle 5 outlines the need to reduce overreliance on OCS, reflected in a section on *treatment*. These indicators cover key issues related to OCS use, the availability and uptake of other treatments, and data on prescribing trends. The indicators included aim to contextualise overreliance on OCS and treatment and/or pharmaceutical management. Principles 3, 4 and 6 outline the need for quality and timely care, reflected in a section on *care delivery* with key indicators of performance in resource utilisation, access to care for people living with SA, the quality of care provided, and communication and management structures. Each of these sections seeks to incorporate indicators on clinical quality and appropriateness of care, looking at both processes and outcomes, the responsiveness of the health system to experience and satisfaction of people living with SA, and equity in care (as described in Smith et al., 2009).

Three additional sections aim to provide important contextualisation factors. The *epidemiology* section covers prevalence, incidence, and mortality rates, classified by Smith et al. (2009) as 'population health'. The *policy structure and organisation* section provides an understanding of the regulatory structure available at a system level. The final section contextualises *socio-economic impact*, reflecting the productivity measure described by Smith et al. (2009) through consideration of the financial impact on the individual and the health system.

Table 1: Conceptual framework

Theme	Sub-theme	Indicator	Principle
Epidemiology	Prevalence	Number and percentage of prevalence	n/a
	Incidence	Number and percentage of incidence	n/a
	Morbidity	Number and percentage of asthma DALYs	n/a
	Mortality	Number and percentage of asthma-related deaths	n/a
Policy structure and organisation	Guidelines	Existence of clinical or practice guidelines on asthma / SA	n/a
	Structure	Existence of patient organisations	n/a
		Existence of specialist care / characteristics of specialist care	n/a
Diagnosis	Diagnostic testing	Use of diagnostic tests	Principle 2
	Specialist referral	HCP/person responsible for referral and referral criteria used	Principle 1
		Time to specialist referral	
	Definitive diagnosis	Number of people living with SA in registries	Principle 2
		Number or ratio of people living with SA receiving a clear diagnosis	
		Provision of disease diagnosis and explanation in an understandable format	Principle 3
	Materials and education	Provision of knowledge and awareness building tools	
		Provision of training on the use of inhalers or any other medical devices	
		Patient information available in multiple formats and languages	
Treatment	OCS use	Average usage of OCS prior to specialist care referral	Principle 5
		Individual episodes of OCS use in a year	
	Available biologic treatment	Reimbursement status of relevant drugs / biologics	
		Existence of early access opportunities	
		Number of people living with SA offered full range of potential treatment options with an emphasis on biologics	
	Biologic use	Number of people living with SA using biologic treatments	
	Prescribing	Prescribing data on asthma / SA	
		Number of decisions taken by HCP or MDT to prescribe biologics	
		Variations in regional prescribing	
Care delivery	Resource utilisation	Value of healthcare resource use (unscheduled)	Principle 4, 5
		Number of clinical episodes in a year (planned / unscheduled)	
		Hospital admission rates for people living with asthma/SA	
		Hospital length of stay (days)	
	Access to care	Ratio of people living with SA who access specialist care services	Principle 6
		Geographic distribution of specialist care centres	
		Average travel distance for people living with SA to specialist and ongoing care	
		Length of waiting times for specialist appointment	
		Waiting times on the day of care interaction	
	Communication and management of care	Details on proportion of people living with SA being managed by MDT	Principle 2, 4, 5
		Availability of specialist nurses and educators and role in treatment and education of people living with SA	Principle 3
		Level of communication between specialist centres and referring sites	n/a
		Involvement of people living with SA in decisions about care	Principle 5
	Quality of care	Availability of a national quality standard for SA	Principle 4
		Availability of financial incentives around SA care/outcomes	
		National strategy or plan on asthma/SA	
Socio-economic impact	Absenteeism	Absenteeism associated with SA	n/a
	Cost of illness data	Individual-level costs	n/a
		System-level costs	n/a

Source: Authors.

3.2. Data availability

3.2.1. Epidemiology & policy systems

Table 2 outlines the availability of existing information from national or other sources on the indicators included in the framework for the epidemiological context of SA, and policies within the healthcare system.

Table 2: Data availability and information sources across countries: epidemiology and policy systems

	AUS	BR	CAN	FR	GER	IT	JPN	SP	SE	UK
Epidemiology										
Prevalence	✓	✓	✓	✓	✓	✓	✓✓	✓	✓	✓
Incidence	-	-	-	-	-	-	-	-	-	-
Mortality	-	-	-	-	-	✓✓	-	✓✓	-	✓✓
Morbidity	-	-	-	-	-	-	-	-	-	-
Policy systems										
National guidelines	✓✓	✓✓	✓✓	✓✓	✓✓	✓✓	✓✓	✓✓	✓✓	✓✓
Organisation of care	✓✓	✓	-	✓	✓✓	✓✓	-	-	-	✓✓

Key: ✓✓ : Information available from national sources
✓ : Information available from the literature
- : No information available
n/a : Indicator is not applicable to the relevant setting or system
Note: AUS: Australia; BR: Brazil; CAN: Canada; FR: France; GER: Germany; IT: Italy; JPN: Japan; SP: Spain; SE: Sweden; UK: United Kingdom
Note: Prevalence data may refer to severe asthma or severe uncontrolled asthma.
Source: Authors.

Prevalence rates for SA are scarce, possibly due to difficulties in tracking and monitoring of individuals suffering from SA in a specific country. International estimates suggest SA prevalence sits between 3% (Hekking et al., 2015) and 10% (Chung et al., 2014) of all asthma sufferers, ranging from 4% to 10% in western European countries, 5% to 10% of the asthma population in Canada and 2.4% of people living with asthma in Japan. However, data using different definitions give higher estimates: SA estimates for Germany range from 30% to 38%, 16.9% in UK, and 18.4% in France (Myers et al., 2017). Even though SA prevalence rates have been identified for each country (Appendix Table 2), issues arise as to the strength and comparability of this evidence since it comes from several sources, largely literature based and not from national sources. *Mortality and morbidity rates* are also scarce, highlighting the need for large multicentre studies with control data to look for drivers and predictors of mortality in SA. A relevant study using data from five European electronic health care databases found that the standardised all-cause mortality rates ranged between 11.3 and 14.8/1000 person-years (PY) across the respective national databases (see Appendix Table 3) (Engelkes et al., 2020).

All study countries have national *asthma guidelines*, although in Italy these are adapted from the Global Initiative for Asthma (GINA) guidance. Many of these national guidelines provide guidance on appropriate treatments and care pathways for SA. At an international level, various documents proposing different clinical definitions of SA in adults and children have been published by international taskforces, workshops, networks and guideline committees (i.e., GINA, the taskforce of the European Respiratory Society and the American Thoracic Society, and the WHO). Nevertheless, a lack of consensus on the definition and diagnosis of SA still exists as the various definitions proposed employ different inclusion/exclusion criteria and nomenclature to define and describe SA and people living with SA respectively (c.f section 3.2.2) (Lommatzsch and Virchow, 2014; Bel et al., 2011). Further challenges in defining and/or diagnosing SA arise due to notable differences in adherence and implementation of guidelines for diagnosis and management of asthma observed among asthma care clinicians (Cloutier et al., 2018).

Only some study countries have established *national registries* and associations as part of their national policies on the organisation of care for SA. Only some study countries have policy systems in place to facilitate the diagnosis, management and organisation of care for SA. Information on national policies around the organisation of care for people living with SA was not always available from national sources.

Evidence around *misdiagnosis* of SA and/or around unawareness of difficult or SA symptoms in those living with SA suggests that there are numbers who may benefit from improved assessment, diagnosis, management and/or treatment.

Key findings on epidemiology and policy systems

- Prevalence, mortality and morbidity rates for SA are scarce.
- All study countries have national asthma guidelines, many of which provide guidance on appropriate treatments and care pathways for SA. Some evidence suggests non-compliance with the respective guidelines.
- Only some study countries have established national registries and associations.

