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REVIEW ARTICLE

Association and correlation of patient symptom perception and asthma control – a rapid literature review

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Abstract

Background: Several studies suggest that patients often under-estimate their asthma symptoms and over-estimate their level of asthma control, potentially putting them at risk of undertreatment with inhaled corticosteroids.

Objective: To determine the association and correlation between patient symptom perception and asthma control.

Methods: A rapid literature review comprising searches in MEDLINE, Embase and Cochrane Library identified English language articles published between 2011–2021 that included a statistical measure of the association or correlation between perceptions of symptoms and asthma control in patients with asthma (adults and/or children). [PROSPERO CRD42021230152]. The Joanna Briggs Institute (JBI) instrument was used for study quality appraisal.

Results: Of 22 identified studies, nine presented association data and 13 reported correlation analyses. Eight of nine association studies showed a discordance between patients perceived symptoms and level of asthma control or lung function; among these, patients more frequently overestimated their asthma control than they underestimated their asthma control. Of 10 studies reporting correlation coefficients, all reported a statistically significant correlation between increased symptoms and worse asthma control; however, the strength of the correlation was shown to be only weak or moderate in most studies (coefficients numerically ranged from 0.12 to 0.74).

Conclusion: Many patients with asthma tend to overestimate their level of asthma control. Although more frequent or worse symptoms were shown to be statistically significantly correlated with worsening asthma control, there was wide variation in correlation strengths, most showing weak or moderate correlations. Research to further understand the reasons for patient symptom misperceptions are warranted.

Key words: Association, asthma control, correlation, symptom-based treatment, symptom perception

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Introduction

Asthma is a heterogeneous disease characterized by chronic airway inflammation and a range of symptoms (wheeze, shortness of breath, tight chest, cough) that vary over time and in intensity.[1] To achieve good symptom control is one of the primary long-term goals of asthma management but it is estimated that approximately half of patients with asthma have poor asthma control.[2,3] Several studies have shown that patients often underestimate their symptoms and overestimate their level of asthma control.[4-11]

In questionnaire-based surveys, approximately 50% to 80% of patients with asthma perceived their asthma to be at least well-controlled when in fact a substantial proportion had experienced frequent symptoms of asthma (range 42% to 65% of patients over varying time periods) or had required emergency care treatment or received oral corticosteroids due to asthma in the past 12 months (≥ 25%).[7-10,12] Patients may unnecessarily accept symptoms, assuming that frequent symptoms, exacerbations and lifestyle limitations are an inevitable consequence of having asthma, leading to poor asthma control.[7]

The Global Initiative for Asthma (GINA) recommends a symptom driven approach for Track 1, treating mild asthma (Step 1 and 2) with low dose inhaled corticosteroid (ICS)-formoterol taken as-needed for symptom relief, and ICS-formoterol maintenance and reliever therapy (MART) for treating moderate to severe asthma at Steps 3 and 4. The alternative Track 2 recommendation being as-needed short-acting β_2-agonist (SABA) plus ICS (Step 1) and regular daily dosing with an ICS-containing maintenance therapy plus SABA as-needed over Steps 2 to 4.[1] For patients with mild asthma treated under Track 1 (Steps 1 and 2), the decision on when to take ICS for symptom relief is directed by the patients. Patients who underestimate or under-report their symptoms may be at risk of undertreatment of the underlying inflammation with ICS and therefore at increased risk of exacerbations.[13,14] In a prospective cohort study of 189 individuals with asthma, patients who were poor perceivers of bronchoconstriction and dynamic hyperinflation (based on their perceptions of breathlessness during methacholine challenge testing) had higher rates of emergency department visits and hospitalizations due to asthma in a two-year follow-up period compared with patients who were considered normal perceivers.[15] Understanding and addressing the issues of discordance between patients' perception of their asthma control and their actual symptoms is important when it comes to managing patients with asthma treated with a symptom-driven approach.

The aim of this rapid literature review was to determine and quantify the association between patients' perception of their asthma symptoms and asthma control, with a specific focus on studies that included a statistical analysis, including any correlation (linearity). The review was limited to studies published in the previous 10 years to evaluate the most current literature on the issues of discordance between patients' perceptions of symptoms and asthma control, and over a period that coincided with the recent changes to GINA asthma management recommendations.

