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Treatment gaps in severe asthma across nine OECD countries and recommendations for addressing them

An international survey of clinicians

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Abbreviations

DMP	Disease Management Programme
GAAPP	Global Allergy and Airways Patient Platform
GINA	Global Initiative for Asthma
GP	General practitioner
HCP	Healthcare professional
ICD	International Classification of Diseases
ICS	Inhaled Corticosteroid
KOLs	Key Opinion Leaders
LABA	Long-Acting Beta Agonist
LSE	London School of Economics and Political Science
MDT	Multi-disciplinary team
mOCS	Maintenance oral corticosteroids
NHS	National Health System
OCS	Oral corticosteroids
PAGs	Patient Advisory Groups
PEF	Peak Expiratory Flow
QoC	Quality of Care
SA	Severe asthma
SABA	Short Acting Beta Agonist
UK	United Kingdom

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Abstract

OBJECTIVES: Despite recent advancements in the pharmacological management of severe asthma (SA), there is a significant lack of robust, system level data on the diagnostic, prescribing and care practices in SA. This hinders performance measurement and improved quality in SA care outcomes. This paper aims to capture clinician and patient insights on outcomes relevant to the clinical and pharmacological management of SA and understand the extent to which this evidence can facilitate performance and quality measurement efforts in SA care.

METHODS: Following an in-depth review of the relevant literature, we developed a robust framework of SA relevant indicators around: a) policy structure and organisation; b) diagnosis; c) treatment; and d) care delivery. We conducted an international web survey of respiratory specialists to capture information on the above indicators and provide comparative insights and benchmarking of performance in SA across 9 countries.

RESULTS: Twenty-six responses were received from respiratory specialists in Australia, Brazil, Canada, France, Germany, Italy, Japan, Spain, and UK. The insights revealed that SA-specific quality-of-care frameworks are largely unavailable across all study countries, while discrepancies exist across and within settings on practices and timings for specialist referral and appointment booking: the former ranging from 19 days in Germany and up to 24 months in Brazil. Variation is more prominent in the diagnostic criteria and tests used, with only about a third of surveyed clinicians reporting using SA diagnostic pathway guidelines. A disconnect both between and within countries exists in the prescribing pathways followed to treat and manage SA, especially in relation to the use of oral/systemic corticosteroids.

CONCLUSION: Data around the clinical and pharmacological management of SA is not routinely available, and despite the increased use of biologics there are still significant gaps in patient care holding back improved outcomes. In light of the COVID-19 pandemic, action in the form of measures to enhance outcomes in SA care is vital now more than ever. These include measures for: i) the systematic collection of outcomes data in SA, ii) improved referral pathways and capacities in SA, and iii) measures to support increased understanding and incentivisation of guidelines in the prescribing of treatment and SA diagnostic criteria.

1. Background & Objectives

> Severe asthma is the most serious and life-threatening form of asthma.
>
> *(Asthma UK, 2020)*

Severe asthma (SA) is a debilitating condition characterised by a lack of response to standard asthma treatments and more intense, persistent symptoms than other types of asthma (GAAPP, 2020). There is an incontestable need to enhance SA care and practices at both national and inter-country level: people with SA have higher risk of asthma-related symptoms (such as shortness of breath or chest pain), comorbidities, and exacerbations, with significant effects on patients, carers, and society more widely (Maltby et al., 2020). A person's quality of life is impacted by asthma-related exacerbations, and SA continues to contribute substantial direct and indirect costs to the healthcare system (Hossny et al. 2017; Lloyd et al. 2007; Menzella et al., 2019; FitzGerald et al., 2017; Trevor and Chipps, 2018; Ivanova et al. 2012; Antonicelli et al. 2004).

In addition, substantial mortality due to asthma still occurs in many settings (Trevor and Chipps, 2018; Asthma UK, 2017). A UK review of asthma deaths categorised over half of asthma-related deaths as avoidable (Royal College of Physicians, 2015), suggesting continuing issues in the care, treatment, and management of asthma, in general, and of people with SA in particular. Mortality rates are suggested to be higher for people with SA treated with OCS (Bourdin et al., 2017). While it has been found that mortality rates for asthma could be improved through more effective management techniques, improvements in mortality rates in asthma have stagnated in recent years (Royal College of Physicians, 2015; Jenkins, 2017).

Improving healthcare and treatment for SA requires system-level information on the diagnostic experience, treatment pathway and service delivery practices, which is currently not collected extensively or systematically in many countries (Kamphuis et al., 2021). Kamphuis et al. (2021) conclude appropriate and thorough data needs to be collected for SA to allow countries to conduct improved performance reviews, as well as identify key bottlenecks which contribute to high avoidable mortality and quality of care. In this context, the burden posed by the condition remains significant and challenges for respiratory specialists and other clinicians treating people with SA are strenuous.

Healthcare professionals involved in the treatment of SA are in a unique position to understand where a lack of asthma control, and potential subsequent morbidity, arises both at an individual and system-wide level, and how people with SA may be better managed, policies amended, or guidelines improved to maximise care and clinical outcomes. Healthcare providers are crucial in ensuring the quality of care in SA is as high as possible. This study aims to contribute a greater evidence base for SA, through a qualitative survey of clinicians treating people with SA, exploring:

1. The importance of treatment choices for severe asthma. Oral corticosteroids (OCS) are a widely used asthma treatment, recommended in short courses for the treatment of asthma exacerbations (Bleecker et al., 2020). It is estimated that 25–60% of people with SA may be prescribed OCS during their care (Chung et al., 2020; Shaw et al., 2015; Sweeney et al., 2012), with long-term or frequent acute OCS use reported in 15-64% of people with SA globally (Broder et al., 2017; Heffler et al., 2019; Shaw et al., 2019). Acute and long-term OCS use has been linked to continued exacerbations, the development of OCS-linked comorbidities including hypertension, cardiovascular disease and diabetes, negative impact on the quality of life of people living with severe asthma, increased emergency room visits and potentially fatal outcomes (Bourdin et al., 2017; Chung et al., 2020; Prazma et al., 2014; Price et al., 2017; Suruki et al., 2017; Sweeney et al., 2012; Lee et al., 2019; Zeiger et al., 2020; Voorham et al., 2019). Acute OCS use has also been associated with an increased risk of acute and chronic adverse events (Bleecker et al., 2020). Concurrent asthma guidelines advocate for the relegation of OCS use for acute exacerbations and as a GINA Step 5 option for long-term use (GINA, 2020; Haughney et al., 2020). However, there is currently a dearth of information on both the use and uptake of newer treatments for SA, such as biologics, which are thought to improve symptoms and reduce asthma attacks and therefore reduce reliance on OCS (Asthma UK, 2020).

2. Multidisciplinary care and effective decision-making in line with guidance. Multidisciplinary team care is essential because of the complexity of SA. It remains unclear whether multidisciplinary care is easily accessible by people living with SA across countries so that they can receive a holistic treatment approach and education to manage their condition (Chung et al., 2018). Asthma healthcare professionals (HCPs) with limited knowledge about guideline-recommended therapies, as well as inconsistent diagnostic and referral pathway issues, communication gaps, and low adherence to guidelines (Majellano et al., 2019) can all contribute to poor asthma management and inconsistent treatment approaches. In addition, the extent to which national treatment guidelines for SA are being adhered to by clinicians across countries is unclear, though evidence from specific settings suggests adherence is potentially low (Baldacci et al., 2019; Reddel et al., 2015; Jo et al., 2020). This may hinder further efficient decision-making in the pharmacological management of SA.

3. Opportunities for open communication and dialogue with patients. Positive interaction between clinicians and people living with asthma has a significant impact on maintaining asthma control and ensuring correct treatments are administered. Patient-physician communication has an important role to play in asthma management: good communication leads to improved outcomes for the patient (Majellano et al., 2019). Similarly, a 2017 study looking at patient-physician agreement on expectations for treatments and management across a group of Spanish people living with moderate-severe asthma found that discordance may be contributing to poorer asthma control (Crespo-Lessman et al., 2017). Clinicians also play an active role in the management of symptoms and risk. As such, they must ensure that people living with asthma and SA are adequately involved in their asthma management and assist them with developing necessary self-management tools and an understanding of the impact of their treatments. It has been reported that people living with asthma, who have limited knowledge of asthma symptoms and management are at risk for poorer asthma control (Majellano et al., 2019).

Report aims

1. Understand key challenges in SA care and management.
2. Capture clinician and patient insights on outcomes relevant to the clinical and pharmacological management of SA.
3. Understand the extent to which evidence can facilitate performance and quality measurement efforts in SA care.

2. Methods

The design and implementation of the clinician survey was based on the following methodological steps: a) the adaptation of an earlier developed framework for SA care and treatment (Kamphuis et al., 2021), to a revised framework that reflects indicators relevant to SA clinical practice and SA clinicians' perspectives; b) the creation of a respective online survey/questionnaire that captures data on the above indicators; and c) country selection and identification of clinicians for survey participation.

2.1. Adaptation of framework

Kamphuis et al. (2021) developed a framework of SA relevant indicators (Appendix Table 1) which was applied to investigate the performance of health systems and assess the level of evidence that exists in the current literature across all relevant aspects/indicators relevant to the experiences of people with SA including diagnosis, treatment, care delivery and socio-economic impact in ten countries. A wider system aspect was added to ensure that the framework also assessed the suitability of the policies and guidelines in place for SA. Most importantly, this framework was created with the contribution of an expert panel consisting of clinical experts, academic experts in health policy and other stakeholders in the respiratory field.

The initial framework of Kamphuis et al. (2021) (Appendix Table 1) comprised 44 indicators across six sections: a) epidemiology; b) policy structure and organisation; c) diagnosis; d) treatment; e) care delivery; and (f) socio-economic impact. For the clinician survey, the framework was tailored to reflect the specific information we wanted to obtain from clinicians on SA care and pharmacological management, given the respective gaps of the literature as identified by Kamphuis et al. (2021). Therefore, the sections on epidemiology and socio-economic impact were excluded from the current framework, whereas the rest of the sections were adapted to reflect indicators on SA clinical care and treatment where further understanding and in-depth information was needed.