3.2.2. Diagnosis

Table 3 outlines the availability of existing information from national or other sources on the indicators included in the framework around the diagnostic procedures for SA, including specialist referral, diagnostic testing and educational material provided following diagnosis of SA.

Table 3: Data availability and information sources across countries: diagnosis

	AUS	BR	CAN	FR	GER	IT	JPN	SP	SE	UK
Specialist referral										
Time to specialist referral	-	-	-	-	-	n/a	-	-	-	-
Referral guidance / criteria	✓✓	-	-	-	✓	n/a	-	✓✓	-	✓✓
Testing										
Use of diagnostic tests	-	-	-	-	-	-	-	-	-	✓✓
Definitive diagnosis										
Number of people living with SA in registries	-	-	-	-	-	-	-	-	-	-
Number of people with SA receiving clear diagnosis	-	-	-	-	-	-	-	-	-	-
Provision of disease diagnosis and explanation in an understandable format	-	-	-	-	-	-	-	-	-	-
Materials and Education										
Provision of knowledge building and self-management tools	✓✓	✓✓	✓✓	✓✓	-	-	✓✓	-	-	✓✓
Provision of training on the use of inhalers or any other medical devices	✓✓	✓✓	-	-	-	-	-	✓✓	✓✓	-
Patient information available in multiple formats and languages	-	-	-	-	-	-	-	-	-	-

Source: Authors.

The evidence on diagnostic procedures for SA, including information on specialist referral and diagnostic testing, is scarce and not available at all for a significant number of indicators (Table 4). Time to specialist referral following first awareness of symptoms, and engagement with a clinician or secondary care professional are key indicators for the diagnostic context of a given healthcare system. Barriers to receiving a timely referral may include travel distance, waiting lists, unclear reasons for referral, and patient-specific factors (Chung et al., 2018). Appendix Table 6 shows the wide range of referral criteria used.

Severity is defined differently across countries. For example:

- In Canada, guidelines for diagnosis and management of people living with asthma do not provide a specific definition for SA and solely refer to people with severe uncontrolled asthma (SUA) (Myers et al., 2017). The Canadian guidelines highlight the need to understand the difference between uncontrolled asthma due to poor management, and SA conditions which exist despite correct management (FitzGerald et al., 2017).
- The Japanese guidelines provide a system for the assessment of asthma severity of asthma, noting this is key in appropriate asthma management and pharmaceutical treatment (Ichinose et al., 2017).
- While no international agreed upon definition exists for SA, in the UK SA has been described as asthma that remains uncontrolled under GINA treatment Steps 4 or 5 (including additional

add-on therapies, high-dose therapies, continuous or frequent use of oral steroids), the highest treatment steps in the GINA guidelines (Myers et al., 2017).

Criteria for referral of people living with SA to a specialist practitioner or clinic are described by the GINA guidelines, though a lack of clinical consensus on when to refer people with suspected difficult/SA remains (Asthma UK, 2018). Canadian guidelines note there are reports of up to one third of individuals with an asthma diagnosis who are eventually recognised as having alternative diagnoses and advises caution in making a clinical diagnosis of SA (FitzGerald et al., 2017). Additionally, in Spain, despite national guideline recommendations for the referral of people living with severe uncontrolled asthma to asthma units where people can receive multidisciplinary management, it is estimated that more than 40% of people living with SA may not be referred to a specialist (Pola-Bibian et al., 2016; GEMA, 2020). Challenges in SA diagnostic procedures and testing arise due to variation in the inclusion/exclusion criteria and nomenclature that are employed by different national and international guidelines to define and describe SA and people living with SA respectively (Lommatzsch & Virchow, 2014).

Evidence on the availability and utilisation of SA educational materials was more readily available across countries compared to other indicators studied in this section. Data shows limited availability of educational programmes/material and variability in the level of detail provided in clinical guidance on education programmes.

- Brazilian guidelines have a 'pre-consultation' period, targeting the people during waiting times or support provided by the nursing team, relevant students, or community volunteers, the medical consultation itself, and a 'post-query' period, including inhaler training by the nursing team and a one-day-a-week scheduled education program (Brazilian Guidelines, 2006).
- Survey data from Canada suggested 82.5% of respondents received information or education about asthma from at least one source, including family physicians (61.2%), specialists (51.8%), the Asthma Society of Canada (51.8%), and the Internet (49.4%) (Asthma Canada, 2017). In another survey, respondents indicated they referred to their physician (85%), online resources (41%) and ancillary providers such as nurses or physician assistants (40%) to improve their understanding of managing their symptoms (Genentech, 2018).
- In Germany, education tools mentioned were printed media (non-professional, non-scientific), targeted at the general public and distributed in pharmacies free of charge (Lingner et al., 2017) whereas a study of asthma schooling programmes found that participants regretted quickly forgetting information with no opportunity to "refresh the information" (Lingner et al., 2017).

While types of asthma management and levels of involvement of people living with SA vary per country, research suggests that room remains for improved education for both people living with SA and physicians on the use of asthma management plans and validated tool (Chapman et al., 2017). Additional education sources and formats (such as support groups) could be available for those who are unable to see a healthcare professional, or for those who are seeking support from others who are experiencing similar issues (Asthma Society of Canada, 2017).

Key findings on diagnostic processes for SA

- Evidence on diagnostic procedures for SA is scarce.
- Asthma severity is defined differently across countries and highlight a lack of clinical consensus on when to refer people with suspected difficult or severe asthma.
- Evidence on the availability and utilisation of educational materials was largely available across countries, though the data shows variability in the level of detail provided in guidance.
- Room remains for improved education for both people living with SA and physicians.

3.2.3. Treatment

Table 4 outlines the availability of existing information from national or other sources on the indicators in the framework around prescribing and pharmacological management of SA, including the availability and use of biologics.

Table 4: Data availability and information sources across countries: treatment

	AUS	BR	CAN	FR	GER	IT	JPN	SP	SE	UK
OCS use										
Average usage of OCS prior to referral to specialist care	-	-	-	-	-	-	-	-	-	-
Individual episodes of OCS use in a year	-	-	-	-	-	-	-	-	-	-
Available treatments (Biologics)										
Reimbursement status of drugs / biologics	✓✓	✓✓	✓✓	✓✓	✓✓	✓✓	✓✓	✓✓	✓✓	✓✓
Existence of early access opportunities for biologics	-	-	-	-	-	-	-	-	-	-
Biologics use	-	-	-	✓	✓	✓	-	✓	-	✓
Number of people living with SA offered full range of potential treatment options with an emphasis on biologics	-	-	-	-	-	-	-	-	-	-
Prescribing										
Prescribing data on SA	-	-	✓	✓	✓	✓	-	✓	✓	✓
Number of decisions taken by average MDT to get biologic	-	-	-	-	-	-	-	-	-	-
Variations in regional prescribing	-	-	-	-	-	-	-	-	-	-

Source: Authors.

Studies reporting *acute or chronic OCS usage* in SA are extremely limited and no evidence was found measuring the use of OCS prior to specialist referral and/or annual OCS bursts. A comparative study across countries found that, overall, the use of OCS varies between settings, and, in Australia, maintenance OCS was prescribed in up to 25% of SA cases and the median daily dose for people living with SA was estimated to be 10 mg/day (prednisolone equivalent), although a wide dose range is reported (2–50 mg) (Chung et al., 2020). Similar data was reported for the UK where the median prednisolone dose was 10–15 mg/day across several specialist UK centres. However, the International Severe Asthma Registry (ISAR) reports 59.6% of people living with SA in the UK were prescribed OCS maintenance treatment, while a longitudinal UK study from 2005 to 2012 of over 60,000 people living with SA found 75% of them were exposed to OCS (Chung et al., 2020). Fewer OCS users have been reported in Italy (33.3%) (Van Ganse et al., 2006) and Spain (21.7% and 30.2%) (Pérez de Llano et al., 2019; Sicras-Mainar et al., 2020).

