



## Original Research

## Is asthma control more than just an absence of symptoms? An expert consensus statement



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## ABSTRACT

**Purpose:** Definitions and measures of asthma control used in clinical trials and in clinical practice vary considerably. There is also misalignment between patients and healthcare professionals (HCPs) in terms of understanding and managing asthma control. This study aimed to progress towards a consensus definition of asthma control, and evaluate disparities between HCP and patient perspectives.

**Basic procedures:** A two-stage Delphi questionnaire involving asthma specialists sought to identify areas of consensus on aspects of asthma control in clinical practice. Results were compared with those of a structured literature review to assess if existing guidance and measures of asthma control used in studies correlated with practice. Eighty-two panelists took part in the Delphi questionnaire. The structured literature review included 185 manuscripts and 31 abstracts.

**Main findings:** Panelists agreed that there was no standard definition of asthma control, confirmed by a total of 19 different composite consensus/guideline definitions and/or validated measures of control being identified across the Delphi study and literature review. Panelists agreed on the positive associations of well-controlled asthma with patient outcomes, but not on the components or thresholds of a working definition of control.

**Principal conclusions:** A universally accepted definition and measure of asthma control that is utilized and understood by patients, HCPs, and researchers is required.

**Abbreviations:** ACQ, Asthma Control Questionnaire; ACT, Asthma Control Test; ATS/ERS, American Thoracic Society/European Respiratory Society; GINA, Global Initiative for Asthma; HCP, Healthcare professional; SABA, Short-acting  $\beta_2$ -agonist.

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## 1. Introduction

The goal of asthma management is to achieve and maintain symptom control, and reduce future risk of adverse outcomes, including exacerbations, lung function decline, and side-effects of medications, irrespective of asthma severity [1]. Periodic assessment and ongoing asthma control monitoring can confirm treatment optimization or alert the healthcare professional (HCP) to the need for treatment adjustment, further investigations, or patient education. Asthma control has been described as having two distinct components: one patient-focused, based on symptoms, and one HCP-focused, based on objective measures of pathophysiological abnormalities [2]. Well-controlled asthma is associated with good symptom control and maintenance of normal activity levels [3], yet many patients and HCPs overestimate their level of symptom control [4], with patients potentially tolerating symptoms and reduced quality of life, and HCPs accepting a sub-optimal level of control [5]. Indeed, the lack of a universally accepted definition of asthma control [6] can potentially result in HCPs underestimating the level of control. HCPs often define well-controlled asthma as minimal symptoms and impact upon activities, while patients often define it as effective management of symptoms that potentially exceed their individually-defined threshold [7,8].

Following the American Thoracic Society (ATS)/European Respiratory Society (ERS) task force's recommendations [6], a combined approach to assessing asthma control from both symptom control and future risk is widely accepted. Yet, although measures and definitions for asthma control exist, there is no "gold standard" definition [6]. The Global Initiative for Asthma (GINA) and the National Asthma Education and Prevention Program provide definitions of control that appear to encompass both the patient's clinical disease characteristics and limitations, including diurnal and nocturnal symptoms, activity limitation, and use of reliever medication [3,9]. One of the long-term goals of asthma management as stipulated by GINA is "to minimize future risk of asthma-related mortality, exacerbations, persistent airflow limitation and side-effects of treatment", which is often overlooked in short-term questionnaires. There are also several standardized questionnaires, e. g., the Asthma Control Questionnaire (ACQ) [10] and the Asthma Control Test (ACT) [11]. However, it should be noted that HCP bias may have influenced the development of these tools. For example, symptoms identified in the ACQ were selected based upon HCP opinion of those most important [10]. During ACT development, stepwise regression methods were used to select a subset of items that showed the greatest discriminant validity regarding the HCP's rating of asthma control, for which no accepted system of defining control in relation to these goals has been articulated [11]. In addition to clinical disease characteristics and limitations, some definitions/measures of asthma control consider exacerbations and pulmonary function [11,12], highlighting disparities between definitions and measures. Different measures of asthma control can also be useful for various functions, such as quickly screening for poor control [12], highlighting when an intervention is needed [3], or longitudinal evaluation of the efficacy of an intervention [10].

Given these disparities between definitions and expectations of asthma control, there is a need for an expert consensus regarding challenges and approaches in achieving well-controlled asthma. The current study aimed to progress towards reaching a consensus on asthma control, by examining the validity and utility of current measures of asthma control, evaluating which factors additional to those included in standard definitions of asthma control should be considered, and providing expert recommendations on the future assessment of asthma control in clinical practice.

## 2. Methods

The study was composed of two parts. Firstly, a two-stage Delphi method was used to reach expert consensus on definitions of asthma control used in clinical practice, HCP understanding of asthma control,

and disparities in HCP perceptions on patient opinion and understanding. The Delphi survey method is a recognized group facilitation technique designed to transform opinion into group consensus [13]. While the authors acknowledge that patient opinion is also extremely important, circulation of the Delphi survey to patients was outside of the scope of the current study due to regulatory-imposed constraints. We were therefore limited to HCP perceptions of patient opinion and understanding only. Secondly, a structured literature review examined measures of asthma control used in clinical trials and real-world studies. Findings from both the Delphi study and literature review were compared to provide a consensus regarding challenges and approaches in achieving asthma control in clinical practice. Both the Delphi study and literature study were carried out by a research team at Ashfield MedComms, an Inizio company.