A total of four sections and 32 indicators were finally included (Table 1): a) policy structure and organisation (four indicators on guidelines and structure); b) diagnosis (eight indicators on diagnostic testing, specialist referral, definitive diagnosis and materials and education); c) treatment (five indicators on biologics use and prescribing); and d) care delivery (fifteen indicators on resource utilisation, access to care, communication, management and quality of care).

Table 1. Indicators covered by the clinician survey

Theme	Sub-theme	Indicators
Policy structure and organisation	Guidelines & Policy structure	Existence of clinical guidelines, quality of care or performance management systems and/or national strategy for asthma and SA
		Sources of up-to-date information on SA diagnosis, treatment and management
	Organisation of care	Existence of patient organisations
		Existence and geographic distribution of specialist care for SA
Diagnosis	Diagnostic testing	Diagnostic criteria used for SA diagnosis
	Specialist referral	Healthcare professional /person responsible for referral
		Time to referral and whether before or after official SA diagnosis
	Definitive diagnosis	Average time between first symptoms of SA and official diagnosis
		Benchmark in time between first symptoms of SA and official diagnosis after which diagnosis is classified as "delayed"
		Causes of delayed diagnosis
	Materials & education	Provision of educational materials to newly diagnosed people with SA
		Provision of (self-) management plans to people living with SA for their SA treatment
Treatment	Biologic use	Criteria/conditions for biologic prescribing & time of prescribing following official diagnosis
		Attributes important for selecting biologic treatment
		% of people living with SA currently receiving biologics
		Reasons for not prescribing biologics
	Prescribing	Prescribing pathway & rationale for prescribing followed under points 5 and 6a/6b of the GINA severe asthma decision tree
Care delivery	Resource utilisation	Scheduled/unscheduled consultations and, if scheduled, are these guidelines recommended
		Average % of people living with SA hospitalised within 1 year due to SA complications
		Average % of overnight vs. not overnight admissions
	Access to care	Geographic distribution of specialist care centres
		Average travel time for appointment
		Time to appointment after referral
	Communication and management of care	% of people living with SA managed by Multidisciplinary Team (MDT) & barriers to MDT use, if any
		% of people living with SA seeing specialist nurses and educators
		Contact hours between patients and specialist nurses and educators
		Barriers to using specialist nurses and/or education services
		Level of communication between specialist centres and referring sites
		Involvement of people living with SA in decisions about their treatment
	Quality of care	Existence of a national quality standard for SA
		Availability of financial incentives in SA prescribing
		Existence of a national strategy or plan on asthma/SA

2.2. Selection of countries and identification of clinicians

The geographical scope of this survey initially covered 10 countries: Australia, Brazil, Canada, France, Germany, Italy, Japan, Spain, Sweden and the United Kingdom (UK). We used the same countries as the Kamphuis et al. study (2021), which were selected based on: a) approaches to health care financing, organisation and delivery; and b) geographical spread (Appendix Table

2). A total of 137 SA clinicians were contacted across the ten countries, including general practitioners, pulmonologists, allergists and respiratory specialists identified as Key Opinion Leaders (KOLs) on SA in their country of practice. However, due to responses from Sweden being inadequate for inclusion in the analysis, our results are based on the responses received from the remaining nine countries.

2.3. Insights from people living with severe asthma

Based on the above framework, a short survey of people living with SA was also conducted which asked questions in relation to the relevant study indicators around: a) policy structure and organisation of care (one indicator on structure); b) diagnosis (six indicators on diagnostic testing, specialist referral, definitive diagnosis and materials and education); c) treatment (four indicators on OCS use, access to biologics and prescribing); and d) care delivery (thirteen indicators on resource utilisation, access to care, communication, management and quality of care). Due to issues in respondent recruitment and a subsequent small sample of people living with SA, this survey serves as supplementary evidence to the clinicians' survey to provide further insights across specific indicators and countries.

A total of 14 asthma relevant PAGs across the ten countries (Australia, Brazil, Canada, France, Germany, Italy, Japan, Spain, Sweden and UK) were contacted via e-mail and invited to voluntarily share the questionnaire with their network of people living with SA via e-mail, electronic newsletter, blogs and social media accounts. All people living with SA were informed about the study objectives and data confidentiality procedures in place and were asked to provide online written informed consent to indicate their understanding of the study conditions and their agreement to participate. The study protocol was submitted to, and approved by, the LSE Research Ethics Committee (REC reference: 1040).

2.4. Data management and analysis

Both surveys were hosted online on the Qualtrics® software under an LSE-verified account and remained open for a period of 12 weeks; the clinicians' survey between January and April 2020; and the people living with SA survey between October and December 2020. Responses were extracted, coded and analysed qualitatively, using descriptive statistics (Excel®). Clinicians' responses were also analysed by means of a comparative analysis and benchmarking of the clinicians' perspectives across countries. Additionally, a comparative analysis and benchmarking of those living with SA as well as clinicians' perspectives and experiences across countries was also performed for applicable indicators.

3. Results

3.1. Sample characteristics

Of the 137 clinicians invited to participate in the survey, 26 returned a fully completed survey resulting in a response rate of 19%. More specifically, responses were received from Australia (n=1), Brazil (n=5), Canada (n=4), France (n=2), Germany (n=4), Italy (n=1), Japan (n=4), Spain (n=2) and UK (n=3). The majority of respondents were pulmonologists (42%, n=11), followed by respiratory specialists (35%, n=9), allergists (11.5%, n=3) and general/family practitioners (11.5%, n=3). The median age of participating clinicians was 54.5 years, while their average number of years in practice was 25. Finally, the majority of respondents practice in a university hospital (n=17). Other practice sites included community hospital (n=4), private hospital/centre (n=3), General Practitioner (GP) surgery (n=1) and a private practice office (n=1).

In addition, 54 patient surveys were completed covering Australia (2%, n=1), Brazil (2%, n=1), Canada (26%, n=14), France (4%, n=2), Germany (5%, n=3), Italy (2%, n=1), Spain (15%, n=8), Sweden (31%, n=17) and UK (13%, n=7).

3.2. Policy structure and organisation of care

Table 2 summarises the information provided by surveyed clinicians on the structure of the respective national policies and guidelines available for the diagnosis and management of SA. It also outlines how care for SA is organised at the local/regional level, including information on the availability of specialist centres for people living with SA.

Guidelines & policy structure

Our results report that clinical practice guidelines for asthma exist in all study countries and clinical practice guidelines specifically for SA exist in all study countries except Australia.

However, national quality standards specifically for SA (defined as a prioritised set of concise and measurable recommendations to support quality improvement in care provided specifically for SA) were reported to be lacking in all study countries apart from Germany and the UK, where there are performance and care quality management systems in place through the German Disease Management Programme (DMP) Asthma and NHS England’s Quality Dashboard.

Despite this, surveyed clinicians reported that scientific publications and congresses were the most popular sources for current, up-to-date information on SA. Our survey also found that discussions with colleagues were more frequently used as a source of information than clinical guidelines. Other sources mentioned by surveyed clinicians included scientific training courses, pharmaceutical representatives and social media (Appendix Table 3).

Organisation of care

Although national patient advocacy groups covering asthma exist in all study countries, there are no organisations specifically for SA. Clinicians from Brazil, Japan and Spain also reported that a national strategy or plan for asthma and/or SA does not exist in their respective countries.

More than 90% of surveyed clinicians reported that, although specialist care for SA exists in all study countries, the geographical distribution of these facilities is insufficient as they are concentrated in, or near, large city centres. Respective insights from people living with SA suggest that only a minority receive, or have received, care at a specialist asthma centre in a large city setting. This serves to highlight discrepancies in the availability/utilisation of these facilities across countries, as well as across regions within countries (Appendix Table 7).

Key findings on policy structure and care organisation

- Although clinical practice guidelines exist in all countries (with the exception of Australia), there is a lack of national quality standards and/or performance measurement systems in all countries apart from the UK and Germany, hindering quality assessment and improvement in the care provided for SA.
- Although specialist centres for SA do exist, the majority of clinicians reported concerns around their geographic distribution which impacts the accessibility of these services for people living with SA.

Table 2. Clinician survey results for indicators on policy structure and SA care organization across countries

	AUS (n=1)	BR (n=5)	CAN (n=4)	FR (n=2)	GER (n=4)	IT (n=1)	JPN (n=4)	SP (n=2)	UK (n=3)	Total (n=26)
Guidelines & Policy structure										
Clinical guidelines for asthma	Yes (International)	Yes (National, International)	Yes (National, International)	Yes (National, International)	Yes (National, International)	Yes (International)	Yes (National, International)	Yes (National)	Yes (National)	Yes (100%)
Clinical guidelines for SA	No	Yes (National, International)	Yes (National, International)	Yes (National, International)	Yes (National, International, European)	Yes (International)	Yes (National)	Yes (National, International)	Yes (National, European)	Yes (89%)
General QoC/ performance management system	No	No	No	No	Yes (DMP Asthma)	No	No	No	Yes (QOF, Quality incentives in some hospitals)	Yes (22%)
Existence of a national quality standard for SA	No	No	No	No	Yes (DMP Asthma)	No	No	No	Yes (NHSE Quality Dashboard)	Yes (22%)
National strategy or plan for asthma and SA	Yes (Asthma Australia)	No	Yes (unspecified)	Yes (SPLF)	Yes (NVL)	Yes (SANI)	No	No	Yes (NHSE specs)	Yes (67%)
Organisation of care										
Existence of patient organisations	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes (100%)
Existence of specialist care for SA (% of respondents)	Yes (100%)	Yes (100%)	Yes (100%)	Yes (50%) No (50%)	Yes (100%)	Yes (100%)	Yes (100%)	Yes (100%)	Yes (100%)	Yes (92%) No (8%)
Sufficient geographic distribution of SA specialist care (% of respondents)	No (100%)	No (100%)	Yes (50%) No (50%)	No (100%)	Yes (100%)	n/a	No (100%)	Yes (100%)	Yes (66%) No (33%)	Yes (40%) No (60%)
Reasons for insufficient geographic distribution of specialist care for SA	Many have to travel long distances	Concentrated in big centres/ cities of the south/ southeast areas	Mostly in large urban centres	Some empty areas	n/a	n/a	No specialist in some areas	n/a	Number of specialists up to 8 times higher in cities	n/a

Key: n/a: Indicator is not applicable to the relevant setting

Note:
- AUS: Australia, BR: Brazil, CAN: Canada, FR: France, GER: Germany, IT: Italy, JPN: Japan, SP: Spain, UK: United Kingdom.
- DMP: Disease-Management-Programme, MSLs: Medical Science Liaisons, NHSE: National Health System England, NVL: Nationalen Versorgungs-Leitlinie, QOF: Quality Outcomes Framework, SANI: Severe Asthma Network Italy, SPLF: Société de pneumologie de langue française.