Methods

Rapid review design

The study protocol followed the methodology outlined by the Cochrane Collaboration, Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.[16,17] The study protocol was registered in the PROSPERO database, International prospective register of systematic reviews (ID CRD42021230152).[18]

Search strategy and study selection

Literature searches were conducted in MEDLINE, Embase and Cochrane Library to identify English-language articles published from January 2011 to January 2021. Additionally, proceedings from scientific conferences were searched to identify meeting abstracts between January 2019 and January 2021; and the reference lists of relevant review articles were manually checked for additional evidence.

The included studies were in patients (adults and children) with asthma that reported patient symptom perceptions and asthma control, and were either non-interventional studies or interventional studies where the intervention was not an investigational product.

The generated list of studies was exported to Endnote X8 and duplicate references were removed. Unique study references were then downloaded to Excel for sorting and screening. Studies were screened and selected for inclusion by one reviewer and a 10% sample was randomly selected for independent review by a second. Any conflicts between reviewers were identified and resolved by a third independent reviewer.

Data extraction and quality assessment of included studies

Data extraction was performed by one person and verified by a second, using a data extraction template developed in Microsoft Excel (Version 2017). The quality of each included study was assessed using the Joanna Briggs Institute (JBI) suite of critical appraisal tools.[19,20]

Summary measures and synthesis of results

Results of included studies were evaluated to confirm the presence of quantitative data reporting a statistical correlation (e.g., Pearson correlation coefficient or Spearman's rank-order correlation coefficient) or statistical association (e.g., odds ratios, relative risk ratios, prevalence ratios, chi-squared tests, or independent t-tests reporting 95% confidence intervals) between asthma control and the perception of asthma symptoms. Studies that only reported descriptive statistics of the relationship between the two outcomes were excluded.

Heterogeneity was expected in reported measures of both patients' symptom perception and asthma control. Consequently, our intention was to present the results as a qualitative synthesis, with side-by-side presentation of studies reporting similar outcome measures to determine recurring patterns in the data.

Results

Search results

A total of 3,946 unique publications were identified by database searches and following screening, 22 met the eligibility criteria and were included in the analysis (**Figure 1**).

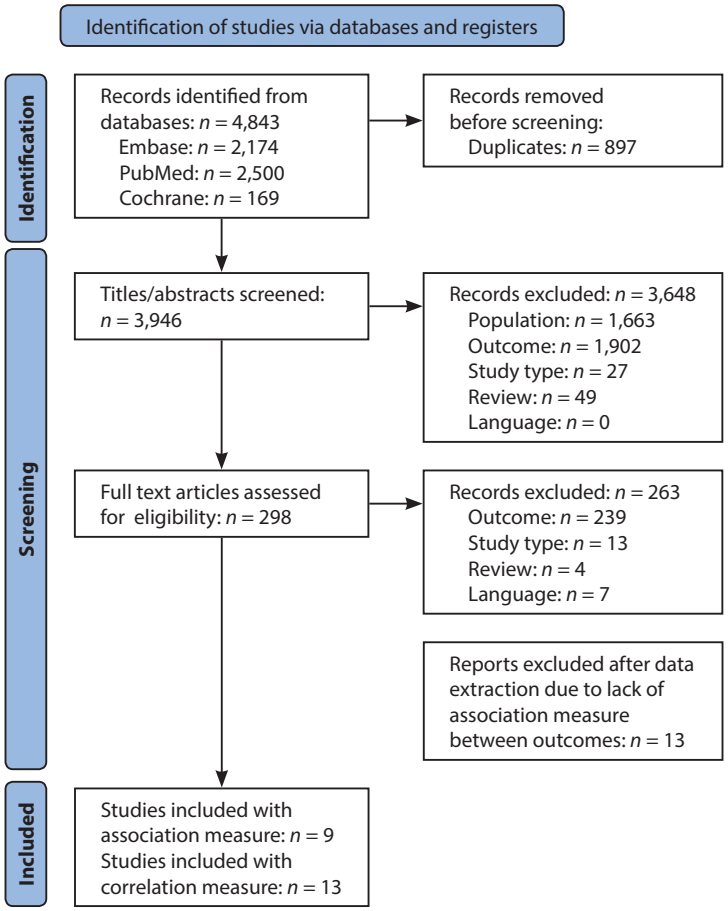

Figure 1. PRISMA flow diagram depicting the flow of information through the different phases of the review.