### 2.1. Delphi survey method

#### 2.1.1. Questionnaire development

The Delphi method consisted of two rounds of questionnaires, which were developed, reviewed, and approved by all authors. The first and second questionnaires were disseminated to panelists in March 2021 and April 2021, respectively. Further details on the questionnaires are provided in the Online Repository.

#### 2.1.2. Panelists

Nine of the authors are practicing clinicians (GWC, AS, LPdL, CDR, JDB, GG, HI, MD, DY) and completed the questionnaire. Seventy-three additional HCPs with a professional interest in asthma were also invited to complete the questionnaire. This provided an additional eight panelists per one practicing clinician author to offer representative information and greater generation of data. Panelists who were invited to participate through SERMO (a third-party, centralized database of HCPs) received an honorarium which was compliant with GSK's fair market value evaluation for each country; authors did not. All panelists provided written informed consent to participate. Further details on recruitment and screening are available in the Supplementary Methods within the Online Repository.

#### 2.1.3. Analysis and interpretation of responses

Descriptive summaries were produced for closed questionnaires. Responses to Likert scale-based questionnaires were grouped into three categories: disagree, neither agree nor disagree, and agree. Consensus on an item was reached when  $\geq 66\%$  of panelists voted within the agree or disagree category. Further details on coding of responses are available in the Online Repository.

### 2.2. Structured literature review

A structured literature review was undertaken to identify measures and guidelines for asthma control in clinical publications. The review sought to identify all relevant publications since the Gaining Optimal Asthma Control study in 2004 by Bateman et al. [14] until search end in March 2021. Congress abstracts from 2018 to 2021 were included as it was presumed that abstracts published prior to this would have been published as full manuscripts. PubMed, Cochrane, and Embase databases were searched for relevant articles. All titles and abstracts were manually screened by a reviewer from the research team. Publications were included if they met pre-defined criteria, namely: (1) adult study population (aged  $\geq 18$  years); (2) control used as a study endpoint; and (3) an appropriate study design was used (i.e. randomized controlled trial, systematic review, meta-analysis, and/or real-world evidence).

Following initial screening, the following details were extracted from the included publications to quantify the results: (1) trial design; (2) control as primary/secondary endpoint; (3) population; (4) total N; (5) center type; (6) country; (7) measure of control used (guidelines, validated measure [e.g. ACT, ACQ], symptomatic measure of control [e.g.

frequency of exacerbations, use of rescue medication], patient-reported measures of control [e.g. sleep disturbances, impact on day-to-day activities]); and (8) any further details. Details were extracted and recorded from the publications as written; no assumptions were made by the research team (full details of the data extraction are available in [Table E1](#) in the Online Repository). Results of the structured literature research were reported descriptively.

Further details on the literature review, including search criteria and strategy, inclusion/exclusion criteria for relevant papers, and information on secondary and tertiary reviewers, are provided in the Online Repository.

### 3. Results

#### 3.1. Delphi survey method

In total, 82 panelists, including the nine authors, completed the first-round Delphi questionnaire. Overall, 63 panelists, including the nine authors, took part in the second-round Delphi questionnaire (19 panelists were lost in follow up). Panelist demographics are detailed in [Table 1](#).

#### 3.2. Structured literature review

The literature research identified 664 manuscripts and 89 abstracts. Following exclusions, 185 manuscripts and 31 abstracts were included in the full data extraction. A PRISMA flow diagram of included and excluded publications, stratified by study design, is detailed in [Figure E1](#) in the Online Repository. Asthma control was a primary endpoint for 36% and secondary endpoint for 17% of included publications. Nearly half of publications used a single measure to define/measure asthma control (49%), 20% used two measures, and 29% used 3–6 measures.

**Table 1**  
Delphi questionnaire respondent demographics.

Demographic	First-round questionnaire (N = 82)	Second-round questionnaire (N = 63) <sup>a</sup>
<b>Primary medical specialty, n</b>		
Allergist	14	8
General practitioner/ primary care physician	30	20
Pulmonologist	38	35
<b>Years qualified in specialty,<sup>b</sup> n</b>		
>10	18	
11–15	17	
15–20	22	
20–25	23	
25–30	17	
30+	14	
<b>Mean time spent on activities,<sup>b</sup> %</b>		
Actively treating patients	82%	
Academic/research	11%	
Admin/other	7%	
<b>Number of patients treated in a typical month<sup>b,c</sup></b>		
0–30	17	
31–60	26	
61–90	10	
91–120	12	
121+	17	
<b>Location, n</b>		
Argentina	12	9
Australia	11	9
Brazil	11	8
China	12	6
Italy	12	11
Japan	11	9
Spain	13	11

<sup>a</sup> All respondents also took part in the first-round questionnaire.