National, publicly available information exists about the reimbursement status of biologic therapies for SA. According to this evidence, there is significant variation across the study countries on the final reimbursement decisions taken about the biologic therapies for SA and more importantly, on whether positive reimbursement decisions for the same medicine across countries are unconditional or conditional upon clinical and/or pricing restrictions. Additionally, country-specific discrepancies between the reimbursement status and actual availability of biologics might exist, such as in Italy, where a number of biologic treatments have been approved but regional reimbursement restrictions are in place that impede access to and availability to people living with SA. Appendix Table 9 details the reimbursement status of these biologics across the ten countries. Some level of information on the *use and prescribing of biologics* exists from secondary sources. For example, a recent Italian and German study highlighted that 12% of people being treated by GPs and private, office-based respiratory consultants were eligible for a specific biologic, but did not receive this therapy (Price et al., 2017). In the UK, around 50,000 individuals of approximately 200,000 to 250,000 living with SA are reported to be on the highest level of treatment (Asthma UK, 2017). Detailed information also exists on the *numbers of people living with* SA *receiving biologic therapy*, showing a small fluctuation in the numbers of SA OCS users between countries, particularly in the use of Xolair®, but more importantly, showing discrepancies between percentage of use reported by people living with SA and the physician-stated percentage of people living with SA that receive biologic therapy (Adelphi 2018, see Appendix Table 10). Studies capturing prescribing patterns specifically in SA were not identified.

Key findings on treatments for SA

- Studies reporting acute or chronic OCS usage in SA are extremely limited. A comparative study across countries found that the use of OCS varies between settings.
- The reimbursement status of biologic therapies is publicly available. Significant variation exists across final reimbursement decisions for biologic therapies and whether decisions are conditional upon clinical and/or pricing restrictions.
- Cross-country discrepancies observed in the percentage of physicians prescribing biologics and mOCS.

3.2.4. Care delivery

Table 5 outlines the availability of existing information from national or other sources on the indicators included in the framework around care delivery in SA, including resource utilisation, access to care, communication practices and quality of care.

Table 5: Data availability and information sources across countries: care delivery

	AUS	BR	CAN	FR	GER	IT	JPN	SP	SE	UK
Resource utilisation										
Value of healthcare resource use (unscheduled)	-	-	✓	-	✓	✓	-	✓	✓	✓
Number of clinical episodes in a year (planned and unscheduled)	-	-	✓	-	✓	✓	-	✓	✓	-
Hospital admissions for people living with asthma/ SA	✓✓	✓✓	✓✓	✓✓	✓✓	✓✓	✓✓	✓✓	✓✓	✓✓
Average length of stay in hospital	-	-	-	✓✓	✓✓	✓✓	-	✓✓	✓✓	✓✓
Access to care										
Ratio of people living with SA accessing specialist care services	-	-	✓✓	-	-	✓✓	-	-	-	-
Geographic distribution of specialist centres	✓	-	-	-	-	-	-	-	-	-
Average travel distance for people living with SA to specialist care	✓	-	-	-	-	-	-	-	-	-
Length of waiting times for specialist appointment	-	-	-	-	-	-	-	-	-	-
Waiting times on day of care	✓	-	-	-	-	-	-	-	-	-
Communication and management										
Level of communication between specialist centres and referring sites	-	-	-	-	-	-	-	-	-	-
Availability of specialist nurses and educators and role in treatment and education of people living with SA	-	-	-	-	-	-	-	-	-	-
% people living with SA managed by a multi-disciplinary team	-	-	-	-	-	-	-	-	-	-
Involvement of people living with SA in decisions about their care	-	-	-	-	✓	-	-	-	-	-
Quality of care										
Availability of a national quality standard on care for SA	-	-	-	-	✓✓	-	-	✓	-	-
Availability of financial incentives around SA care/outcomes	-	-	-	-	-	-	-	-	-	-
National strategy or plan on asthma/SA	-	-	-	-	-	✓✓	-	-	-	-

Source: Authors

No data were found on *barriers of access to care*, such as waiting times for specialist appointments, waiting times on the day of care interaction and travel distance for people living with SA to specialist and/or ongoing care. A limited number of studies in Australia were identified that measured and discussed these factors as barriers in Australian settings. A survey of people living predominantly with severe (and some mild) asthma reported a typical one or two hour wait to see the doctor on the day of care (Douglass et al., 2004).

Access to specialist care services is suggested to be low, with only a minority of people living with SA managed by specialists in countries where evidence was found. Findings include:

- In Australia, a subspecialised SA service offers the advantage of a structured, multidimensional approach to confirm the diagnosis, asthma severity and phenotype and manage risk factors and comorbidities which 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 (Chung et al., 2018). Information on the extent of access to and utilisation of this service by Australian people living with SA was not identified.

- In Canada the ratio of total people living with asthma accessing specialist services was 2.3% in 2011/12, although this did not refer to people's asthma severity (Health Infobase Canada, 2018).
- According to the SANI database, in Italy, there were 65 reference centres with 437 enrolled people living with SA in 2018 (PRECISION, 2018), although only a minority of Italian people living with asthma is followed by specialists, and many are never seen by a doctor (Global Initiative for Asthma, Italian Group, 2017).
- In the UK, despite recommendations for people to be referred to specialist care when on high dose treatment or continued oral corticosteroids, many are not under specialist care and rely on their local GP (Asthma UK, 2017; Asthma UK, 2020b). The reason could be that there are only a small number of specialist asthma centres spread out across the country, with large catchment areas. For access, individuals need to meet a set of criteria: for example, number of life-threatening asthma attacks, steroid doses, duration of reliance on steroids (Asthma UK, 2020a). Exact information on the number of people living with SA in specialist care was not identified.

A significant lack of evidence was identified for indicators on the level of communication between specialist centres and referring sites, the availability of specialist nurses and educators and the level of MDT utilisation by people living with SA. With regards to the latter, some evidence was found on the existence and offer of MDT to people living with SA in Australia (McDonald et al., 2016) and the UK (SIGN Guidelines, 2019), although the proportion of people living with SA that actually access these services remains unclear. Levels of people's involvement in decisions about their care was also studied, with the suggestion that the quality of interactions that people living with SA have with their physician play a role in either enhancing or impeding long-term use of inhaled corticosteroids (Pelaez et al., 2015). Only one relevant study of a focus group of German people living with SA was found to discuss the extent of their involvement in shared decision-making about their care, where none of the participants recalled a shared decision-making process with their doctor (Linger et al., 2017).

Only a few studies with reference to unscheduled healthcare resource utilisation were identified. A randomised controlled trial in a UK primary care setting reported a novel approach using an electronic asthma risk registry was found to reduce asthma hospitalisations, ER presentation and unscheduled GP visits by 50%, 26% and 21%, respectively (Chung et al., 2018). Some studies were found on scheduled and unscheduled clinical episodes in SA, although not for all study countries; Appendix Table 11 shows the available evidence on the annual, planned and unplanned, number or clinical episodes in SA. Information on hospital admissions and average length of stay (LOS) specifically for people living with asthma was more comprehensive and available for most study countries through OECD and Eurostat sources; Appendix Table 12 shows the range of asthma-related hospital admissions and respective LOS across the study countries where such evidence was available. The lowest number of admissions was 7.61 per 100,000 people (Italy), while the highest was 70.97 per 100,000 people (UK). High rates are also reported in Australia and Spain. Additionally, some individual, country-specific sources on asthma hospital admissions and average LOS were identified for Australia, Brazil, Canada, Japan, Spain and the UK (Appendix Table 13).

Finally, a number of quality-of-care indicators were studied, for which only information around the availability (or not) of a national quality standard on care for SA was available (Appendix Table 14). Evidence on the availability of financial incentives or Quality of Care frameworks/data around SA care or outcomes was particularly limited.

Key findings on care delivery in SA

- Access to specialist care services is suggested to be low, with only a minority of people living with SA managed by specialists in countries where evidence was found.
- No data found on length of waiting times for specialist appointments, waiting times on the day of care interaction and travel distance for people living with SA to specialist and/or ongoing care.
- Barriers in the delivery of care includes long waiting lists due to lack of specially trained HCPs, the limited availability of local centres and the resulting distance to treatment, and access to adequate staffing and objective testing.