Study characteristics

A summary of study characteristics is presented in **Table 1**. Nine studies presented data on associations between patients' symptom perception and asthma control,[21-29] and 13 presented correlation analyses of the relationship.[10,30-41] Most studies were cross-sectional in design, and study sample sizes ranged from 59 to 8,000 participants. Six studies enrolled adolescents and children; four of these were conducted solely in pediatric populations. Twelve of the studies were conducted in Europe, the rest were conducted in the USA, Central/South America/Caribbean, the Middle East, Africa and Oceania.

In most studies, asthma control was assessed using either the Global Initiative for Asthma (GINA) assessment of asthma control questionnaire,[1] or the Asthma Control Test (ACT),[42] whereas, greater heterogeneity was observed in the reporting of patients' perception of symptoms. Across the 22 studies, nine different approaches to measuring symptom perception were identified. Differences were also noted within some of these approaches. Among the five studies using a visual analogue scale (VAS), there were differences in how the scale was utilized. Janssens et al. used the VAS to assess the intensity and unpleasantness of symptoms,[36] while Tosca et al. used the VAS to measure breathlessness.[40,41] Other studies measured general perception of asthma symptoms using the VAS. Six studies measured patients' symptom perception with study-specific questions. These questions were variable; for example, Price et al.,[10] asked patients to evaluate their day with symptoms, normal activities affected by symptoms and night-time awakening. Beharry et al.,[31] evaluated patients' perceptions of chest pain, chest tightness, cough, nocturnal awakening in the last week, daytime symptoms in the last week, symptoms preventing routine work and disease control.

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Table 1. Characteristics of studies included in the rapid literature review.

Study[Reference]	Study Design	Region	N	Asthma Severity	Mean Age (SD) Years	Population	Subgroups	Current Asthma Medication
Studies measuring a statistical association between asthma symptoms and asthma control								
Al-Busaidi and Soriano, 2011[21]	Cross-Sectional	Middle East	201	NR	Range, % 5–15: 21% 16-29: 33% 30-49: 35% ≥ 50: 10%	Adults, adolescents and children	Adults: 16 and older Children: < 16	Reliever inhaler: 92%ICS: 5%
Bereznicki et al., 2017[22]	Cross-Sectional	Oceania	1960	NR	38.6 (16.6)	Adults	Overestimation of control, Age, Level of education	NR
Bosnic-Antcevich et al., 2018[23]	Cross-Sectional	Oceania	200	NR	47.7 (15.8)	Adults	NR	FDC ICS + LABA: 100%
Forno et al., 2018[24]	Longitudinal‡	North America (United States)	59	NR	11.4 (3.1)	Adolescents and children	NR	NR
Janssens et al., 2012[25]	Cross-Sectional	Europe	94	Intermittent: 10.64% Mild: 30.85% Moderate: 53.19% Severe: 4.26%	37.87 (18.56)	Adults	Young adults, students (17-35) Adults and seniors (18-79)	NR
Kritikos et al., 2019[26]	Cross-Sectional	Europe	4274	NR	Group A: 50.0 (14.4) Group B: 51.4 (14.2)	Adults	Group A: GINA-defined controlled asthma who accurately self-assessed being well-controlled Group B: GINA-defined controlled asthma who inaccurately self-assessed being well-controlled	FDC ICS + LABA: 100%
Ozoh et al., 2019[27]	Cross-Sectional	Africa	405	NR	32.9 (18.1)	Adults, adolescents and children	Children Adults (> 16 years) Treatment by asthma control	ICS + LABA: 11.6% Oral steroids: 2.7% Inhaled salbutamol: 24.4% Oral salbutamol: 14.1% Oral aminophylline: 11.1% Oral montelukast: 6.4% Others: 1.2%
Silva et al., 2020[28]	Cross-Sectional	NR	149	Moderate-to-severe	NR	NR	NR	NR
Varsano et al., 2020[29]	Longitudinal*	Middle East	69	Severe-controlled	56 (12)	Adults	ACT score < 20 (uncontrolled) or ≥ 20 (well controlled)	ICS + LABA: 97% No controller medication: 1.4% Omalizumab:1.4%