<sup>b</sup> Question asked in first-round questionnaire only.

<sup>c</sup> Patients were asked to give their response as it was pre-COVID-19 pandemic.

#### 3.3. Outcome measure indicative of well-controlled asthma

Panelists agreed that there is no agreement that there is a clear, published definition of asthma control ([Table 2](#)). This was confirmed by the identification of 19 different composite consensus/guideline definitions or validated measures of control across the Delphi study and literature review ([Table 3](#)).

Notwithstanding the above finding, panelists agreed that the currently accepted definition of asthma control is appropriate ([Table 2](#)). When asked how asthma control is defined in clinical practice, panelists noted that they largely used GINA, ATS/ERS, ACT, or ACQ definitions. Panelists agreed that GINA, the most commonly cited document by panelists, clearly defines well-controlled asthma symptoms ([Table 2](#)). When the definitions cited by panelists were compared with the literature, their use was more varied, with asthma control defined using multiple other measures, such as other guidelines, symptomatic measures, or patient-reported outcomes ([Table 3](#) and [Figure E2](#) in the Online Repository).

Consensus was reached by Delphi panelists that asthma control should be considered as a continuum, yet panelists also agreed that asthma control should be considered as a categorical variable, with level of control defined as poor, good, or total ([Table 2](#)). When asked what level of outcome measure they consider indicative of well-controlled asthma, the majority of panelists reported that they use ACT values (59% of panelists; [Figure E3](#) in the Online Repository). Of those that provided a specific score, the majority stated they defined well-controlled asthma as an ACT score of >19 or >20 (40 and 33%, respectively). In the literature, only 23% of included publications used ACT as a measure of asthma control; of those that noted specific values, 57% stated that an ACT score  $\geq 20$  was indicative of well-controlled asthma. The second most commonly used outcome measure was ACQ (16% of panelists, 27% of included publications), and of those that utilized ACQ, 73% of panelists advised a score of <0.75 as being indicative of well-controlled asthma, while 95% of publications advised a score of  $\leq 0.75$ .

When asked specifically about the frequency of short-acting  $\beta_2$ -agonist (SABA) reliever medication in a 4-week period that they would consider indicative of poorly controlled asthma in clinical practice, responses from the surveyed HCPs varied widely (see [Figure E4](#) in the Online Repository). Only seven of the included publications included rescue medication (SABA [ $n = 4$ ] or other [ $n = 3$ ]) as a measure of control, all with different definitions for SABA use indicative of poorly controlled asthma.

#### 3.4. Most important measures of asthma control from the HCP and patient perspective

Consensus was reached by panelists that when categorizing the level of control, both the HCP and the patient's perspective is considered ([Table 2](#)). When asked to report which measures of asthma control they thought were most important from both their perspective and the patient's perspective, most panelists reported the number/frequency of exacerbations (HCP 40% vs. patient 39%) and severity of symptoms (HCP 33% vs. patient 36%) as the most important (see [Figure E5](#) in the Online Repository). Despite this apparent close alignment of the patient and HCP, as perceived by the panelists, it was agreed that there is a misalignment between the patient's most important measures of control and those of the HCP ([Table 2](#)).

When asked specifically, consensus was reached by panelists that symptoms represent an important component of the assessment of asthma control in clinical practice ([Table 2](#)), symptom burden is directly related to asthma control, and asthma control is the same as symptom control ([Table 2](#)). Consensus was also reached by panelists that airway obstruction represents an important component of the assessment of asthma control in clinical practice ([Table 2](#)). However, few publications appear to explore symptom severity, exacerbations, or airway