3.2.5. Socio-economic impact

Table 6 outlines the availability of existing information from national or other sources on the indicators included in the framework around absenteeism and cost of illness of SA, both at the individual and system level.

Table 6: Data availability and information sources across countries: socio-economic impact

	AUS	BR	CAN	FR	GER	IT	JPN	SP	SE	UK
Absenteeism										
Absenteeism associated with SA	✓	✓	✓	-	-	✓	-	✓	-	✓✓
Cost of illness data										
Individual-level costs	-	✓	-	-	-	✓	-	✓	-	✓✓
System-level costs	✓✓	✓	✓	✓	✓	✓	✓	✓	✓	✓✓

Source: Authors.

Costs to the system

System-level cost-of-illness studies for SA were more readily available, although the definitions of SA used therein were not consistent, with costs measured corresponding to SA, persistent asthma, poorly controlled asthma, severe atopic asthma, and other definitions across studies. Discrepancies also existed in the asthma populations studied across countries, including children, adults, or total asthma population within a setting. The cost of unscheduled care is suggested to be higher than scheduled care in some settings (France, Germany, and Italy), while unscheduled care is less expensive than scheduled care in others (Spain, Sweden, and the UK) (Williams et al., 2006). A combined mean annual cost per person in the adult severe persistent asthma group amounted up to €1,400 (Williams et al., 2006). A study of urgent care costs of uncontrolled asthma in Canada found a total cost CAD$33,107,133 based on a unit cost of an unscheduled family physician visit of $27.85 (Seung & Mittman, 2004). Another comparative study of asthma-related resource use and cost by GINA classification of severity in three European countries measured direct medical costs (including costs from ED and hospitalisations, asthma related drugs, physician visits) and indirect costs and found that total mean annual costs per person living with SA ranged from €3,300 in Italy, to €4,100 in France and between €8,554 and €10,000 in Spain (Melero Moreno et al., 2019; Van Ganse et al., 2006). Costs identified by all country specific studies are presented in Appendix Table 15.

Healthcare costs for asthma are generally estimated to be significant: from CAD$46 million in British Colombia in Canada up to AUD$1.2 billion in Australia (Ismaila et al., 2013; Australian Centre of Excellence in Severe Asthma, 2016). A large portion of these costs is driven by severe or uncontrolled asthma: in Spain, Australia and Canada estimates suggest SA accounts for 50%, 60% and 94% of total asthma costs respectively, while in the UK people living with severe or uncontrolled asthma are estimated to cost the system up to four times as much as those with non-severe asthma (Pérez de Llano et al., 2016; Australian Centre of Excellence in Severe Asthma, 2016; Asthma UK, 2018; CIHI, 2018). High annual costs per person are reported in the literature (see Appendix Table 16). Management and treatment choices have a direct implication for costs as well: a Swedish study found that those treated with regular OCS had greater direct costs compared to those not receiving regular OCS treatment and reported significantly lower HRQOL (Jannson et al., 2020).

Cost to the individual

Evidence on the cost-of-illness of SA at the individual level was limited. Some evidence was identified for Brazil, Italy, Spain, and the UK but challenges in the interpretation and comparability of this evidence across countries arise due to the different levels of costs measured in different studies. Individual level cost-of-illness data from Brazil reported an average annual hospital cost per person of 135 USD and 733 USD, whereas from the family perspective, average annual direct costs per person varied from 764 USD to 929 USD (Stirbulov et al., 2016). In Italy, individual/social burden due to asthma was measured in terms of resource utilisation (e.g., 87.5% of people living with severe persistent asthma reported at least one medical consultation in the last 12 months, 37.5% reported emergency department visits and 26.7% reported a hospitalisation (Maio et al., 2012)). The annual cost of OCS side effects (e.g., annual costs per person related to OCS-related adverse events) in SA groups were equal to €1,957.50 (Canonica et al., 2019). In Spain, mean annual direct costs were estimated at €7,472 per person, with the cost per exacerbation amounting up to €1,410 per person (Melero Moreno et al., 2019). Finally, a study using data from the British Thoracic Society Difficult Asthma Registry estimated direct healthcare costs and the annual mean treatment costs among people living with severe refractory asthma in the UK to be £2,912 (SD £2,212) to £4,127 (SD £2,449) (NHS England, 2017).

Work impact

Data on absenteeism and productivity losses due to SA was scarce. Comparability of figures across settings is not always feasible due to different types of measurement. Data found includes:

- A study in Australia, in which participants with SA reported much higher presenteeism and activity impairment than those with non-severe asthma, but no significant difference in absenteeism (Hiles et al., 2018).
- A study in the UK which found that 26% of participants were not working due to SA, 73% of whom were on sustained oral corticosteroids (Asthma UK, 2017).
- An Italian cost-of-illness study across asthma severity groups which found 25% of people living with SA reported work/school absenteeism (n=13) (Maio et al., 2012).
- A literature review of Canadian studies, which reported that 9.1% of people living with SA were absent for 7 or more days (Ismaila et al., 2013).
- Two studies of Spanish adult asthmatics: a study of 226 people living with SA measuring productivity loss using the lost workday equivalent index, reporting 3.67 mean days of

absenteeism during the last month and decreased productivity by 58.77% (95%CI, 55.07-62.47) (Ojeda et al., 2013). A more recent study including 303 people living with SA estimated that mean sick leave due to SA was 9.1 days per person per year, with mean annual indirect costs up to €1,082 per person (Melero Moreno et al., 2019).

- A Canadian study which reported that a person with uncontrolled asthma would avoid CAD$184.80 in productivity loss by achieving clinical control during a week, CAD$167.50 (90.6%) of which would be due to presenteeism (Sadatsafavi et al., 2014). A study assessing asthma and its socio-economic reality in Brazil which reported that people with severe and moderate asthma reduced their mean family incomes during the duration of the study (Costa et al., 2013).

Key findings on the socio-economic impact of SA

- The cost of unscheduled care is higher than scheduled care in some settings, while unscheduled care is less expensive than scheduled care in others.
- Data on absenteeism and productivity losses due to SA was scarce. Comparability of figures across settings is not always feasible due to different types of measurement.
- Studies suggest participants with SA reported much higher presenteeism and activity impairment than those with non-severe asthma, but no significant difference in absenteeism.
- Evidence on the cost-of-illness of SA at the individual level was limited.
- System-level cost-of-illness studies are prevalent and available across all study countries, although the definitions of SA and asthma populations used were not consistent.

4. Discussion

4.1. Current availability of data for performance assessments in severe asthma

Key findings on data availability

Existing performance assessments: Very few performance assessments of respiratory diseases, let alone SA, exist.

Existing data and guidelines: Limited data found on indicators in framework across all countries; No current performance assessment data collected for SA; National guidelines adhere to the GINA international guidelines to an extent, but not in full.

Data on severe asthma: Most available data across both national and literature sources is for asthma, not SA.

Sources: Little information available from national sources, reliance on literature sources.

Existing performance assessments in SA

Performance assessments of healthcare provided in a specific disease area are generally scarce. A review of the literature reveals few efforts at assessing health system performance for respiratory disease, let alone for SA in particular. Some countries do conduct these to a certain degree: for example, the Swedish National Body of Health and Welfare conducted a performance assessment of asthma and COPD healthcare and adherence to national guidelines in Sweden in 2018, and the UK published an outcomes strategy for asthma and COPD in 2012 (See: Swedish National Board for Health and Welfare, 2018; UK Department of Health, 2012). However, even where performance assessments are conducted (e.g., Sweden, the UK), documents are often focused on asthma and COPD, not SA. As SA is a complex diagnosis, numerous metrics are necessary for performance measurement to assess SA treatment and care. Internationally ISAR has started collecting data across a number of countries but is currently focused primarily on demographic and clinical data of those in care for SA (Wang et al., 2019).