4. Diagnosis of severe asthma

Table 3 outlines the insights provided by clinicians on the availability and characteristics of diagnostic, referral, and educative pathways/practices in SA across the study countries.

4.1. Diagnostic testing

Several key criteria were reported as commonly used by clinicians across all countries, including the 'number of Oral Corticosteroid (OCS) bursts in 12 months', followed by 'number of exacerbations per month/week' and 'number of hospital admissions'. Other diagnostic criteria included a review of inhaler techniques to exclude suboptimal adherence, spirometry and /or Peak Expiratory Flow (PEF) with reversibility test, and assessments of respiratory symptoms (e.g. wheeze, shortness of breath, cough) for intensity, occurrence, and triggers (Appendix Table 4).

The use of the diagnostic pathways included in clinical guidelines as a diagnostic criterion varied according to the clinicians surveyed. All clinicians based in Australia, France, Germany, and the UK indicated they did not use them, while all clinicians based in Spain and Italy, and some clinicians in Brazil, Canada, Japan indicated they did use the diagnostic pathways included in clinical guidelines (Appendix Table 4).

4.2. Referral, diagnostic & educative pathways

Just over half of the surveyed clinicians reported that specialist referral is most commonly instigated by a GP or primary care physician and usually the referral comes before an official SA diagnosis (62% of clinicians), although there is some variation between countries, with clinicians in Brazil and France indicating that referral to specialist care occurs after an official SA diagnosis. In Canada, Sweden, and the UK, people living with SA reported being diagnosed by asthma-related specialists (for example pulmonologists or respirologists) followed by asthma specialist doctors and allergists.

Similarly, insights from people living with SA also showed that in some cases official SA diagnosis was received from a non-asthma specialist (i.e. prior to specialist referral) (Appendix Table 7).

According to clinicians' responses, the average time from referral from primary care to specialist level is approximately 5.5 months, although this ranged from 19 days in Germany to between 6 to 24 months in Brazil. The average time reported by people living with SA was approximately 4.5 months, again ranging from 14 days in Germany to up to 5 and 24 months in Canada and Brazil respectively (Appendix Table 7).

Insights from surveyed clinicians showed that the average time between first symptoms and official SA diagnosis was two years, with variation between and/or within countries, such as less than one year (e.g. Japan and Germany), to between two and three months (e.g. Australia, France, the UK) and even to more than five years (e.g. Brazil). Furthermore, responding clinicians' estimates of when diagnoses are considered 'delayed' ranged from 3 to 24 months between observing first symptoms of SA and receiving an official diagnosis. There is a lack of consensus and/or no common guidelines across countries which define the time after which a diagnosis is classified as delayed, although one of the commonly reported reasons for a delayed diagnosis was a lack of specialist training in primary care.

Finally, just over 70% of clinicians surveyed across all study countries reported that they provide educational materials to newly diagnosed people living with SA, although some regional variation was observed in responses from Brazil, Germany, Japan, Spain, and the UK. Similarly, a large proportion of surveyed people living with SA reported receiving further information or material by a medical professional when they were newly diagnosed, with some minor discrepancies. (Appendix Table 7).

Key findings on the diagnostic, referral and educative pathways

- Key diagnostic criteria commonly used across countries included number of OCS treatment courses (bursts) in 12 months, exacerbations per month/week, and hospital admissions.
- The use of the diagnostic pathways included in clinical guidelines as a diagnostic criterion varied according to the clinicians surveyed, with only a minority of clinicians in Spain, Italy, Brazil, Canada, and Japan reporting their use.
- There are inconsistencies in specialist referral pathways across countries, with both clinicians and people living with SA reporting an average time from primary care to specialist referral of 5.5 months, ranging from 19 days in Germany to two years in Brazil.

Table 3. Clinician survey results for the indicators on diagnostic, referral and educative pathways/practices in SA across the study countries

	AUS (n=1)	BR (n=5)	CAN (n=4)	FR (n=2)	GER (n=4)	IT (n=1)	JPN (n=4)	SP (n=2)	UK (n=3)	Total (n=26)
Specialist referral										
HCP responsible for referral (% of respondents)										
▪ GP or primary care physician	100%	40%	75%	0%	50%	0%	100%	100%	0%	54%
▪ Pulmonologist/Respirologist	0%	60%	25%	100%	25%	100%	0%	0%	0%	31%
▪ Other (e.g. Allergist, Nurse)	0%	0%	0%	0%	25%	0%	0%	0%	100%	15%
Time to referral (months)	12	6-24	3-4	3	19 days	1	3-12	1.5	4- >12	5.5
Referral before/after SA official diagnosis (% of respondents)	Before (100%)	After (60%)	Before (75%)	After (100%)	Before (75%)	Before (100%)	Before (100%)	Before (100%)	Before (66%)	Before (62%)
Definitive diagnosis										
Average time between first symptoms of SA & diagnosis (years)	2-3	1 - >5	1- 4	2-3	<1 - >5	1-2	< 1	1	2-3	2
Benchmark between first symptoms of SA and official diagnosis after which diagnosis is "delayed"? (months)	12 (ERS/ATS)	6 (GINA)	24 (estimation)	12 (GINA)	3-6 (GINA, NVL, DGP)	24 (GINA)	3 (JRS)	6 (SEPAR)	6-12 (BTS)	11
Causes of delayed diagnosis (% of respondents)										
▪ Lack of SA diagnostic guidelines	100%	0%	0%	0%	0%	0%	0%	0%	33%	8%
▪ Lack of specialist training	0%	80%	0%	0%	100%	100%	25%	50%	33%	48%
▪ Lack of communication between GP - specialist	0%	0%	0%	0%	0%	0%	0%	50%	0%	4%
▪ Other	0%	20% Infrequent appointments	100% Unrecognized severity by the GP/ failure to refer by GPs	100% Limited awareness of OCS harmfulness	0%	0%	75% Patients' cooperation Outpatient frequency Dropout	0%	33% Some patients accept symptoms/opt out of medication	40%

Materials and Education										
Provision of educational materials to newly diagnosed people with SA (% of respondents)	100%	60%	100%	100%	75%	100%	50%	50%	66%	73%
Provision of (self-) management plans to people living with SA for their SA treatment (% of respondents)	100%	80%	100%	100%	100%	100%	75%	100%	66%	92%

Key: n/a: Indicator is not applicable to the relevant setting

Note:

- AUS: Australia, BR: Brazil, CAN: Canada, FR: France, GER: Germany, IT: Italy, JPN: Japan, SP: Spain, UK: United Kingdom.
- ATS: American Thoracic Society, BTS: British Thoracic Society, DGP: German Respiratory Society, ERS: European Respiratory Society, GEMA: Spanish Guideline on the Management of Asthma, GINA: Global Initiative for Asthma, HCP: Healthcare Professional, JRS: Japanese Respiratory Society, NVL: Nationalen Versorgungs-Leitlinie, OCS: Oral Corticosteroid, SEPAR: Spanish Society of Pulmonology and Thoracic Surgery.

5. Management of severe asthma

Table 4 outlines results on the pharmacological management of SA reported by clinicians across the study countries, including indicators specific to the use/selection of biologics, and the prescribing patterns followed by clinicians after official diagnosis of SA[1].

5.1. Pharmacological management pathways

Based on the clinician responses, there is inconsistency in the types of pharmacological treatments used to manage SA. For example, the use of oral and/or systemic corticosteroid treatment under point 5 of the GINA severe asthma decision tree was reported by clinicians in some countries (e.g., Italy, Japan, France) but not by those in others (e.g., Australia, Spain).

For oral corticosteroids (OCS) specifically, although clinicians reported prescribing OCS less frequently on average in point 6 of the GINA severe asthma decision tree than in point 5, there was still significant variation in prescribing patterns across all countries. For example, survey results suggested that clinicians in Italy and Japan commonly prescribe OCS in both decision points 5 and 6a/6b of the GINA severe asthma management decision tree, in France, respondents reported using OCS only in point 5 and in Spain only in point 6a/6b, while according to respondents based in Australia, OCS is not chosen at all as a treatment option.

Insights from surveyed people living with SA, also indicated that utilisation of OCS was lower at the later SA treatment stages compared to initial stages (n=12 and n=25 of surveyed people living with SA respectively). Nevertheless, in the later treatment stages utilisation of OCS remained prominent in Australia, France, and Spain, whereas in Italy and Germany it was not reported at all (Appendix Table 7). Additionally, responses from people living with SA also indicated variation between countries, as well as discordance with the clinician respondents.

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[1] Asthma management in general, is classified into 5 different steps based on the severity level of asthma, whereby a diagnosis of "severe asthma" corresponds to the highest step (i.e., Step 5) of asthma management (GINA, 2020). Furthermore, within Step 5 of asthma management, a distinct decision tree has been recommended by the Global Initiative for Asthma that describes specifically the pathway for managing difficult-to-treat and severe asthma (GINA, 2019). The GINA severe asthma decision tree comprises 8 decision points around diagnosis confirmation & referral (points 1-4), assessment and treatment of severe asthma phenotypes (points 5 and 6a/6b), and treatment review/monitoring (points 7 and 8) (GINA, 2019). The indicators studied in this section focus on the pharmacological management pathways of severe asthma and therefore, the results presented herein present evidence about clinicians' prescribing patterns under decision points 5 and 6a/6b of the severe asthma decision tree.