**Table 2**  
Level of agreement to statements presented to healthcare professionals.

Statement	Proportion of panelists, % <sup>a</sup>			Consensus reached?
	Net agree	Net neither agree nor disagree	Net disagree	
<b>Outcome measure indicative of well-controlled asthma</b>				
There is a clear, published definition of asthma control (1)	65	28	7	X
The currently accepted definition of asthma control is appropriate (1)	71	24	5	✓
GINA clearly defines well-controlled asthma symptoms (in the past four weeks: daytime asthma symptoms less than twice a week, no night waking due to asthma, SABA reliever use for relief of symptoms two or fewer times/week, no activity limitation due to asthma) (2)	95	2	3	✓
Asthma control is best considered as a continuum (1)	85	7	7	✓
Categories of control should be defined as poor/good/total (1)	67	21	12	✓
<b>Most important measures of asthma control from the HCP and patient perspective</b>				
When categorizing the level of control, both the physician and patient's perspective is considered (1)	87	7	6	✓
Physicians and patients share the treatment goal of good asthma control (1)	85	9	6	✓
There is misalignment between the patient's most important measures of control and those of the physician (2)	68	11	21	✓
Symptoms represent an important component of the assessment of asthma control in clinical practice (1)	98	2	0	✓
Symptom burden is directly related to asthma control (2)	98	0	2	✓
Asthma control is the same as symptom control (2)	71	8	21	✓
Airway obstruction represents an important component of the assessment of asthma control in clinical practice (1)	85	12	2	✓
<b>Poorly controlled asthma and future risk</b>				
Patients understand the importance of asthma control, and the link between good asthma control and future risk (1)	66	16	18	✓
Well-controlled asthma is associated with improved quality of life (2)	95	3	2	✓
Well-controlled asthma is associated with reduced future risk (of exacerbations, loss of control, unscheduled healthcare use, and long-term adverse outcomes) (2)	94	3	3	✓
Well-controlled asthma is associated with improved quality of life and reduced future risk, but there are many confounding factors (2)	84	10	6	✓
Well-controlled asthma is associated with ability to perform normal day-to-day activities (including minimal sleep disturbances) (2)	98	0	2	✓
Patients who achieve good control of asthma, according to a guideline-based composite measure (e.g. the patient has good asthma control according to GINA/ATS/GEMA etc. definition of control), also achieve greater improvements in quality of life (1)	95	4	1	✓
<b>Asthma control and asthma exacerbations</b>				
There is a clear, published definition of asthma exacerbations (1)	79	13	7	✓
A reduction in frequency of exacerbations is indicative of improved asthma control (2)	94	5	2	✓
<b>The importance of HCP and patient education</b>				
It is important to educate patients on the significance of good asthma control on current and future risk and health outcomes (1)	100	0	0	✓
It is important to educate healthcare professionals on the significance of good asthma control on current and future risk and health outcomes (1)	95	5	0	✓
Well-controlled asthma is associated with a good patient-doctor relationship (2)	81	17	2	✓
<b>Asthma control and adherence</b>				
Patients understand that they should continue to adhere to their medication regimen, even when they are not experiencing any symptoms of asthma (1)	63	12	24	X
Adherence to therapy should be considered as part of the assessment of a patient's level of asthma control (2)	89	5	6	✓
Well-controlled asthma is associated with minimal use of as-needed reliever medication (SABA use) (2)	90	3	6	✓
Well-controlled asthma is associated with good adherence with the minimal effective treatment dose of inhaled corticosteroids (2)	87	10	3	✓
Well-controlled asthma is associated with using the most cost-effective treatment (2)	84	13	3	✓

Net agreement defined as total percentage of panelists answering "somewhat agree" or "strongly agree". Net disagreement defined as total percentage of panelists answering "strongly disagree" or "somewhat disagree". Consensus on an item was reached when  $\geq 66\%$  of panelists voted within the agree or disagree category. Number in brackets indicates Delphi questionnaire round in which statement was posed to panelists.

ATS, American Thoracic Society; GEMA, Spanish Guideline on the Management of Asthma; GINA, Global Initiative for Asthma; HCP, healthcare professional; SABA, short-acting  $\beta_2$ -agonist.

<sup>a</sup> Due to rounding, totals may not equal exactly 100%.

obstruction as measures of asthma control. When the individual domains of asthma control were analyzed, nearly all definitions and measures cited by panelists or in literature included aspects on diurnal and nocturnal symptoms, but only seven (35%) cited measures of control included exacerbations as a considered domain, and none included airway inflammation (Table 3).

### 3.5. Asthma control and adherence

Panelists did not agree that patients understood the importance of adhering to their medication regimen, even when not experiencing any symptoms of asthma (Table 2). It was suggested that there was a need for better patient education on the importance of adherence, even when not symptomatic (Table 4). None of the included publications assessed

adherence to therapy as a specific measure when assessing study participant's level of asthma control.

Panelists were asked to score on a scale of 1–10 (1 being not at all important and 10 being very important) how important each of the factors were for achieving well-controlled asthma. NET important was defined as the total percentage of panelists answering 8–10, Net neutral was defined as the total percentage of panelists answering 4–7, and Net not important was defined as the total percentage of panelists answering 1–3. Consensus on an item was reached when  $\geq 66\%$  of panelists voted within the important or not important category.