Existing data and guidelines

Limited data was found in each setting across the epidemiological features of SA and the identified elements of the trajectory of people living with SA: diagnosis, treatment, and care delivery. While all countries have asthma guidelines in place, some for SA specifically, gaps for performance assessment remain. For example, diagnosis pathways and referral systems for those with suspected SA were found to be laid out in guidelines across countries to some degree, but no clear performance data is collected to understand how people living with SA move through the system at any stage of care. While there is some evidence for performance indicators in asthma or SA, such as morbidity, hospital visits or length of stay of hospitalisation, the complexity of SA and asthma more generally is not widely reflected in current data collection or performance assessment of national healthcare systems.

Notably, despite guidelines on care for people living with asthma, a lack of consensus within and across countries when those with suspected SA should be referred to a specialist remains, and often asthma guidelines do not provide a specific definition of SA to guide these decisions. Similarly, although some relevant information is available through national bodies due to their remit, such as treatment approved to use for people living with SA by regulatory bodies, little to no information is made available elsewhere in the system on the use of these treatments, prescribing trends, or the decision-making process clinicians use.

National guidelines adhere to the international guidelines for SA set out by GINA to an extent, but not in full. For example, GINA outlines the identification of poor adherence, incorrect technique, and the provision of an asthma management plan as essential to the diagnosis and management of SA (GINA, 2018). And while guidelines in a majority of countries provide information on the provision of self-management tools and/or the provision of training for the use of inhalers, only the Australian and Brazilian guidelines detail standards for both.

Severe asthma specific data

Some data identified from either national sources or other sources only existed for asthma, and not SA. For example, epidemiological endpoints, such as the prevalence of and the mortality and morbidity were found for asthma, but limited information is available for those same endpoints with reference to SA specifically. This could potentially be due to the relatively recent introduction of the diagnostic code in the ICD, and thus the collection of accurate collection of data, and the difficulty in assessing and diagnosing SA. Resource utilisation and cost data, such as hospital admissions, length of hospital stays and system level costs, were often only available for asthma and not for SA.

Sources

Limited information was available through national sources, with many data points only available through literature sources, including data on productivity impact or costs for the health care system or the individual. And yet other information, such as care delivery processes or outcomes, were unavailable from either national or literature sources. A majority of countries did not have any mortality or morbidity data available in either the literature or within national sources.

This study shows a scarcity of readily available data on SA from national sources. Data often focuses on asthma more widely or relies on third-party sources and research. Additionally, available information is often prevalent for primarily factual metrics, and not directly conducive to comprehensive performance assessment. Figures from the current literature are extremely useful in assessing the potential size and impact of the SA burden, treatment and care, and should not be underestimated. However, data from literature is not always ideal for assessing current performance levels across countries, as significant intra- and inter-country variation in these figures may result from small sample sizes, limited datasets, specific definitions or cut-off points for determining SA, or contain other variations resulting from the limited potential for other research bodies to conduct large-scale investigations into national performance in SA care. There is a need for countries to collect this data in a more centralised, systematic and consistent manner.

4.2. Existing data collection infrastructure and policies

Addressing the deficit in the collection of suitable data for performance assessment identified in this study should, at least in part, be the responsibility of the state in settings where healthcare is publicly provided: as Smith et al. (2009) state, performance information is ‘unlikely to develop optimally within a health system without the guidance and encouragement of governments.’ Ensuring data collection is conducted appropriately, frequently, and for the right indicators, and subsequently used to review suitable targets and monitoring, requires governments to ensure adequate data collection efforts are in place.

Key findings on existing infrastructure and policy

Willingness: Countries are open to improved data collection and reform in healthcare data.

Room for improvement: Reviews of current efforts in Australia and Brazil conclude limited use of data for research, unsystematic and /or unstructured data collection processes, and limited metrics.

Innovative efforts: Some countries are developing more innovative efforts to improve data collection across health services.

Countries seem to be open to improved data collection and reform in healthcare data collection with many countries included in this study currently collecting data at a national level: the Canadian Institute for Health Information (CIHI) in Canada, the Ministry of Health, Labour and Welfare in Japan, and the Swedish National Board of Health and Welfare (CIHI, 2013; Matsuda, 2019; Swedish National Board for Health and Welfare, 2019). In the UK, the collection of and access to healthcare data is highlighted as a critical policy endeavour, aligned with the National

Information Board (NIB) 2020 programmes, and wider government strategies and agendas (McNeil, 2017). Canada and the UK have also recently reviewed either the processes or the data collected in 2018 and 2017, respectively (CCA, 2018; McNeil, 2017).

However, room for improvement remains. In Australia, the National Innovation and Science Agenda outlined the government's aims to use data to drive better quality services, but Canaway et al. (2019) concluded 'limited use of primary health care data for research and for data linkage between health care settings' remained. Similarly, Brazil was found to have unsystematic and unstructured data collection processes, and collection only for limited metrics (Greca and Fitzgerald, 2019).

Some countries are also developing more innovative efforts to improve data collection across health services; examples include the French Health Data Hub, aiming to facilitate the sharing of big data in health, and the German Medical Informatic Initiative, which plans to integrate clinical data into medical research (Cuggia and Combes, 2019). It is important to note that all of these efforts, however, seem to be at national level for across-the-board health data generation, and do not outline what metrics should be covered. This all leads to the suggestion that the atmosphere is one of readiness and willingness, but that the actual collection and application of health data, especially for disease-specific outcomes, remains to be seen.

5. Recommendations

Policy recognition of these issues has to be accompanied by practical efforts to perform good measurement and monitoring, which require adequate technology and infrastructure. While the review in this study suggests there are systems in place for recognising the use of and burden on hospital resources, there are many key pieces of information currently excluded from any kind of data collection or where the burden relies mainly on peer-reviewed literature.

Key recommendations

1. Building strong technological infrastructure
2. Designing a system with effective communication and management
3. Identifying and measuring appropriate metrics
4. Establishing political will

1. Building strong technological infrastructure

Efforts to improve technological infrastructure in order to collect data will be part of a larger system overhaul or redesign in many countries and may require contemplating sources such as electronic health records as a means of collecting clinician data points. Clinical sources could be key in addressing a component of SA treatment and care as there is an absence of available data from a clinical setting on OCS use and other treatments.

2. Designing a system with effective communication and management

Implementing necessary infrastructure should also include adequate communication to or prompting of physicians (and possibly of people living with SA) to collect the necessary data with sufficient regularity. The kind of prompt or incentive that may work in a given setting will need to be considered in context by decision-makers. Additionally, beyond an involvement in design, the inclusion of all stakeholders in performance measurement is considered essential to ensure all components are captured (Smith et al., 2009) and is ultimately also key in ensuring health care provision is as efficient and effective as ideally possible for the health care system. This is particularly relevant to disease-specific efforts to ensure the data collected is useful, relevant and appropriate.

3. Identifying and measuring appropriate metrics

Policymakers and clinical leaders must consider the features of the health system in which they operate: the need for or design of certain indicators will invariably depend on characteristics of available pathways and treatments. Governments should reflect needs and experiences of people living with SA, physicians and other stakeholders in addition to system-based indicators. Smith et al. (2009) highlight the importance of tailoring performance measurement to specific disease areas, as condition or disease-specific indicators are key in ensuring the right information is collected. While common process-based indicators (such as LOS) are essential, they often do not reflect the full reality of the care and treatment provided or where the issue in the system really lies, unless they are, for example, adjusted by the severity of illness. While such indicators may capture whether or not people living with SA require an emergency department visit or an overnight hospital stay, they do not contribute directly to understanding why their symptoms are not controlled and whether there are decisions made earlier on in care which affect the use of secondary or tertiary care. Ultimately, this would result in better outcomes for both the individual and the wider system.