Treatment choice can be influenced by the type of clinician and whether prescribing occurs at the primary care or specialist level. As such, it is worth mentioning that the divergent responses observed in the above countries were all provided by specialist clinicians. Nevertheless, some common patterns in clinician prescribing were reported across countries, including the use of Long-Acting Beta Agonist (LABA) with ICS (reported by 100% of responding clinicians), followed by ICS (95%) and long-acting anticholinergics (86%) in point 5, and the use of biologics (79%), long-acting anticholinergic (74%) and LABA with ICS (74%) in point 6a/6b of the GINA severe asthma decision tree. When questioned, people living with SA also reported utilisation of biologics most commonly in the later stages of the severe asthma treatment pathway (Appendix Table 7).

5.2. Biologic use

In terms of biologic use, almost all clinicians reported currently having people living with SA on biologics. Insights from people living with SA report a moderate utilisation rate of biologics, with only half of respondents saying they were offered the option to be treated with a biologic (Appendix Table 7).

According to clinicians, the average time to initiate biologic treatment following SA diagnosis was 6.5 months across all countries, though this varied significantly across and within countries, with responses ranging between 2 to 12 months. Nevertheless, as biologics are initiated by specialists only, it is worth noting that average time to specialist referral was also around 6 months on average across all countries (see section 4.3), suggesting that time to biologic initiation may be influenced by time to specialist referral.

Nearly all surveyed clinicians indicated that a key reason for biologic treatment initiation is the "requirement for maintenance treatment of people living with SA with OCS", followed closely by "exacerbations and/or poor symptom control after high dose Inhaled Corticosteroid (ICS) with LABA" and by "more than a specified number of exacerbations in 1 year". Interestingly, "exceeding a maximum of two OCS courses per year" was highlighted as a key reason for biologic initiation by all clinicians in Australia, France, Italy, Spain, by most clinicians in other countries (Brazil, Canada, Germany, Japan) but by none of the clinicians in the UK.

Finally, criteria such as effectiveness, SA phenotype (e.g., severe Type 2 (T2) high asthma, the sub-type eligible for receiving biologic treatment) and safety are also paramount criteria across all clinicians in selecting a biologic therapy, all achieving an average score of 5 (on a scale of importance from not considered (0) to very important (5)) (Appendix Table 5).

Key findings on treatment pathways and pharmacological management

- Based on the clinician responses, there is inconsistency in the types of pharmacological treatments used to manage SA. A disconnect across/within countries is reported specifically in the prescribing of oral/systemic corticosteroids under both points 5 and 6a/6b of the GINA severe asthma decision tree. Overall, prescribing rate of OCS was lower in the later treatment stages, although it remained prominent among clinicians in Italy, Japan and Spain.

- Some agreement between surveyed clinicians across countries exists specifically in the prescribing of LABA with ICS under point 5 and biologics under point 6a/6b of the GINA severe asthma decision tree.

- The average time to initiate biologic treatment following SA diagnosis was reported to be 6.5 months across all countries, though this varied significantly across and within countries, with responses ranging between 2 to 12 months

Table 4. Results for indicators on treatment pathways and pharmacological management of SA in the study countries

	AUS (n=1)	BR (n=5)	CAN (n=4)	FR (n=2)	GER (n=4)	IT (n=1)	JPN (n=4)	SP (n=2)	UK (n=3)	Total (n=26)
Biologic use										
Time of prescribing after SA diagnosis (months)	3-6	2-12	3-12	7-12	3-6	3-6	2-12	7-12	2-6	6.5
Criteria considered for biologic use (% of respondents)										
▪ OCS has failed	0%	40%	25%	100%	0%	100%	100%	0%	50%	48%
▪ ICS has failed	0%	80%	25%	50%	50%	0%	25%	0%	0%	36%
▪ Exacerbations/ poor symptom control after high dose ICS with LABA	100%	100%	100%	100%	75%	100%	50%	50%	100%	84%
▪ Type 2 biomarkers above specified level (e.g., Eos ≥300/µl L, FeNO ≥25 ppb L)	100%	40%	50%	50%	75%	100%	50%	0%	100%	56%
▪ Maintenance OCS required	100%	100%	100%	100%	75%	100%	100%	100%	100%	96%
▪ > than a specific no. of exacerbations in 1 year	100%	80%	50%	100%	75%	100%	75%	50%	100%	76%
▪ > 2 OCS bursts in 1 year	100%	60%	75%	100%	75%	100%	75%	100%	0%	72%
Clinicians having people with SA on biologics (% of respondents)	100%	100%	100%	100%	100%	100%	100%	100%	66%	96%
Reasons for not prescribing biologics	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	GPs can't prescribe	n/a

	AUS (n=1)	BR (n=5)	CAN (n=3)	FR (n=1)	GER (n=4)	IT (n=1)	JPN (n=1)	SP (n=2)	UK (n=3)	Total (n=21)
Prescribing under point 5 of GINA severe asthma decision tree (% of respondents, n=21)*†										
Controller medications										
▪ ICS (e.g., Beclometasone, Fluticasone propionate/ furoate, Budesonide)	100%	100%	100%	100%	100%	100%	100%	50%	100%	95%
▪ LABA with ICS (e.g., Beclometasone/Formoterol, Fluticasoe/Salmeterol, Fluticasone/ Vilanterol)	100%	100%	100%	100%	100%	100%	100%	100%	100%	100%
▪ Leukotriene modifiers (e.g., Montelukast)	0%	40%	66%	0%	75%	100%	100%	50%	100%	62%
▪ OCS (e.g., prednisolone, hydrocortisone)	0%	80%	33%	100%	50%	100%	100%	0%	66%	57%
Add-on controller medications										
▪ Long-acting anticholinergic (e.g., tiotropium)	100%	80%	100%	100%	75%	100%	100%	50%	100%	86%
▪ Biologics (subcutaneous)	100%	60%	33%	100%	50%	100%	100%	0%	66%	57%
▪ Systemic corticosteroids (oral or IV) (e.g., prednisolone, hydrocortisone)	0%	20%	0%	100%	25%	100%	100%	0%	66%	33%
Reliever medications										
▪ SABA (e.g., salbutamol, terbutaline)	0%	80%	33%	0%	75%	100%	100%	50%	100%	67%
▪ Low dose ICS formoterol (e.g., beclometasone-formoterol or budesonide-formoterol)	0%	60%	66%	0%	50%	100%	100%	0%	66%	48%

▪ Short-acting anticholinergics (e.g., ipratropium)	0%	60%	0%	0%	25%	0%	100%	50%	33%	33%

	AUS (n=1)	**BR (n=5)**	**CAN (n=3)**	**FR (n=1)**	**GER (n=4)**	**IT (n=1)**	**JPN (n=1)**	**SP (n=2)**	**UK (n=0)**	**Total (n=18)**
Prescribing under point 6a/6b of GINA severe asthma decision tree (% of respondents, n=18)*‡										
Controller medications										
▪ ICS (e.g., Beclometasone, Fluticasone propionate/ furoate, Budesonide)	100%	20%	66%	100%	100%	100%	100%	50%	n/a	63%
▪ LABA with ICS (e.g., Beclometasone/Formoterol, Fluticasone/Salmeterol, Fluticasone/ Vilanterol)	100%	20%	100%	100%	100%	100%	100%	100%		74%
▪ Leukotriene modifiers (e.g., Montelukast)	100%	0%	100%	0%	75%	100%	100%	50%		53%
▪ OCS (e.g., prednisolone, hydrocortisone)	0%	20%	66%	0%	50%	100%	100%	100%		47%
Add-on controller medications										
▪ Long-acting anticholinergic (e.g., tiotropium)	100%	20%	100%	100%	100%	100%	100%	100%		74%
▪ Biologics (subcutaneous)	100%	60%	100%	100%	75%	100%	100%	100%		79%
▪ Systemic corticosteroids (oral or IV) (e.g., prednisolone, hydrocortisone)	0%	0%	0%	100%	50%	100%	100%	0%		26%
Reliever medications										
▪ SABA (e.g., salbutamol, terbutaline)	0%	20%	0%	0%	100%	100%	100%	50%		42%
▪ Low dose ICS formoterol (e.g., beclometasone-formoterol or budesonide-formoterol)	0%	20%	33%	0%	50%	100%	100%	0%		32%
▪ Short-acting anticholinergics (e.g., ipratropium)	0%	20%	0%	0%	25%	100%	100%	50%		26%

Key: n/a: Indicator is not applicable to the relevant setting, *: Total number of available responses is n=21 and n=18 for the indicators on Prescribing under points 5 and 6a/6b of the GINA severe asthma decision tree respectively.

†: Point 5 of GINA severe asthma decision tree refers to assessing SA phenotype while optimising management, including pharmacological and non-pharmacological interventions, inhaler technique, adherence and treatment of comorbidities.

‡: Point 6a/6b of GINA severe asthma decision tree refers to considering add-on biologic Type 2 targeted treatments or alternative options if add-on Type 2 biologic therapy is not available/ affordable.

Note:

- AUS: Australia, BR: Brazil, CAN: Canada, FR: France, GER: Germany, IT: Italy, JPN: Japan, SP: Spain, UK: United Kingdom. Eos: Eosinophil, FeNO: Fractional Exhaled Nitric Oxide, ICS: Inhaled corticosteroid, LABA: Long-acting beta-agonist, OCS: Oral Corticosteroid, SABA: Short-acting beta-agonist.

6. Delivery of care in severe asthma

Table 5 outlines the information provided by the respondents on indicators relevant to hospitalisation and resource utilisation, access to, management, and quality of care.

6.1. Resource utilisation & access to care

Clinicians surveyed reported that on average, they have 6 consultations with their SA patients over a 12-month period, and around 85% of these consultations are scheduled. Insights from people with SA suggested fewer consultations take place over a 12-month period, with the majority of these consultations being scheduled (Appendix Table 8).