### 3.6. Asthma control and asthma exacerbations

There was consensus that there is a clear, published definition of

**Table 3**  
Domains and components of guideline/consensus definitions and validated measures of control.

	Cited measure of control	Number of panelists noting measure, n (%)	Number of publications citing measure, n (%)	Recall period	Domains and components measured									
					Nocturnal symptoms	Diurnal symptoms	Activity limitation	Use of reliever medication	Exacerbations	Patient self-assessment	Spirometry/pulmonary function	ED visits or hospitalizations	Use of OCS	Eosinophil testing
<b>Guidelines/recommendations</b>	GINA	61 (84)	47 (13)	4 weeks	✓	✓	✓	✓						
	ATS/ERS taskforce	42 (58)	8 (2)	Not specified	✓	✓		✓	✓	✓	✓			
	GEMA	5 (7)	0 (0)		✓	✓	✓	✓	✓	✓	✓			
	SBPT	3 (4)	0 (0)	4 weeks	✓	✓	✓	✓	✓					
	Australian Asthma Handbook	1 (1)	0 (0)	4 weeks	✓	✓	✓	✓						
	EPR-3	0 (0)	8 (2)	1 week (symptoms), since last visit (exacerbations and hospitalizations)	✓	✓	✓	✓	✓	✓	✓	✓		
<b>Validated measures</b>	CDC's National Asthma Survey	0 (0)	1 (0)	1 year for exacerbations, ED/hospitalizations and activity limitation	✓	✓	✓		✓			✓		✓
	ACT	30 (41)	84 (23)	4 weeks	✓	✓	✓	✓		✓				
	ACQ	23 (32)	97 (27)											
	ACQ-7		87 (24)	1 week	✓	✓	✓	✓			✓			
	ACQ-6		8 (2)	1 week	✓	✓	✓	✓						
	ACQ-5		4 (1)	1 week	✓	✓	✓	✓						
	PCAQ-6	0 (0)	4 (1)		✓	✓	✓	✓		✓				
	ATAQ	0 (0)	3 (1)	1 week	✓	✓	✓	✓	✓					
	ACSS	0 (0)	1 (0)	1 week	✓	✓	✓	✓			✓			
	CARAT	0 (0)	1 (0)		✓	✓	✓	✓						✓
	SASCQ	0 (0)	1 (0)	30 days	✓	✓	✓	✓	✓					
	AIRQ	0 (0)	1 (0)	2 weeks for impairment measures and 12 months for risk measures	✓	✓	✓	✓		✓		✓		✓
JACS	0 (0)	1 (0)	4 weeks	✓	✓	✓	✓		✓					
RCP3	0 (0)	1 (0)	1 month	✓	✓	✓	✓							

ACQ, Asthma Control Questionnaire; ACSS, Asthma Control Scoring System; ACT, Asthma Control Test; AIRQ, Asthma Impairment and Risk Questionnaire; ATAQ, Asthma Therapy Assessment Questionnaire; ATS/ERS, American Thoracic Society/European Respiratory Society; CARAT, Control of Allergic Rhinitis and Asthma Test; CDC, Centers for Disease Control; ED, emergency department; EPR, Expert Panel Report; GEMA, Spanish Guidelines on the Management of Asthma; GINA, Global Initiative for Asthma; JACS, Japan Asthma Control Survey Questionnaire; OCS, oral corticosteroids; PCAQ-6, Six-item Perceived Control of Asthma Questionnaire; RCP3, Royal College of Physicians 3-item asthma questionnaire; SASCQ, Seattle Severity and Control Questionnaire; SBPT, Sociedade Brasileira de Pneumologia e Tisiologia.



asthma exacerbations (Table 2). Whilst the authors acknowledge that reductions in exacerbation frequency in a clinical trial setting often does not correlate with asthma control, the panelists agreed that a reduction in frequency of exacerbations is indicative of improved asthma control in a clinical setting (Table 2). When asked about the frequency of exacerbations in a 12-month period that they would consider indicative of poorly controlled asthma in clinical practice, responses were varied, with 74% of panelists stating 1–3 exacerbations per year (see Figure E6 in the Online Repository). Fifteen of the included publications noted frequency of exacerbations as an outcome measure. Of these, the majority calculated the total number of exacerbations during the study period, while only one of the publications included specified that poor asthma control could be indicated by  $\geq 2$  exacerbations in the past year.

### 3.7. Poorly controlled asthma and future risk

Panelists concurred that, in their opinion, patients understand the importance of asthma control, and the link between good asthma control and future risk of worsening asthma symptoms (Table 2). They agreed that well-controlled asthma is associated with reduced future risk and improved quality of life, including the ability to perform normal day-to-day activities and minimal sleep disturbances, despite there being many confounding factors (Table 2). When asked specifically, panelists reported that severe exacerbations, decline in lung function, and loss of asthma control were the most important future risk factors associated with poorly controlled asthma (see Figure E7 in the Online Repository).

### 3.8. The importance of HCP and patient education

Panelists considered it important that both patients and HCPs are educated on the significance of well-controlled asthma on current/future risk of worsening asthma and health outcomes (Table 2). It was suggested that it is important to increase patient understanding of the correlation between asthma control and improved outcomes, and the impact that treatment and lifestyle choices can have on control (Table 4). Panelists suggested that setting functional goals with the patient could also help to improve asthma control (Table 4). When asked how the importance of asthma control could be best communicated to the patient, panelists felt that good communication and the patient-doctor relationship were very important, as were materials to share with the patient (Tables 2 and 4). HCP panelists did not feel it was as important to increase consultation time or endeavor for more effective history and note taking in consultations, nor use media outlets such as social media for disease education (Table 4).