4. Establishing political will

Beyond these three focus points, there must be *political will* to drive change and review performance on a wider scale. The effective combination of appropriate infrastructure, data sources, encouragement of data collection, and the identification and the setting of targets and prioritisation of indicators will require stable leadership. Policy-makers need to consider prioritisation of key indicators, both to ensure the feasibility of the system 'as an unfeasibly large set of data may result from seeking to satisfy all information needs' (Smith et al., 2009). International collaboration may also be desirable: even with data collection in key indicators and/or performance assessments, variable data collection in national asthma registries and statistical bodies and different regulations on these issues create an obstacle for country comparisons and understanding best practice in context (Wang et al., 2019). Efforts at sharing metadata (data providing information on other data) or aggregate data across countries exist at national or cross-national level in Europe, but often focus on specific topics such as rare diseases (Cuggia and Combes, 2019).

6. Conclusion

This study outlines the kind of metrics necessary in order to conduct a full review of care and treatment of SA in ten countries and highlights the current lack of data in each setting for epidemiological measures and diagnosis, treatment, and care delivery for people living with SA.

While several countries are currently cultivating an atmosphere of readiness and willingness for the collection of health data, the actual collection and application of health data for disease-specific performance reviews has not been fully realised. With recognition of how effective management of SA could dramatically reduce avoidable mortality, the impact of comorbidities, and healthcare resource utilisation, as well as improve the quality of life of those diagnosed with SA, there is an essential need to improve SA care and practices at national and inter-country level.

Governments should take advantage of the general atmosphere of readiness and willingness for the collection of health data, and the effects of the COVID-19 pandemic to maintain political willingness and traction. Governments should consider a number of aspects in designing data collection efforts for SA: effective policy efforts and target setting, appropriate infrastructure and data collection methods, stakeholder involvement, and suitable indicators and metrics. A database of relevant, adequate and accurate information allows:

a) countries to conduct improved performance reviews and to identify key bottlenecks which contribute to high avoidable mortality and quality of care.

b) decision-makers to make quality decisions to ensure appropriate interventions and changes are enacted where necessary to improve health outcomes and optimal care is received by people living with SA.

c) the system to feedback on performance and action to practicing clinicians.

Where governments are currently constrained in collecting and assessing suitable data, they should look to instituting a mid- to long-term plan. In the meantime, the burden remains with other stakeholders to contribute to the understanding of quality of care and treatment in SA.

7. Further research

This research is part of a wider initiative looking at current policy and practices in SA care and treatment. The aims of the initiative are threefold:

- to provide insight into the value of performance assessment for improved outcomes and an overview of current country practices in performance assessment for SA.
- to create a list of metrics which are key to assessing performance in SA care.
- to supplement current knowledge on current policy and practices in SA care across these metrics through surveying clinicians practicing in the SA field and people living with SA.

The findings of the research are relevant for policymakers in designing improved performance measurement structures and in understanding current limitations of healthcare systems in SA care.

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9. Appendices

Appendix Table 1: Health system financing

Country	Health system financing source	Health system type
Australia	Public funding through general and income taxes	National healthcare system (the Medicare Benefits Scheme, MBS)
Brazil	Government expenditure with high levels of private costs	Universal healthcare system (the Unified Health System, SUS)
Canada	Provincial/federal general tax revenue	Universal public insurance system (Regionally administered)
France	Employer/employee earmarked tax; General tax revenue	Statutory health insurance system
Germany	Employer/employee earmarked tax; General tax revenue	Statutory health insurance system
Italy	National earmarked corporate and value-added taxes; general tax revenue and regional tax revenue	National healthcare system (the Servizio Sanitario Nazionale)
Japan	General tax revenue; insurance contributions	Statutory health insurance system
Spain	Public funding	National healthcare system (the Sistema Nacional de Salud, SNS)
Sweden	Public funding through general taxes	National healthcare system
United Kingdom	Public funding through general taxes	National healthcare system (the National Health System, NHS)

Sources:	Australia, Canada, France, Germany, Italy, Japan, Sweden, UK: Commonwealth Fund (n.d.) Brazil: World Bank (2014) Spain: Bernal-Delgado et al. (2018)

Appendix Table 2: Prevalence of Asthma and SA

	Asthma Prevalence		**Severe (Uncontrolled) Asthma Prevalence**		**Asthma Incidence**	
	Prevalence	*Prevalence*	*SA prevalence*	*SUA prevalence*	*Incidence*	*Incidence*
	(number, 2017)	*(%, 2017)*	*(%, 2002-2017)*	*(%)*	*(number, 2017)*	*(%, 2017)*
Australia	2,253,963.11	10.16	-	3% to 10%[3]	136,774.89	0.13
Brazil	8,761,260.45	4.28	-	8% to 74.3%[2]	1,744,839.16	0.16
Canada	1,827,688.00	5.40	55.0-10.0	-	216,828.03	0.12
France	4,081,981.93	6.63	2.8	3.2% to 18.4%[3]	219,071.16	0.07
Germany	3,763,983.40	4.77	5.7	30%[3] 38%[2] 66.2%[1]	202,839.14	0.05
Italy	2,128,990.45	3.66	2.0	14.2%[1] 34.6%[2]	137,926.94	0.07
Japan	5,883,268.59	4.84	2.4	-	457,671.22	0.08
Spain	2,373,107.50	5.38	-	3.9% 55.7%	112,870.46	0.05
Sweden	810,102.54	8.50	4.2	-	44,587.82	0.09
UK	5,578,169.69	8.87	8.5	16.9%[3]	282,058.63	0.08

Source:	Australia	Centre of Excellence in Severe Asthma, 2019
	Canada	FitzGerald et al., 2017
	Brazil; France, Germany; Italy, UK	Myers et al, 2017
	Japan	Sato et al., 2019
	Spain	Quirce et al., 2011
	Sweden	Larsson et al., 2018
Notes:	[1]	SUA among uncontrolled asthma
	[2]	SUA among severe asthmatics
	[3]	SUA among all asthma severities
	-	no evidence found

Appendix Table 3: Crude and age & sex standardised mortality rate (distribution of CPRD as reference population)

	Asthma			Severe Asthma		
	Overall MR	*Overall MR standardised*	*95% C.I*	*Overall MR*	*Overall MR standardised*	*95% C.I*
HSD (IT)	6.0	5.2	4.9-5.5	11.9	11.6	9.2-13.9
CPRD (UK)	6.5	6.5	6.4-6.6	14.8	14.8	14.1- 15.5
SIDIAP (SP)	8.8	6.4	6.1-6.7	25.3	13.0	10.5-20.6

Source: Engelkes et al., 2020
Note: Mortality Rates (MR) = number of deaths/per 1000 PY

Appendix Table 4: National clinical guidelines for asthma and or SA

	National Asthma Guidelines	Year last updated
Australia	Australian Asthma Handbook (AAH)	2017
Brazil	Brazilian Guidelines for the management of asthma	2006
Canada	CTS	2017
France	Société de Pneumologie de Langue Francaise (SPLF)	2016
Germany	Nationale Versorgungs Leitlinie (NVL), German Agency of Medicine	2013
Italy	GINASMA / Italian GINA guidelines	2019
Japan	JSA	2017
Spain	GEMA	
Sweden	Läkemedelsbehandling vid astma – behandlingsrekommendation	2015
UK	BTS (SIGN)	2019

Appendix Table 5: Availability of national registries and associations as part of their national policies on the organisation of care for asthma and/or SA

	Stakeholders/associations	National registry
Australia	National Asthma Council Australia	Severe Asthma Web-Based Database
Brazil	-	-
Canada	Asthma Canada	-
France	-	-
Germany	Ärzteverband Deutscher Allergologen AeDA; German Allergy and Asthma Association (DAAP)	German Asthma Net (GAN); https://erj.ersjournals.com/content/52/suppl_62/PA647
Italy	-	Severe Asthma Network (SANI)
Japan	Japanese Society of Allergology (JSA)	-
Spain	-	-
Sweden	Swedish Asthma and Allergy Association (https://astmaoallergiforbundet.se/)	-
UK	Asthma UK	UK Severe Asthma Registry