Clinicians reported that the percentage of people hospitalised in a year due to SA complications ranged from 1% to 9% in Italy and Spain, 10% to 29% in Australia and the UK, and up to 49% or more than 50% in Germany or Brazil and Japan respectively. On average, clinicians estimated that the number of hospitalised people living with SA in a period of 12 months can range from 9% to 37%, with 47% of hospitalisations perceived to be overnight. Insights from people living with SA supported this, indicating that one-third of surveyed people were hospitalised at least once over a 12-month period, although a higher number of overnight admissions was reported compared to the one indicated by the clinicians' survey (Appendix Table 8).

Finally, in terms of access to care, surveyed clinicians reported that the average travel time to an appointment for their patients was 90 minutes, and average time to booking an appointment after referral was 1.5 months. However, this ranged from 7 days in Japan to 90 or 120 days in France. On average, people living with SA reported slightly shorter travel times, ranging from as little as 20 minutes in Australia and to approximately 70 minutes in Canada. Furthermore, discrepancies in the average time to specialist appointment were reported by some people living with SA, with experiences ranging 7 days in Germany to nearly 120 days in Canada and UK and 150 days in Sweden (Appendix Table 8).

6.2. Communication & management of care

Availability and use of multidisciplinary teams (MDTs) for SA and asthma specialist nurses and/or educators varies significantly both between and within countries. For example, according to the SA clinicians surveyed, the percentage of people living with SA managed by MDTs in France, Spain and UK can be more than 80%, compared to 0% in Italy. In Brazil and Germany regional variation is significant with the reported percentage of people living with SA managed by MDTs ranging from 0% to more than 80% and 0% to 29% respectively. Overall, the clinicians who responded reported that the average percentage of people living with SA across all countries using MDTs and seeing specialist nurses/educators varies hugely (ranging from 28% to 62% and

19% to 72% respectively) with local or regional unavailability cited as a common barrier to accessing these services.

Additional issues in the delivery of care/treatment due to COVID-19 were reported by people living with SA who provided their insights. For the majority of these people this change was negative, primarily due to cancellation of physical appointments and the non-feasibility of objective examination with virtual consultations (Appendix Table 8) (e.g., "*My follow up care and spirometry were cancelled so we couldn't confirm change of medication is effective*.", "*Phone consult only; while my doctor was attentive, it was a lot harder to have objective measures, examination.*", "*Physically not being assessed in person doesn't permit a physician to hear your breathing or when you are inflamed from triggers and become quite unwell*.", "*Not been able to do spirometry and therefore only based the treatment on the symptom picture, which made me worse.*").

According to the clinicians surveyed, the level of communication between specialist centres and referring sites was deemed either adequate (by 52% of surveyed clinicians) or less than adequate (by 32% of surveyed clinicians), with only select clinicians in Germany and the UK indicating better than adequate levels of communication.

Inadequate levels of communication were also underscored by the responses received from people living with SA, who suggested that there is an average wait time of two months (ranging from less than 14 days and up to 11 months) for diagnosis or treatment information exchange between referral and specialist sites across all countries (Appendix Table 8).

Finally, in terms of peoples' involvement in decisions about their treatment, around half of clinicians who responded indicated that they prefer to share responsibility of deciding for treatment and around a quarter prefer to make the final selection of the treatment after seriously considering the person's opinion (Appendix Table 6).

6.3. Quality of care

Financial incentives in SA prescribing were reported by less than a third of clinicians and only available for some types of treatment. For example, one clinician from the UK mentioned incentives exist in the ratio of controller to reliever medication prescribing, as the ratio is a measure of treatment and prescribing quality for people living with asthma at the general practice level (Appendix Table 6).

Key findings on delivery of care

- Availability and use of multidisciplinary teams (MDTs) for SA and asthma specialist nurses /educators is reported to vary significantly both between and within countries. Additional issues in the delivery of care/treatment due to COVID-19 were reported by SA patients who provided their insights. For the majority of these patients this change was negative, primarily due to cancellation of physical appointments and the non-feasibility of objective examination with virtual consultations.
- According to the surveys, there is significant variation in hospitalisation rates and reported overnight admissions for people living with SA.
- Financial incentives in SA prescribing were reported by a minority of clinicians and only available for some types of treatment.

Table 5. Results for indicators on the structure and pathway of SA care delivery across the study countries

	AUS (n=1)	BR (n=5)	CAN (n=4)	FR (n=2)	GER (n=4)	IT (n=1)	JPN (n=4)	SP (n=2)	UK (n=3)	Total (n=26)
Resource utilisation										
No. of consultations in 12 months (scheduled vs. unscheduled, %)	n/a* (95% vs.5%)	8 (64% vs.36%)	4 (88% vs.12%)	4 (90% vs.10%)	8 (83% vs.17%)	2 (100% vs.0%)	12 (96% vs. 4%)	6 (70% vs.30%)	2-10 (75% vs.25%)	6 (85% vs.15%)
If scheduled, are these recommended by guidelines?	No	Yes (GINA)	Yes (GINA, CTS)	No	Yes (DGP, GINA, NVL)	Yes (GINA)	No	Yes (GEMA)	No	Yes (56%)
% of SA patients hospitalised in 1 year	10% - 29%	10% ->50%	1% – 29%	0% - 29%	0% - 49%	1% - 9%	>50%	1%-9%	10%-29%	9% - 37%
% overnight vs. not overnight admissions	20% vs 80%	47% vs 53%.	37% vs. 63%	85% vs 15%	70% vs 30%	100% vs. 0%	12.5% vs. 87.5%	12.5% vs. 87.5%	43% vs. 57%	47% vs. 53%
Access to care										
Travel time to appointment (hrs)	1	2	1.5 hrs	1	1.5	>24 (overnight)	0.5-1	1-2	1-2	1.5
Time to appointment after referral (days)	30	60	60	90-120	16	30	7-30	10-30	45	45
Communication and management of care										
% of people living with managed by MDT	30% - 49%	0% - >80%	1% - >80%	>80%	0% – 29%	10% - 29%	0%	>80%	>50% - >80%	28% - 62%
% of people living with SA seeing specialist nurses/ educators	>80%	0% - >80%	0% - >80%	0% - >80%	0% - >50%	10% - 29%	0%	30% - >80%	>50% - >80%	19% - 72%
Contact hrs/year between people living with SA and specialist nurses	3	4	1	n/a	6	5	n/a	n/a	1-2	3.5
Barriers to accessing specialist nurse/educator	n/a	Local/regional unavailability	Local/regional unavailability	Local/regional unavailability	Local/regional unavailability	n/a	Local/regional unavailability	n/a	n/a	n/a
Level of communication between specialist centres and referring sites	Less than adequate	Less than adequate (60%)/ Adequate (40%)	Adequate (66%)/ Less than adequate (33%)	Adequate	Adequate (50%)/ Better than adequate (50%)	Less than adequate	Adequate (75%)/ Less than adequate (25%)	Adequate (50%)/ Less than adequate (50%)	Adequate (33%)/ Better than adequate (66%)	Adequate (52%) / Less than adequate (32%)
Quality of care										
Financial incentives in SA prescribing (% respondents)†	100%	60%	0%	0%	0%	100%	0%	0%	33%	23%

Key: n/a*: Invalid response, n/a: Indicator is not applicable to the relevant setting, †: Financial incentives tailormade for SA.

Note:

- AUS: Australia, BR: Brazil, CAN: Canada, FR: France, GER: Germany, IT: Italy, JPN: Japan, SP: Spain, UK: United Kingdom.
- CTS: Canadian Thoracic Society, DGP: German Respiratory Society, GEMA: Spanish Guideline on the Management of Asthma, GINA: Global Initiative for Asthma, NVL: Nationalen Versorgungs-Leitlinie, MDT: Multidisciplinary team.

7. Discussion

This study reveals significant differences in the clinical practices followed by clinicians who responded to our survey both between and within countries, with a reported unavailability of standardised information across several major indicators in SA pharmacological management and clinical care. Specifically, key findings include:

- A reported lack of national quality standards and/or performance measurement systems in all countries bar the UK and Germany, hindering quality assessment and improvement in care provided for SA.
- Inconsistencies across and within countries on timings to specialist referral and appointment booking and a general lack of agreement on what is considered acceptable or delayed timings within the referral pathway.
- Inconsistencies across and/or within countries on: i) availability and utilisation of SA multidisciplinary teams and ii) diagnostic pathways and criteria used in SA; importantly, only a third of clinicians reported using severe asthma diagnostic pathway guidelines and only in a limited number of the study countries.
- Concerns over the insufficient geographic distribution of specialist centres for SA, which can impact on accessibility of these facilities for people living with SA.
- A disconnect across and within countries in the prescribing pathways followed under points 5 and 6a/6b of the GINA severe asthma decision tree, especially including the use of oral/systemic corticosteroids.

7.1. Policy structure and organisation of care

Our survey reports a lack of national quality standards specifically for SA, as well as limited performance management systems to track quality of care. These insights reinforce the findings reported by Kamphuis et al. (2021), who highlighted that evidence on the availability of quality-of-care frameworks for SA care outcomes is particularly scarce across all study countries. Additionally, although most countries seem to have specialist care facilities for SA, the clinicians surveyed suggest the geographic distribution of these facilities is insufficient and often unavailable in areas further from main city centres. Travel distance has been reported elsewhere as one of the key barriers to receiving a timely referral in SA care (Chung et al. 2018).

Finally, clinicians surveyed reported that they rely more commonly on discussions with colleagues than on clinical guidelines as a source of up-to-date information on care and management of SA, linking to findings reported elsewhere around the poor adherence and implementation of guidelines for diagnosis and management of asthma (Hasegawa et al., 2020;

Haughney et al., 2020; Cloutier et al., 2018). Poor adherence to clinical guidelines can have significant implications for the long-term management of SA exacerbations, with subsequent impact on the socioeconomic burden of the disease (Haughney et al., 2020). Opportunities for improved compliance may exist through provision of enhanced scientific training to SA clinicians; for example, research on primary care physicians showed that those who follow courses of continued education adhere to clinical guidance in the treatment of people living with SA more closely compared to those clinicians not attending these courses (GINA, Italian Group, 2017).