## 4. Discussion

The present expert opinion of practicing pulmonologists, allergists,

and general practitioners, coupled with assessment and analysis of published literature, demonstrated that there is a need for a genuine consensus definition on asthma control with high penetration. With respect to the validity and utility of current measures of asthma control, while HCPs may believe they are using a universally accepted measure of asthma control, this study highlights that no such universally accepted measure exists. The identification of 19 different composite consensus/guideline/expert paper definitions or validated measures of control identified both in the literature published since 2004, and according to expert clinical opinion, demonstrates the disparities and difference between clinical trials and clinical practice. It is possible that many more outcome measures exist and are used in clinical practice globally. Some validated measures were used more frequently in clinical practice and in clinical trials than others, namely the ACT and ACQ. Yet among these measures, and despite published guidance, there was no standardized, specific value at which the literature or expert panel considered asthma to be well-controlled, and research suggests these measures may not be used as standard in practice [15]. The GINA definitions of asthma control were the most frequently selected document by panelists. GINA highlights that there are many available systems for the assessment of asthma symptom control, which may correlate with one another but are not identical [3]. Panelists agreed that there is no clear, published definition of asthma control. However, they agreed that the currently accepted definition of asthma control is appropriate. It could be suggested that HCPs have confidence in the measure of control they feel is most appropriate for their individual practice.

To reach a universal definition of asthma control, it is important to examine which factors should be considered with those already included in standard definitions of asthma control, while addressing the needs of both HCPs and patients. With respect to the needs of HCPs, while panelists strongly agreed that asthma control should be considered as a continuum, they also suggested that a universally accepted definition of asthma control would require some binary categorization to ensure its usefulness in clinical decision-making. For example, for well-controlled asthma, patients could continue to be monitored and managed using their current treatment regimen, whereas patients with asthma that is not well controlled may require treatment adjustment or further investigation. Concepts of “partial” asthma control may not be as appropriate for use in clinical practice as binary concepts of “well-controlled” or “poorly-controlled” asthma. This suggestion is in line with other studies stating that asthma severity categorization could result in improved care [16]. Furthermore, the semantics of current measures of asthma control may introduce misunderstanding and error: the term “control” may be understood differently by patients compared with HCPs [3]. Although outside the scope of this study, any new universally accepted measure of asthma control should ideally include a numerical scoring system, with values used in a more dichotomous manner to indicate either a need for further evaluation/treatment or that the patient is on adequate

**Table 4**  
Healthcare professional rating of importance of statements presented in Question 3, Round 2.

Statement	Proportion of panelists, %			Consensus reached?
	Net important	Net neutral	Net not important	
<b>The importance of HCP and patient education</b>				
Improving the patient's understanding of the correlation between asthma control and improved outcomes (symptoms, severity, exacerbations, quality of life, etc.)	90	8	2	✓
Increasing patient understanding of treatment and lifestyle choices and the impact upon control	89	11	0	✓
Setting of functional goals with the patient (e.g. to go on a bike ride)	75	25	0	✓
Improving communication between the patient and healthcare professional	86	14	0	✓
Improving patient education, including materials which can be shared with the patient	81	19	0	✓
Use of media outlets including social media to communicate the importance of asthma control	52	44	3	X
Increasing consultation time	54	43	3	X
More effective history and note taking in consultations (e.g. occupational history, social context)	65	32	3	X
<b>Asthma control and adherence</b>				
Better patient education on the need for adherence, even when not symptomatic	83	13	5	✓

HCP, healthcare professional.

treatment and can continue to be monitored, in order to improve usability and reduce misunderstanding between the patient and HCP. GINA documents state that assessment of both symptom control and future risk of adverse outcomes should be described separately [3]. We suggest that, if a patient has good symptom control, but has an increased future risk of adverse outcomes, they should not be classified as “well-controlled”, as to be at future risk indicates they require treatment modification and should be classified as well-controlled with future risk based on therapeutic goals.

To develop a universally accepted definition of asthma control that also meets patients’ needs, it is important to recognize that patient needs differ from those of HCPs, thus HCPs need to fully understand factors of asthma control that are important to the patient. Although there may be some degree of overlap in patient and HCP perceptions of asthma control, they are not consistently matched [17], with patients potentially having their own specific personal meanings and measures to gauge their individual asthma control [8]. Therefore, to facilitate an accurate and objective assessment of asthma control, future measures of control should consider the patient’s perspective and recognize the potential for patient under-reporting of symptoms [18]. Important factors to consider include levels of control among patients in clinical practice, which may be significantly lower than in clinical trials [4], and patients may not recognize their symptoms as indicators of poor control [4].

A qualitative study of 55 adults with asthma reported that patients evaluate their own level of asthma control by considering their level of respiratory symptoms, exacerbations, activity limitations, fatigue, panic/fear relating to symptoms, sleep disturbances, and use of rescue medication [17]. While the panelists agreed that these measures of asthma control are considered by both HCPs and patients when assessing asthma control in clinical practice, this does not occur in commonly used assessments of control, and they suggested misalignment between patients’ most important measures of control and those of HCPs. The panelists suggested that increasing patient understanding of asthma control could improve outcomes. This could be achieved through greater communication and patient–doctor relationships, setting of functional goals, and discussion of the importance of treatment and lifestyle choices. Since the panelists concurred that consultation time should not be increased, potential ways to educate patients and establish functional goals whilst ensuring optimized use of the time available in consultations should be identified, for example the use of educational videos in the waiting room before the patient’s visit. It may also be appropriate to include patients with asthma in future research to help define and create measures of asthma control.