Appendix Table 6: Referral criteria used across study countries (referral from GP only)

		Referral criteria in instances of GP referral							
	Referral initiated by GP or patient	**SA diagnosis; suspicion of SA; or inadequate asthma control**	**Problems in definitive diagnosis**	**Treatment eligibility**	**Comorbidities (e.g. COPD)**	**Exacerbation and/or flare-ups**	**Specific symptoms**	**Recent hospital discharge**	**Poor adherence**
Australia	GP	✓	x	✓	✓	✓	✓	✓	✓
Brazil	GP?	✓	✓	x	x	x	x	✓	✓
Canada		✓	x	x	x	x	x	x	x
France	-	-	-	-	-	-	-	-	-
Germany	Patient / GP	✓	✓			x			
Italy	Patient	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a
Japan	-	-	-	-	-	-	-	-	-
Spain	GP								
Sweden	-	-	-	-	-	-	-	-	-
UK	GP								

Source: LSE, based on primary data and national clinical guidelines.
Note: - No evidence

Appendix Table 7: Key asthma treatment regimens prescribed by physician-reported current severity Q2 2018

	Short acting alone	**ICS/LABA alone**	**ICS-only**	**ICS/LABA +LRA**	**ICS/LABA + LAMA**	**Other LAMA inc. regimen**	**Other regimens**	**mOCS inc. regimen**	**Biologics inc. regimen**
Australia	-	-	-	-	-	-	-	-	-
Brazil	-	-	-	-	-	-	-	-	-
Canada	-	-	-	-	-	-	-	-	-
France	1%	13%	2%	6%	9%	6%	6%	10%	45%
Germany		17%	1%	3%	6%	7%	17%	16%	32%
Italy		16%	1%	7%	7%	10%	11%	22%	26%
Japan	-	-	-	-	-	-	-	-	-
Spain		4%		13%	5%	23%	5%	7%	43%
Sweden	-	-	-	-	-	-	-	-	-
UK		5%	2%	15%	9%	19%	2%	20%	29%

Source: Adelphi, 2018
Note: - No evidence

Appendix Table 8: Secondary evidence found on prescribing patterns across study countries (where available)

Canada	Most frequently prescribed anti-asthmatic drugs as follows: salbutamol and fluticasone. The proportion of patients receiving more than one class of anti-asthmatic drugs were 52% (Bianchi et al., 2010)
Italy	• Level of consumption of the most prescribed drugs, by category (in DDD*/1,000 inhabitants per day), drugs for asthma: 33.6 (2017) (Statista) • Share of patients using prescribed controller medicine for asthma in the past year in Europe, by frequency (2010): every day (41%); 1-6 times a week (8%); less than once a week (8%); as needed for symptoms (14%); did not take controller meds in the past year (27%) (Statista)
Spain	Spanish prescribing of inhaled corticosteroids to asthma patients was the highest among a study of 8 European countries (Jepson et al., 2000).
Sweden	• Medications indicated for asthma and COPD was prescribed to 5.6% of the population in primary care (n = 14,101). Among them, an asthma diagnosis was recorded for 5876 individuals (42%) (2004-2005) (Weidingher et al., 2014) • Use of combination corticosteroid/long-acting bronchodilator inhalers was 34.2% and 48.2% respectively and many patients used their inhaled corticosteroids periodically (Stallberg et al., 2009)
UK	The UK National Review of Asthma Deaths (2014) found evidence of excessive prescribing of reliever medication, under-prescribing of preventer medication, and inappropriate prescribing of long-acting beta agonist (LABA) bronchodilator inhalers (Levy et al., 2014)

Appendix Table 9: Reimbursement status of biologic treatments for SA across the study countries

	Decision-making body	Omalizumab (XOLAIR)	Mepolizumab (NUCALA)	Reslizumab (CINQAIR / CINQAERO)	Benralizumab (FASENRA)	Dupilumab (DUPIXENT)
Australia	*PBAC*	Reimbursed*	Reimbursed*†	Not reimbursed**	Reimbursed*†	Not reimbursed**
Brazil	*CONITEC*	Not reimbursed	Not reimbursed**	Not reimbursed**	Not reimbursed**	Not reimbursed**
Canada	*CADTH*	Reimbursed*	Reimbursed*†	Reimbursed*†	Reimbursed*	Not reimbursed**
France	*HAS*	Reimbursed	Reimbursed	Reimbursed	Reimbursed	Reimbursed
Germany	*IQWIG*	Not reimbursed**	Reimbursed	Reimbursed	Reimbursed	Reimbursed
Italy	*AIFA*	Reimbursed****	Reimbursed****	Not reimbursed	Reimbursed****	Not evaluated
Japan	*PMDA*	Reimbursed	Reimbursed	Not reimbursed	Reimbursed	-
Spain	*AEMPS*	Reimbursed	Reimbursed	Reimbursed	Reimbursed	Not reimbursed**
Sweden	*TLV*	Reimbursed	Reimbursed	Not reimbursed**	Reimbursed	Reimbursed
UK	*NICE*	Reimbursed†	Reimbursed*†‡	Reimbursed*†	Reimbursed*†	Not reimbursed***
	SMC	Reimbursed*	Reimbursed*†	Not reimbursed	Reimbursed*†	Not reimbursed**

Key:
*: Reimbursed, but specific clinical criteria are in place / Reimbursed, but with restricted use
**: Not currently reimbursed, but the product has not been evaluated by main HTA body
***: Not currently reimbursed, but the product is under evaluation
****: Product approved at a national level but not always available to patients due to regional reimbursement restrictions
-: No information found.
†: Discount agreed in patient access scheme or commercial arrangement, and is a condition for reimbursement
‡: Original guidance currently being update

Source: LSE, based on information from national decision-making bodies. Decisions referenced:
Australia: PBAC, a; PBAC, b; PBAC, c.
Brazil: CONITEC, a; CONITEC, b.
Canada: CADTH, a; CADTH, b; CADTH, c; CADTH, d.
France: HAS, a; HAS, b; HAS, c; HAS, d; HAS, e.
Germany: IQWIG, a; IQWIG, b; IQWIG, c; IQWIG, d.
Italy: Gazzetta Ufficiale, a; Gazzetta Ufficiale, b; Gazzetta Ufficiale, c; Gazzetta Ufficiale, d
Japan: PMDA, a; PMDA, b; PMDA, c; KpEGG
Spain: AEMPS, a; AEMPS, b; AEMPS, c; AEMPS, d
Sweden: TLV, a; TLV, b; TLV, c. TLV, d.; TLV, e.
UK: NICE, a; NICE, b; NICE, c; NICE, d; NICE, e; SMC, a; SMC, b; SMC, c; SMC, d.

Note: Information correct as of July 2020.

Appendix Table 10: Proportion of patients receiving biologic therapy Q2 2018 vs. Physician-stated % of patients receiving biologic therapy Q2 2018 (Adelphi, 2018)

	severe eosinophilic patients	severe patients	omalizumab	mepolizumab	reslizumab
Australia	-	-	-	-	-
Brazil	-	-	-	-	-
Canada	-	-	-	-	-
France	Xolair 37% Nucala 20%	Xolair 32% Nucala 13%	pulmonologists 9% allergists 13%	pulmonologists 4% allergists 15%	pulmonologists 4% allergists 13%
Germany	Xolair 11% Nucala 25%	Xolair 15% Nucala 17%	pulmonologists 5% allergists 6%	pulmonologists 4% allergists 4%	pulmonologists 3% allergists 3%
Italy	Xolair 13% Nucala 22%	Xolair 16% Nucala 10%	pulmonologists 7% allergists 8%	pulmonologists 5% allergists 6%	pulmonologists 5% allergists 2%
Japan	-	-	-	-	-
Spain	Xolair 36% Nucala 17%	Xolair 32% Nucala 12%	-	-	-
Sweden	-	-	-	-	-
UK	Xolair 13% Nucala 15%	Xolair 19% Nucala 10%	pulmonologists 6% allergists N/A	pulmonologists 5% allergists N/A	pulmonologists 3% allergists N/A

Source: Adelphi, 2018

Note:
- No evidence available.
n/a Not applicable to the setting.