7.2. Diagnosis of severe asthma

Significant variation existed in the criteria used for the diagnosis of SA between and within countries, although a number of key criteria were commonly identified including the number of OCS bursts in 12 months, the number of exacerbations per month/week and the number of hospital admissions. Substantial variation was also reported by clinicians surveyed across countries on the use of diagnostic pathway guidelines, where in some countries these are not used at all (e.g., Australia, France, Germany, and UK), while in other countries they are used by all (e.g., Spain, Italy) or some clinicians (e.g., Brazil, Canada, Japan). Challenges in SA diagnostic procedures and testing may arise due to variation in the inclusion/exclusion criteria and nomenclature employed by different national and international guidelines to define and describe SA and people living with SA respectively (Lommatzsch & Virchow, 2014).

Additionally, inconsistencies exist in specialist referral pathways across countries, with the average time of referral to a specialist ranging from a reported 19 days in Germany to up to two years in Brazil. Similarly, the average time between first symptoms and official SA diagnosis fluctuated significantly in responses between and within countries, ranging between less than one month (e.g., Japan, Germany), and two to three months (e.g., Australia, France, UK) or over 5 months (e.g., Brazil, Germany). Indeed, despite the clear criteria for patient referral to a specialist practitioner or clinic as described by GINA and other national guidelines, a lack of clinical consensus on when to refer people with suspected difficult/SA remains (Asthma UK, 2018). This variation also links to the finding that some of the key reasons leading to a potentially delayed diagnosis relate to the lack of specialist training in primary care, and the lack of communication between GP/primary care physicians and specialists. Evidence around the level of communication between specialist centres and referring sites is scarce (Kamphuis et al., 2021), although clinicians responding to our survey suggest that the level of communication is most commonly adequate or less than adequate.

Finally, the survey responses suggest that even though provision of (self-) management plans and educational materials to people living with SA for their SA treatment is common across countries, regional variations in availability and access to these materials still exist. Previous research suggests that there is room for improvement in the accessibility and effective utilisation of educational materials, asthma management plans and tools both for people living with SA and physicians across the globe (Chapman et al, 2017).

7.3. Management of severe asthma

Responses received from surveyed clinicians revealed inconsistencies between countries in the types of pharmacological treatments used under points 5 and 6a/6b of the GINA severe asthma decision tree. The prescribing of oral and/or systemic corticosteroid treatments was observed as common practice in some countries, even under point 6a/6b, but not prescribed at all by clinicians in other settings. Several studies exist to suggest that the number of people living with SA exposed to OCS fluctuates significantly across and within settings ranging from 25% of people living with SA in Australia, to nearly 35% in Italy and up to 60% or 75% in UK (Chung et al., 2020; Van Ganse et al., 2006, Shaw et al., 2015; Sweeney et al., 2012). Despite an extensive evidence base and availability of national and international guidelines around the management of SA, people living with SA do not always receive guideline-directed medical therapy. Current prescribing patterns include a continued over-reliance on OCS, and underuse of therapies that can prevent or minimise in the long term the frequency of exacerbations and the associated impact on costs and quality of life (Haughney et al., 2020). Findings reported elsewhere also document poor adherence to and implementation of guidelines for diagnosis and management of asthma among asthma care clinicians (Cloutier et al., 2018; Hasegawa et al., 2020). However, another factor driving increased reliance on corticosteroid treatments may relate to local access restrictions to biologic therapies (Menzies-Gow et al., 2019).

The results from our study indicate that there is some agreement between clinicians on choosing a biologic as a treatment option under point 6a/6b of the severe asthma decision tree. Nevertheless, there is limited evidence available on the actual numbers of people living with SA receiving biologic therapy, while discrepancies have been underscored between biologic utilisation rates reported by people living with SA and those reported by clinicians (Adelphi, 2018).

Finally, there was a consensus among surveyed clinicians across the study countries around the importance of criteria such as SA phenotype and efficacy of biologics in guiding decisions to treat with a biologic; the same criteria have also been emphasised elsewhere as key reasons why specialists may consider a biologic in treating severe T2-high asthma (Pavord et al., 2019).

7.4. Delivery of care in severe asthma

Our survey highlighted important inconsistencies in the availability and access to care across countries; for example, the actual time to booking an appointment after referral could range from 7 days in Japan up to 120 days in France. The availability and use of MDTs for SA and asthma specialist nurses or educators reportedly fluctuated significantly across and within countries. A common barrier and reason listed by clinicians behind regional variation in accessing the above services within countries was local/regional unavailability. Despite some existing evidence around the utilisation and accessibility of multidisciplinary care services for SA in Australia (McDonald et al., 2016) and UK (SIGN Guidelines, 2019), overall, the level of evidence on the above indicators is low and the proportion of people living with SA actually accessing such services remains unclear (Kamphuis et al., 2021).

8. Policy implications & recommendations

The common, overarching observation arising across all areas studied in this international survey relates to the significant lack of robust, system-level data on the diagnostic, prescribing and care practices in SA. As improved outcomes in the management of a complex, chronic conditions such as SA require more efficient quality assessment efforts (Smith et al., 2008) such failures on data availability could signify a serious gap in performance measurement systems and consequently, hinder improved quality in SA care outcomes.

Outcomes measurement is a key step towards improved outcomes as it helps to uncover areas of inadequate care and subsequently understand how to improve them. Therefore, the collection of relevant outcomes data is a fundamental process towards the implementation of effective performance and outcomes measurement. Especially considering the threats currently posed by the COVID-19 pandemic for those suffering from respiratory conditions, it is imperative to introduce systems and measures that will facilitate surveillance practices in SA management and care.

A number of salient observations and respective recommendations towards improved care and enhanced outcomes in SA arise from this study, as well as from the Kamphuis et al. (2021) study, which are reinforced in the literature and acknowledged throughout the SA community.

Key recommendations

1. Systematic collection of outcomes data in SA treatment and care.
2. Enhanced referral and communication capacities in SA specialist care.
3. Restructuring and incentivisation of treatment and diagnostic pathway guidelines in SA.
4. Cross-border, multi-stakeholder collaboration towards optimised quality of care and outcomes in SA.

More specifically, it is strongly recommended that policymakers target their actions around the following aspects:

1. Systematic collection of outcomes data in severe asthma treatment and care

- Measures for the systematic collection of outcomes data in SA are crucial for efficient performance measurement and subsequent quality of care improvement in SA.
- Electronic medical record databases and registries can be a key data source, with the potential to enhance our ability to address the lack of information currently present in the clinical management practices of SA. Therefore, these registries should be dedicated

to severe persistent asthma as an individual condition with its distinguished International Classification of Diseases (ICD) code (J45.5) and should be tailored to represent data collection on indicators and clinical outcomes that are most vital and meaningful for SA care and pharmacological treatment.

- Encouraging the adoption of data collection processes, including data reporting and regular scrutiny, as an integrated part of clinical practices in SA is vital to building the necessary health data infrastructure required to support research and surveillance in SA care outcomes.
- Practical syntheses of best-care experiences/practices reported by people living with SA and their clinicians are needed to guide policy makers and health care professionals in delivering evidence-based care. In order to allow for evidence-based decisions, countries need to develop a way to collect data on a frequent and systematic basis in SA treatment and care.

2. Enhance referral and communication capacities in severe asthma specialist care

- Well-organised systems to support adequate communication between clinicians and healthcare professionals involved in SA care are needed, as well as systems to accelerate/automate referral times and procedures. Prompt referral to specialist care is key to reducing hospitalisations and facilitating timely access to biologics; educating clinicians and people living with SA to recognise SA as a distinct condition with specific symptoms and referral criteria can facilitate referral.
- The current geographic distribution of specialist care centres for SA needs to be re-evaluated as a means of enhancing access to care and optimising referral times, specifically for people living with SA.
- Shared decision-making between people living with SA and their clinicians is essential to minimise the impact of adverse effects of treatment on physical, mental and emotional health and consequently maximise compliance. On that front, significant room exists for improvement in the accessibility and effective utilisation of educational materials, asthma management plans and tools both for people living with SA and physicians across the globe.

3. Restructuring and incentivisation of treatment and diagnostic pathway guidelines

- SA care and outcomes would benefit from measures to support better understanding of - and incentivisation to use - current guidelines on the prescribing of corticosteroids and biologics, as well as those on SA diagnostic criteria and pathways.

- Similarly, incentivising increased accountability of SA care providers through performance measurement and monitoring policies is also vital to ensure a high-level quality standard in SA care provision.

4. Cross-border, multi-stakeholder collaboration towards optimised quality of care and outcomes in severe asthma

- Cross-border, multi-stakeholder action towards the development of a quality-of-care framework specifically for SA is needed. A global position by the "Improve Access to Better Care" Task Force of the AstraZeneca-funded PRECISION Global Steering Committee for severe asthma suggests that collaborative effort between policymakers, health care providers, and patient advocacy groups is essential to build consensus on the definition and expectations of quality care in SA, promote patient-centric care, identify gaps and areas for improvement in care, and reduce the burden of illness for people with SA (Haughney et al., 2020).
- A set of core indicators, best practices and standards for improvement in SA care is essential to monitor outcomes and facilitate research and cross-country learning. To promote optimal implementation of best practices, where possible, quality standards should be tailored to meet the local/regional requirements of health care systems. Quality metrics to define these standards have been proposed by the AstraZeneca-funded PRECISION Task Force under the following key areas: (1) organisation of services, (2) timely identification, diagnosis and specialist referral, (3) specialised assessment and management of SA to optimize outcomes, and (4) patient-centric care that reflects people living with SA's expectations, priorities, and values (Haughney et al., 2020).
- The inclusion of all stakeholders, including patient communities and advocacy groups, in quality improvement is essential to establish the highest attainable levels in quality of care (Haughney et al., 2020; IPPF, 2016; Smith et al., 2008). Similarly, patient-centric care whereby SA communities are educated about their health needs and prospective health outcomes is essential for them to ensure that they demand health services that fulfil certain quality standards, as is the provision of education about the role of patient self-referral for specialty asthma care.
- People living with SA and other key stakeholders need to be included throughout the process of continual assessment. This engagement includes the design, implementation, analysis and assessment of gaps and needs, as well as identifying potential solutions for improved care. Countries can establish a working group comprised of all stakeholders to ensure requirements and experiences are adequately reflected in efforts.