Another key insight gained from this study is that the impact of treatment adherence on asthma control is not considered as standard in either clinical trials or in validated measures of asthma control. Although it is possible that patients can be well controlled and non-adherent, lack of therapeutic compliance can cause poor control. In clinical practice, non-adherence can be high, with low adherence associated with a higher risk of exacerbations [19]. Evaluation and measuring of adherence should be more greatly recognized as an important factor in well-controlled asthma [19]. When providing the patient with further information and education on the need for well-controlled asthma, as highlighted within this study’s results, it could be appropriate to provide the patient with information and education on treatment adherence, even when they believe they are not experiencing symptoms with asthma. A further issue highlighted by this study with regard to treatment is the disparity in use of reliever medication as a measure of asthma control. In our study, per available measures/definitions [3,10], panelists were asked to quantify SABA reliever medication use indicative of poorly-controlled asthma in clinical practice. However, over-use of SABA therapy is associated with an increased risk of exacerbations [20]. GINA has recently recommended as-needed inhaled corticosteroid plus rapid-onset long-acting  $\beta_2$ -agonist as preferred reliever therapy [3]. As this recommendation becomes implemented in clinical practice, it may become more complex to

quantify and distinguish a patient’s reliever medication use from controller medication use, and simple frequency of reliever medication use may not be appropriate as a measure of asthma control.

There are several strengths and limitations to this study. A strength of the Delphi study is that experts with extensive experience in asthma management across different healthcare systems, cultures, and languages were recruited using strict criteria; thus, their individual responses and opinions reflect current knowledge and perceptions within the field of asthma, which were transformed into a group consensus [13]. In addition, sample size was relatively large, providing representative information and limiting any potential influence of the authors on the consensus opinion (authors constituted a minority of the sample size). A limitation of the Delphi study design is that there is no universally accepted proportion of panelists indicative of consensus [13]. In this study, a proportion of  $\geq 66\%$  agreement was considered to be a consensus, per a recently published Delphi consensus study of inhaled therapy in asthma experts [21]. A further limitation is that concerns about the frequency of as-needed inhaled corticosteroids plus rapid-onset  $\beta_2$ -agonist as reliever and the assessment of symptom control were not covered in this study. The results of the Delphi survey were made more robust by comparing with the results of a comprehensive, structured literature review. A limitation of the literature review is the potential for bias, which was not assessed.

## 5. Expert opinion on future goals of asthma control and conclusions

It is the authors’ expert opinion that:

- There is a need for a universally-accepted measure of asthma control to permit alignment between clinical practice, clinical studies, and patient/HCP understanding. The lack of a universally accepted measure of asthma control should be acknowledged and addressed by HCPs.
  - **Expert response:** While the findings of the current study may not be unexpected, it is critical that this is acknowledged so that we can move forward. A greater collaboration between international thoracic societies could help promote a universally accepted measure of asthma control, utilized across clinical trials, and in which HCPs could have confidence. Another interesting target for future development in the clinical management of asthma is minimal clinically important difference (MCID), defined as the smallest change or difference in an outcome measure that is perceived as beneficial and would lead to a change in the patient’s medical management. An expert consensus report on literature evidence about MCID for endpoints to monitor asthma control has been published [22].
- HCPs should be mindful that patients may have their own measures to gauge their asthma control, and should recognize the potential for patients under-reporting symptoms. Treatment adherence and inhaler competence should be evaluated and measured when assessing a patient’s level of control.
  - **Expert response:** Since patients did not contribute to the current study, we were only able to include HCP interpretations of patient values. Future studies, with help from patient advocacy groups, should seek to understand asthma control domains that are important to patients and their concerns around outcomes, as well as compare existing measures or develop and validate new measures of asthma control which encompass both the patient’s perception of their asthma control as well as adherence and inhaler competence. As improved asthma medication adherence is a mediator of asthma control, it is also important to match a patient’s control measures to outcomes important to the patient (i.e., a patient-centered approach), and to address real-world difficulties in measuring medication adherence in patient care.

➤ A future validated measure of asthma control should use a standardized numerical system to indicate whether or not asthma is well-controlled.

There are disparities in the assessment of asthma control among specialists, and between clinical practice and research. Although outside the scope of this study, there is a need for future research, collaboration, and recommendations to develop a universal metric to measure asthma control in clinical practice.

### Ethics approval and consent to participate

This study complied with all applicable laws regarding participant privacy. No direct participant contact, or primary collection of individual human subject data occurred. Study results were in tabular form and aggregate analyses omitted participant identification, therefore informed consent, ethics committee, or Institutional Review Board approval were not required.

### Trademarks and copyright

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### CRediT authorship contribution statement

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### Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.rmed.2022.106942>.