Appendix Table 11: Number of clinical episodes in a year (planned and unscheduled)

Australia	n/a
Brazil	n/a
Canada	Urgent care costs of uncontrolled asthma in Canada, 2004, The number of unscheduled physician visits was based on 88% of uncontrolled asthmatic patients making unscheduled physician visits (2) and, therefore, almost 1.2 million unscheduled (family) physician visits were made (Seung & Mittman, 2004)
France	n/a
Germany	A claims database analysis from the statutory health insurance perspective was conducted. Asthma patients had significantly higher (p = 0.000) outpatient (€217), inpatient (€176), and pharmacy costs (€259). Incremental asthma-related total costs were higher for patients with persistent asthma compared to patients with intermittent asthma (€1,091 vs. €408). (Jacob et al., 2016)
Italy	174 allergists answered the survey. 54% of them reported up to 10 patient visits per week and 35.3% between 10 and 30. (Magnoni et al., 2017)
Japan	n/a
Spain	About biologics and reductions in clinical episodes: Clinical improvement observed with OMA in pts with uncontrolled severe persistent allergic asthma is associated with reductions in healthcare utilisation, and in work or school productivity losses (Martínez Moragón, 2015)
Sweden	Primary care visits because of asthma; visit to a specialist because of asthma; hospitalisations because of asthma; ED visits because of asthma (Larsson et al., 2018)
UK	n/a

Appendix Table 12: Hospital admissions for patients with asthma and average length of stay in hospital

	Age-Sex Standardised Rate, Adults per 100,000 population	**Average length of hospital stay for asthma and status asthmaticus**	
		2010	2015
Australia	64.76 (2015)	-	-
Brazil	n/a	-	-
Canada	15 (2015)	-	-
France	29.56 (2015)	3.6	3.3
Germany	28.74 (2015)	15.6	13.8
Italy	7.61 (2015)	4.9	5.3
Japan	34.6 (2011)	-	-
Spain	44.7 (2015)	5.3	5.8
Sweden	19 (2015)	2.7	2.8
UK	70.97 (2015)	3.4	3.3

Sources: OECD, Eurostat.
Note: - No information available
n/a = Not applicable / not OECD country

Appendix Table 13: Additional, country-specific evidence (where available) on hospitalisation of asthma/SA patients and respective average LOS

	Other sources (where available) on hospitalisations for patients with asthma/SA	**Additional sources (where available) on hospital LOS**
Australia	n/a	Average length of stay associated with asthma/bronchitis (days): 1.5 (public hospitals); 3.5 (private hospitals) (AIHW, 2018)
Brazil	• In 2013, 2,047 people died from asthma in Brazil, meaning approximately 5 deaths/day and more than 120,000 hospitalisations per year. In six years, the absolute numbers of asthma-related deaths and hospitalisations decreased by 10% and 36%, respectively. (Cardoso et al., 2017). • Data from 2005 show that asthma hospitalisations corresponded to 18.7% of those due to respiratory causes and 2.6% of all hospitalisations in the period, also with some decrease from previous decades. In that year, the costs of the Unified Health System with hospitalisations for asthma were 96 million reais, which corresponded to 1.4% of the total annual cost of all diseases. (Brazilian Guidelines)	The mean length of hospital stay due to asthma remained approximately 3 days (Cardoso et al., 2017).
Canada	Number of ED visits admitted: 5,838 (2016-2017) (CIHI) Asthma hospital admission rate (per 100,000 pop.) 15.7 (Fraser Institute, 2013)	Median length of stay for asthma admission following ED visit: 510 mins (2016-2017) (CIHI)
Japan	Number of patients with asthma who continued to visit the hospital (survey, October 2014), was 1,177,000 (515,000 men and 662,000 women) (Japanese Guidelines)	n/a
Spain	n/a	Mean hospital stay of 10.9 days/ patient (Melero Moreno et al., 2019)
UK	Asthma exacerbations lead to over 65,000 hospital admissions (NHS England Service Specification) Prior to discharge, inpatients should receive written personalised asthma action plans, given by healthcare professionals with expertise in providing asthma education. (SIGN Guidelines)	n/a

Appendix Table 14: Availability of a national quality standard on care for SA

	Is there a quality-of-care standard?	Is the standard specific to asthma?	Is the standard specific to SA?	Source
Australia	Not found			
Brazil	Not found			
Canada	Not found			
France	Not found			
Germany	✓	x	x	GBA
Italy	Not found			
Japan	Not found			
Spain	✓	✓	x	(Pinera-Salmeron et al., 2020)
Sweden	Not found			
UK	✓		✓	(NICE, b)

Appendix Table 15: System-level cost of illness studies for SA

Country	System-level costs (aggregate)	System-level costs (per patient)	Economic cost
Australia	$1.2 billion (asthma, estimated 60% severe asthma)		$28 billion in total costs to the economy
Brazil		SA: 135 USD and 733 USD (average annual hospital cost)	
Canada	Across different asthma severities: ~ $46 million in British Columbia to ~ $141 million in Ontario Poorly controlled asthma: 94% of the direct health care costs of asthma (British Colombia)	Across different asthma severities: $366 to $647 (per patient/annum)	
France		Severe asthma: €8,222 (per patient/annum)	
Germany		severe atopic asthma plus seasonal allergic rhinitis: €9,287 (per patient/annum)	
Italy		€2,313.83 (per patient/annum)	
Japan	-	-	-
Sweden		€6,500 (per patient/annum); €2400 and €4100 were direct and indirect costs	
Spain	1.480 and 3.022 million Euros	Between €8,554 to €10,000 per patient per year	

UK	Uncontrolled asthma costs the NHS four times more than other patients: patients with severe uncontrolled eosinophilic asthma c.£840, compared to c.£210 for all asthma patients.	Annual mean treatment costs among SRA patients were £2912 (SD £2212) to £4217 (SD £2449) Long-acting bronchodilator /corticosteroid combination inhalers represent the greatest share of medication-related costs (£885–£1239 for SRA patients (low/high cost scenario) and £425–£678 for non-SRA patients)	

Sources:
Australia: Centre of Excellence in Severe Asthma
Brazil: Stirbulov et al., 2016
Canada: CIHI, 2018; Ismaila et al., 2013
France: Nordon et al., 2018
Germany: Schramm et al., 2003
Italy: Dal Negro et al., 2016
Spain: Melero Moreno et al., 2019; Martínez-Moragón et al., 2009; Van Ganse et al., 2006.
Sweden: Jansson et al., 2020
UK: Asthma UK, 2018; O' Neill et al., 2015

Appendix Table 16: Direct costs to the system per adult SA patient in Euros (per annum)

	Costs in Euro	Cost in national currency
Australia	€214	AUD347
Brazil	€119 – 644^{+}	USD135 - USD733^{+}
Canada	€240 - 425**	CAD366 - CAD647**
France	€8,222**	n/a
Germany	€9,287*	n/a
Italy	€2,313.83	n/a
Japan	-	-
Sweden	€6,500	n/a
Spain	€7,472	n/a
UK	€944***	GBP 840***

Source:
Australia: calculated using cost data from Australian Centre of Excellence in Severe Asthma, population data from the World Bank, and prevalence data in Appendix Table 1.
Brazil: Stirbulov et al., 2016
Canada: Ismaila et al., 2013
France: Nordon et al., 2018
Germany: Schramm et al., 2003
Italy: Dal Negro et al., 2016
Sweden: Jansson et al., 2020
Spain: Melero Moreno et al., 2019
UK: Asthma UK, 2018

Note:
Most recent year found included
Currency conversions based on June 2020 data

Key:

*	Costs for severe atopic asthma and seasonal allergic rhinitis
**	Costs for asthma generally
***	Costs for severe uncontrolled eosinophilic asthma
+	Hospital costs only
-	No evidence