The findings and subsequent recommendations presented here should be interpreted with caution, given the inherent methodological limitations posed by a web-survey based analysis.

Due to time constraints, a limited, convenience sample of clinicians and people living with SA was drawn across the study countries and more importantly, some study countries were represented by one clinician (e.g., Australia and Italy) and one patient (e.g., Australia, Brazil, Italy) only. Therefore, the results presented in this report cannot be viewed as entirely representative of the true environment and clinical practices followed in SA care within the study countries nor of the true outcomes observed in the international population of people living with SA. Furthermore, the use of a web-survey allowed for potentially misinterpreted questions by respondents, an inability to validate respondents' understanding/interpretation of the questionnaire items, and self-reported data based on each clinician's level of knowledge/experience on the specific indicator in question. The latter is particularly relevant to the indicators studied around clinicians prescribing in points 5 and 6a/6b of the GINA decision tree for the management of difficult-to-treat and SA, as this specific guidance is not relevant in all countries and/or recognised by all clinicians that participated in the survey.

As a robustness check to address the above limitations, country specific findings were reviewed and validated by country experts and their feedback was incorporated where needed. Overall, we value the contribution and perspectives of all participants and therefore considered all responses to be relevant and valuable for analysis.

9. Conclusion

Findings of this research demonstrate that data around the clinical and pharmacological management of SA is not routinely available. Despite the increased use of biologics there are still significant gaps in patient care holding back improved outcomes. Given that the significant unmet need currently characterising SA can be addressed by enhanced SA care practices, especially in light of the growing pressure on respiratory-related healthcare resources stemming from the COVID-19 pandemic, action in the form of measures to improve outcomes for people living with SA is vital now more than ever.

Governments should centre their efforts specifically on infrastructure needed to support clinicians in optimising care management and referral pathways, including the ability to collect meaningful, outcomes-relevant data in an automated, systematic way.

A fundamental step towards this effort is to collect data on the effectiveness of routine clinical practices/pathways and support the translation of current diagnostic/treatment guidelines into real-world, meaningful outcomes for people living with SA, caregivers, clinicians and the society. Global, co-ordinated political action and cross-border collaboration is also key to establishing a set of internationally relevant, common standards in performance measurement and quality assessment of the care provided for SA at the international level.

Essentially, the effective combination of enhanced capacities in SA: i) data collection systems, ii) specialist referral and care and iii) quality assessment processes at a global level can drastically address the significant knowledge gaps and unmet need currently present in SA.

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Appendices

Appendix Table 1. Selected indicators (in red) studied in the clinicians' survey.

Theme	Sub-theme	Indicator
Epidemiology	Prevalence	Number and percentage of prevalence
	Incidence	Number and percentage of incidence
	Morbidity	Number and percentage of asthma DALYs
	Mortality	Number and percentage of asthma-related deaths
Policy structure & organisation	Guidelines	Existence of clinical or practice guidelines on asthma / severe asthma
	Structure	Existence of patient organisations
		Existence of specialist care / characteristics of specialist care
Diagnosis	Diagnostic testing	Use of diagnostic tests
	Specialist referral	HCP/person responsible for referral and referral criteria used
		Time to specialist referral
	Definitive diagnosis	Number of SA patients in registries
		Number or ratio of patients receiving a clear diagnosis
		Provision of disease diagnosis and explanation in an understandable format
	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
		Individual episodes of OCS use in a year
	Available biologic treatment	Reimbursement status of relevant drugs / biologics
		Existence of early access opportunities
		Number of patients offered full range of potential treatment options with an emphasis on biologics
	Biologic use	Time of prescribing after SA diagnosis Criteria considered for biologic use Clinicians with SA patients on biologics Reasons for not prescribing biologics Attributes important for selecting biologic treatment Driver of treatment decision/ when prescribing biologics
	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)
		Number of clinical episodes in a year (planned/unscheduled)
		Hospital admissions rates for patients with asthma/SA
		Hospital length of stay (days)
	Access to care	Ratio of patients accessing specialist care services
		Geographic distribution of specialist care centres
		Average patient travel distance 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 patients being managed by MDT
		Availability of specialist nurses/educators and role in patients' treatment
		Level of communication between specialist centres and referring sites
		Patient involvement in decisions about care
	Quality of care	Availability of a national quality standard for SA
		Availability of financial incentives around severe asthma care/outcomes
		National strategy or plan on asthma/severe asthma
Socio-economic impact	Absenteeism	Absenteeism associated with severe asthma
	Cost of illness data	Individual-level costs
		System-level costs

Source: Kamphuis et al., 2021

Appendix Table 2. 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 Service NHS)

Sources: *Kamphuis et al. (2021).*

Appendix Table 3. Sources of up-to-date information on SA care and management

	AUS (n=1)	BR (n=5)	CAN (n=4)	FR (n=2)	GER (n=4)	IT (n=1)	JPN (n=4)	SP (n=2)	UK (n=3)	Total (n=26)
Sources of up-to-date information on SA (% of respondents)										
Guidelines	100% (GINA)	100% (GINA)	100% (GINA, CTS, ERS/ATS)	50% (ERS/ATS GINA)	50% (GINA, DGP)	0%	25% (guide to SA diagnosis & treatment	50% (GINA, GEMA)	66% (BTS / SIGN, GINA, ERS/ATS)	65%
Scientific publication	100%	100%	75%	100%	75%	100%	100%	100%	100%	92%
Scientific congresses	100%	100%	100%	50%	75%	100%	75%	100%	100%	88%
Scientific training courses	0%	80%	0%	50%	0%	100%	25%	100%	66%	42%
Pharma-sponsored symposia	0%	60%	25%	50%	75%	0%	25%	50%	66%	46%
Reps/ MSLs	0%	40%	50%	50%	75%	100%	25%	50%	33%	46%
Discussion with colleagues	100%	80%	75%	50%	50%	100%	25%	100%	100%	69%
Social media	0%	20%	0%	0%	0%	100%	25%	0%	0%	12%

Key: n/a: Indicator is not applicable to the relevant setting

Note:

- AUS: Australia, BR: Brazil, CAN: Canada, FR: France, GER: Germany, IT: Italy, JPN: Japan, SP: Spain, UK: United Kingdom.
- ATS: American Thoracic Society, BTS/SIGN: British Thoracic Society/Scottish Intercollegiate Guidelines Network, CTS: Canadian Thoracic Society, DGP: German Respiratory Society, ERS: European Respiratory Society, GEMA: Spanish Guideline on the Management of Asthma, GINA: Global Initiative for Asthma, MSLs: Medical Science Liaisons

Appendix Table 4. Diagnostic criteria used for SA diagnosis

	AUS (n=1)	BR (n=5)	CAN (n=4)	FR (n=2)	GER (n=4)	IT (n=1)	JPN (n=4)	SP (n=2)	UK (n=3)	Total (n=26)
	Diagnostic testing: diagnostic criteria used for SA (% of respondents)									
Eosinophil count	100%	80%	50%	50%	100%	100%	75%	50%	100%	77%
Spirometry/PEF with reversibility test	100%	100%	75%	100%	100%	100%	50%	100%	100%	88%

Respiratory symptoms (e.g., wheeze, shortness of breath, cough) for intensity, occurrence and triggers	100%	100%	100%	100%	100%	100%	50%	50%	100%	88%
Sputum induction test	0%	0%	0%	50%	25%	0%	25%	50%	33%	19%
Chest x-ray / CT	0%	100%	25%	100%	75%	100%	50%	50%	100%	69%
Bronchoscopy	0%	0%	0%	50%	0%	0%	25%	0%	66%	15%
Nasendoscopy	0%	40%	0%	50%	0%	100%	25%	0%	66%	27%
IgE	100%	100%	50%	50%	100%	100%	50%	50%	100%	77%
Bone densitometry	0%	20%	0%	50%	0%	0%	25%	0%	66%	19%
Skin prick test	100%	100%	75%	50%	100%	100%	50%	50%	100%	81%
Review of inhaler techniques to exclude suboptimal adherence	100%	100%	100%	50%	100%	100%	50%	100%	100%	88%
Risk factors	100%	100%	75%	50%	100%	100%	50%	50%	100%	81%
Comorbidities	100%	100%	100%	50%	75%	100%	50%	50%	100%	81%
Patient's anxiety, depression, and social difficulties	100%	100%	50%	50%	50%	100%	50%	50%	100%	69%
No. of exacerbations per month/ week	100%	100%	100%	100%	100%	100%	75%	100%	100%	96%
No. of hospital admissions	100%	100%	100%	100%	75%	100%	75%	100%	100%	92%
OCS Bursts in 12 months	100%	100%	100%	100%	100%	100%	100%	100%	100%	100%
GP to specialist referral pathway	0%	0%	0%	50%	50%	100%	25%	0%	33%	23%
Diagnostic pathway guidelines	0%	40% (GINA)	25% (CTS 2017)	0%	0%	100% (Eosinophilic)	50% (JGL)	100% (SEPAR GEMA, GINA)	0%	31%

Key: n/a: Indicator is not applicable to the relevant setting

Note:

- AUS: Australia, BR: Brazil, CAN: Canada, FR: France, GER: Germany, IT: Italy, JPN: Japan, SP: Spain, UK: United Kingdom.
- CTS: Canadian Thoracic Society, GEMA: Spanish Guideline on the Management of Asthma, GINA: Global Initiative for Asthma, JGL: Japanese Asthma Prevention and Management Guidelines, PEF: Peak Expiratory Flow, SEPAR: Spanish Society of Pulmonology and Thoracic Surgery.