### References

- [1] C.E. Jia, H.P. Zhang, Y. Lv, R. Liang, Y.Q. Jiang, H. Powell, et al., The asthma control test and asthma control questionnaire for assessing asthma control: systematic review and meta-analysis, *J. Allergy Clin. Immunol.* 131 (2013) 695–703.
- [2] J.D. Blakey, A.J. Wardlaw, What is severe asthma? *Clin. Exp. Allergy* 42 (2012) 617–624.
- [3] Global Initiative for Asthma, Global strategy for asthma management and prevention, Available at: <https://ginasthma.org/wp-content/uploads/2022/05/GINA-Main-Report-2022-FINAL-22-05-03-WMS.pdf>, 2022. (Accessed 4 May 2022).
- [4] D. Price, M. Fletcher, T. van der Molen, Asthma control and management in 8,000 European patients: the REcognise Asthma and Link to Symptoms and Experience (REALISE) survey, *NPJ Prim. Care Respir. Med.* 24 (2014), 14009.
- [5] L. Prieto, C. Badiola, J.R. Villa, V. Plaza, J. Molina, E. Cimas, Asthma control: do patients' and physicians' opinions fit in with patients' asthma control status? *J. Asthma* 44 (2007) 461–467.
- [6] H.K. Reddel, D.R. Taylor, E.D. Bateman, L.P. Boulet, H.A. Boushey, W.W. Busse, et al., An official American Thoracic Society/European Respiratory Society statement: asthma control and exacerbations: standardizing endpoints for clinical asthma trials and clinical practice, *Am. J. Respir. Crit. Care Med.* 180 (2009) 59–99.
- [7] P.M. O'Byrne, C. Jenkins, E.D. Bateman, The paradoxes of asthma management: time for a new approach? *Eur. Respir. J.* 50 (2017), 1701103.
- [8] N. Bidad, N. Barnes, C. Griffiths, R. Horne, Understanding patients' perceptions of asthma control: a qualitative study, *Eur. Respir. J.* 51 (2018), 1701346.
- [9] National asthma education prevention program, Expert panel report 3 (EPR-3): guidelines for the diagnosis and management of asthma—summary report 2007, *J. Allergy Clin. Immunol.* 120 (2007) S94–S138.
- [10] E.F. Juniper, P.M. O'Byrne, G.H. Guyatt, P.J. Ferrie, D.R. King, Development and validation of a questionnaire to measure asthma control, *Eur. Respir. J.* 14 (1999) 902–907.
- [11] R.A. Nathan, C.A. Sorkness, M. Kosinski, M. Schatz, J.T. Li, P. Marcus, et al., Development of the asthma control test: a survey for assessing asthma control, *J. Allergy Clin. Immunol.* 113 (2004) 59–65.
- [12] G. Hoskins, B. Williams, C. Jackson, P.D. Norman, P.T. Donnan, Assessing asthma control in UK primary care: use of routinely collected prospective observational consultation data to determine appropriateness of a variety of control assessment models, *BMC Fam. Pract.* 12 (2011) 105.
- [13] F. Hasson, S. Keeney, H. McKenna, Research guidelines for the Delphi survey technique, *J. Adv. Nurs.* 32 (2000) 1008–1015.



- [14] E.D. Bateman, H.A. Boushey, J. Bousquet, W.W. Busse, T.J. Clark, R.A. Pauwels, et al., Can guideline-defined asthma control be achieved? The Gaining Optimal Asthma Control study, *Am. J. Respir. Crit. Care Med.* 170 (2004) 836–844.
- [15] K.R. Chapman, D. Hinds, P. Piazza, C. Raheison, M. Gibbs, T. Greulich, et al., Physician perspectives on the burden and management of asthma in six countries: the Global Asthma Physician Survey (GAPS), *BMC Pulm. Med.* 17 (2017) 153.
- [16] G.L. Colice, Categorizing asthma severity: an overview of national guidelines, *Clin. Med. Res.* 2 (2004) 155–163.
- [17] K. Rudell, A. Hareendran, N. Bonner, R. Arbuckle, C. Burbridge, L. Abetz, Patients' experience of asthma control and clinical guidelines: perspectives from a qualitative study, *Respir. Med.* 106 (2012) 909–911.
- [18] Y.A. Alzahrani, E.A. Becker, Asthma control assessment tools, *Respir. Care* 61 (2016) 106–116.
- [19] M. Engelkes, H.M. Janssens, J.C. de Jongste, M.C. Sturkenboom, K.M. Verhamme, Medication adherence and the risk of severe asthma exacerbations: a systematic review, *Eur. Respir. J.* 45 (2015) 396–407.
- [20] B.I. Nwaru, M. Ekström, P. Hasvold, F. Wiklund, G. Telg, C. Janson, Overuse of short-acting  $\beta_2$ -agonists in asthma is associated with increased risk of exacerbation and mortality: a nationwide cohort study of the global SABINA programme, *Eur. Respir. J.* 55 (2020), 1901872.
- [21] A.L. Valero, J.A. Trigueros, V. Plaza, Multidisciplinary consensus on inhaled therapy in asthma, *Expert Rev. Respir. Med.* 15 (2021) 425–434.
- [22] M. Bonini, M. Di Paolo, D. Bagnasco, I. Baiardini, F. Braido, M. Caminati, et al., Minimal clinically important difference for asthma endpoints: an expert consensus report, *Eur. Respir. Rev.* 29 (156) (2020 Jun 3), 190137.