Appendix Table 5. Indicators around the attributes important towards biologic treatment initiation, and those important in selecting a biologic treatment

	AUS (n=1)	BR (n=5)	CAN (n=4)	FR (n=2)	GER (n=4)	IT (n=1)	JPN (n=4)	SP (n=2)	UK (n=3)	Total (n=26)
Biologics use										
Driver of treatment decision/ when prescribing biologics										
SA phenotype	✓	✓	✓	✓		n/a	✓	✓		n/a
Patient characteristics & preferences		✓		✓	✓					
Side effects		✓						✓		
Eos		✓	✓				✓			
FeNO			✓				✓			
IgE			✓		✓		✓			
Skin testing		✓								
Comorbidities					✓		✓	✓		
Uncontrolled asthma despite optimised treatment			✓						✓	
Exacerbations			✓				✓			
OCS use							✓			
Guidelines							✓			
Availability of relevant treatment(s)		✓								
Type of inflammation				✓						
Objective to treat				✓						
Route of administration & interval					✓					
Attributes important for selecting biologic treatment (0; not considered to 5; very important)										
Effectiveness	5	5	5	4.5	5	3	5	5	5	5
Tolerability	2	5	4	4.5	5	3	5	4.5	5	4
Cost	4	4	4	2.5	3	4	5	3	2.5	3.5
Patient preference	3	4	3	3.5	3	3	4	3	4.5	3
Convenience/ Easier administration	4	4	3	3	3	3	4	4	4	3.5
Safety	4	5	5	5	5	5	5	5	4	5
Local protocols	1	3	2	2	0.5	5	5	4	2.5	3
Phenotype	5	5	5	4	4.5	5	5	4.5	5	5

Key: n/a: Indicator is not applicable to the relevant setting

Note:

- AUS: Australia, BR: Brazil, CAN: Canada, FR: France, GER: Germany, IT: Italy, JPN: Japan, SP: Spain, UK: United Kingdom.
- Eos: Eosinophil, FeNO: Fractional Exhaled Nitric Oxide, IgE: Immunoglobulin E, OCS: Oral Corticosteroid.

Appendix Table 6. Additional indicators relating to the communication, management and quality of care

	AUS (n=1)	BR (n=5)	CAN (n=4)	FR (n=2)	GER (n=4)	IT (n=1)	JPN (n=4)	SP(n=2)	UK (n=3)	Total (n=26)
Communication and management of care										
Involvement of patients in treatment decisions (% of respondents)										
I prefer to share responsibility of deciding for treatment	100%	60%	33%	50%	66%	100%	25%	0%	100%	54%
I prefer to make the final selection of the treatment after seriously considering the patient's opinion	0%	0%	33%	50%	0%	0%	75%	50%	0%	25%
I prefer to make the final selection about which treatment the patient will receive	0%	40%	33%	0%	33%	0%	0%	50%	0%	21%
Quality of care										
Existence of financial incentives in SA prescribing (% of respondents)										
Biologics	Medication is subsidised	No	No	No	No	Referral	No	No	No	n/a
Anti-inflammatory reliever therapy.		No				Referral			No	
Add-on controller medications		Free of charge				Education			No	
Reliever medications	Purchased w/o Rx					Education			Ratio of controller to reliever is incentivised - avoid high dose controller/reliever)	
Controller medications	No					Electronic devices				

Key: n/a: Indicator is not applicable to the relevant setting

Note:

- AUS: Australia, BR: Brazil, CAN: Canada, FR: France, GER: Germany, IT: Italy, JPN: Japan, SP: Spain, UK: United Kingdom.
- CTS: Canadian Thoracic Society, DGP: German Respiratory Society, GEMA: Spanish Guideline on the Management of Asthma, GINA: Global Initiative for Asthma, NVL: Nationalen Versorgungs-Leitlinie, MDT: Multidisciplinary team.

Appendix Table 7. Patient survey results on selected indicators for diagnostic, referral, educative and treatment pathways/practices in SA across the study countries.

	AUS (n=1)	BR (n=1)	CAN (n=14)	FR (n=2)	GER (n=3)	IT (n=1)	SE (n=17)	SP (n=8)	UK (n=7)	Total (n=54)
Diagnosis										
What medical professional made your diagnosis										
▪ Asthma specialist doctor	0%	0%	29%	0%	33%	0%	12%	25%	29%	21%
▪ Pulmonologist/Respirologist	100%	100%	43%	100%	67%	100%	47%	75%	57%	58%
▪ Allergist	0%	0%	0%	0%	0%	0%	24%	0%	0%	7%
▪ GP/Family doctor	0%	0%	21%	0%	0%	0%	6%	0%	0%	7%
▪ Other healthcare professional	0%	0%	7%	0%	0%	0%	12%	0%	14%	7%
Specialist referral										
Received/receiving care at a specialist asthma centre	0%	0%	29%	0%	33%	0%	59%	63%	71%	46%
Average time to specialist referral (months)	<0.5	24	5	<0.5	0.5	3	3	3	1.2	4.3
Materials and Education										
Provided with educative materials after new diagnosis of SA (% of respondents)	100%	0%	71%	0%	33%	100%	53%	63%	29%	54%
Biologic use										
Offered the option of a biologic (% of all patients)	100%	0%	57%	50%	67%	100%	12%	88%	14%	54%
• Treated with biologic treatment offered (% of patients offered a biologic)	0%	n/a	75%	0%	100%	100%	0%	86%	100%	55%
• Chose not to take biologic treatment offered (% of patients offered a biologic)	100%		0%	100%	0%	0%	0%	0%	0%	7%
Initial treatment received for Severe Asthma										
	AUS (n=1)	**BR (n=0)**	**CAN (n=14)**	**FR (n=2)**	**GER (n=3)**	**IT (n=1)**	**SE (n=17)**	**SP (n=7)**	**UK (n=7)**	**Total (n=52)**
Controller medications ▪ OCS (e.g., prednisolone, hydrocortisone)	100%	n/r	21%	50%	100%	100%	41%	71%	57%	48%
Add-on controller medications ▪ Biologics (subcutaneous)	0%		29%	0%	67%	100%	0%	57%	14%	23%

Subsequent/current treatment received for Severe Asthma (if different from initial)

	AUS (n=1)	BR (n=0)	CAN (n=14)	FR (n=1)	GER (n=2)	IT (n=1)	SE (n=16)	SP (n=6)	UK (n=5)	Total (n=46)
Controller medications ▪ OCS (e.g., prednisolone, hydrocortisone)	100%	n/r	14%	100%	0%	0%	19%	50%	40%	26%
Add-on controller medications ▪ Biologics (subcutaneous)	0%		43%	0%	100%	100%	0%	83%	20%	33%

Note:

- AUS: Australia, BR: Brazil, CAN: Canada, FR: France, GER: Germany, IT: Italy, SE: Sweden, SP: Spain, UK: United Kingdom.
- GP: General Practitioner, SA; Severe Asthma, OCS: Oral Corticosteroid, SABA: Short-acting beta-agonist.
- n/r: not reported/no response, n/a; not applicable

Appendix Table 8. Patient survey results on selected indicators for the access to care, resource utilisation, structure and pathways of SA care delivery across the study countries.

	AUS (n=1)	BR (n=1)	CAN (n=14)	FR (n=2)	GER (n=3)	IT (n=1)	SE (n=17)	SP (n=8)	UK (n=7)	Total (n=54)
Access to care										
Time to specialist appointment (months, average)	2	n/r	3.8	2	<0.5	3	4.7	2.6	3.7	2.8
Travel time to specialist centre (minutes, average)	20		67	30	25	30	48	33	25	35
Wait on the day of care (minutes, average)	10		27	60	30	30	5	32	30	28
Wait for diagnosis/ treatment information exchange between referral site(s) and specialist centre(s) (months, average)	<0.5		<1	<0.5	<0.5	<0.5	11	<1	2.5	2
Resource utilisation										
SA patients hospitalized within the last 12 months	0%	100%	31%	50%	0%	0%	12%	50%	71%	33%
% of hospitalisations that were overnight	n/a	100%	36%	50%	n/a	n/a	100%	100%	100%	84%
Visits to SA specialist within the last 12 months	2	5	4	2.5	5	0	3.2	3.6	3.7	3.3
▪ % of visits planned	100%	20%	75%	71%	89%	n/a	71%	80%	60%	72%

Communication and management of care										
% of SA patients using MDT	0%	100%	43%	0%	33%	100%	70%	50%	43%	52%
% of SA patients seeing specialist nurses/ educators	0%	0%	57%	50%	100%	0%	59%	63%	86%	61%
Barriers to accessing specialist nurse/educator	Not offered (100%)	n/a	Not offered (100%)	Not offered (100%)	n/a	Not available (100%)	Not offered (57%) Not available (14%) Did not need (29%)	Not offered (100%)	Not offered (100%)	Not offered (80%) Not available (10%) Did not need (10%)
COVID-19 & delivery of care										
Change of treatment/care arrangements due to COVI9-19 (% of patients)	100%	0%	64%	0%	33%	0%	59%	62%	71%	58%
• Positive vs. negative vs. neutral change (% of patients that reported a change)	0% vs 100% vs 0%	n/a	33% vs. 56% vs. 11%	n/a	100% vs 0% vs 0%	n/a	0% vs. 70% vs. 30%	20% vs. 40% vs. 40%	20% vs. 40% vs. 40%	19% vs. 55% vs. 26%
% of patients that received additional information/ support in managing SA and their treatment more efficiently or differently during the COVID-19 outbreak.	0%	0%	29%	0%	33%	0%	17%	43%	14%	22%

Note:

- AUS: Australia, BR: Brazil, CAN: Canada, FR: France, GER: Germany, IT: Italy, SE: Sweden, SP: Spain, UK: United Kingdom.
- MDT: Multidisciplinary team, SA: Severe Asthma.
- n/a; not applicable, n/r; not reported/no response.