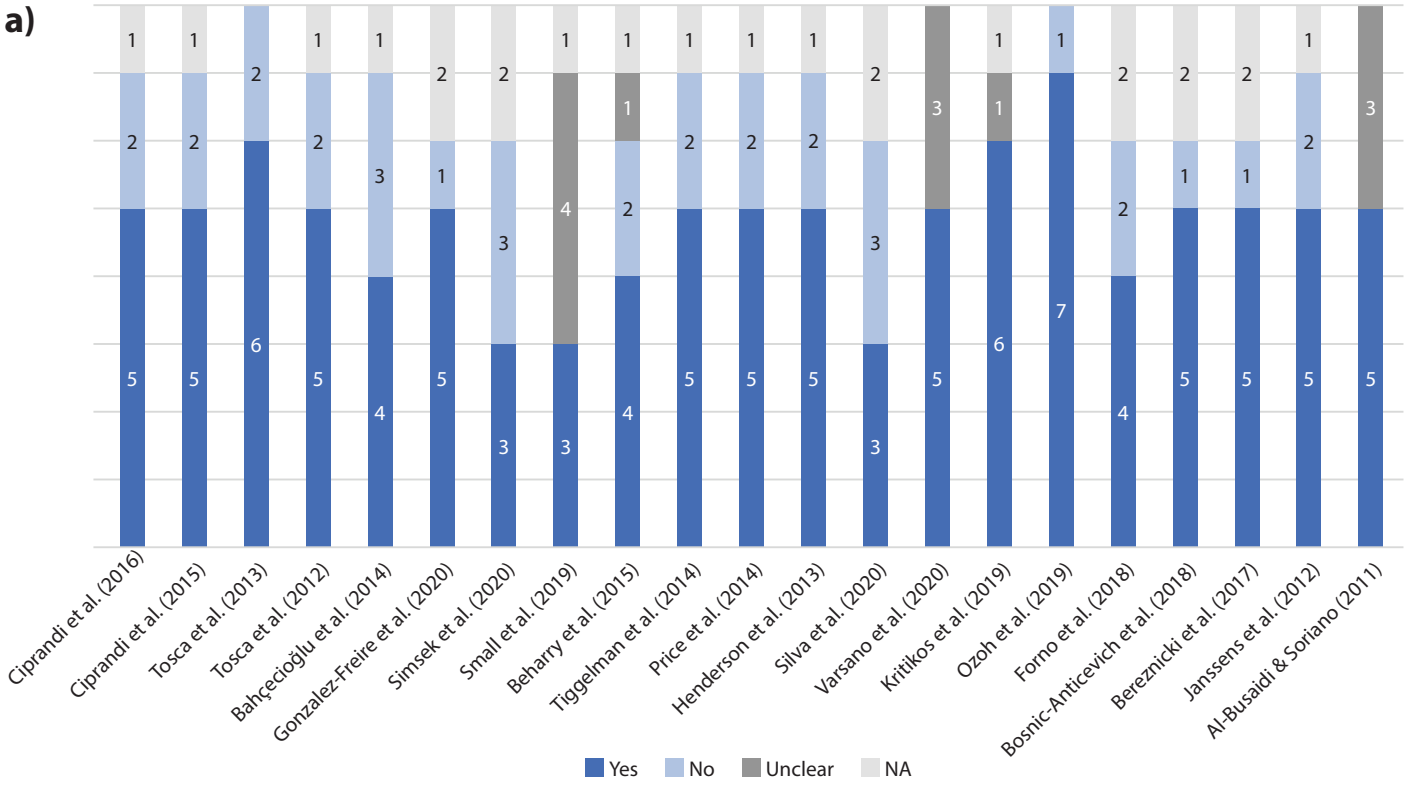
Table 1. (Continued)

Study[Reference]	Study Design	Region	N	Asthma Severity	Mean Age (SD) Years	Population	Subgroups	Current Asthma Medication
Studies measuring a statistical correlation between asthma symptoms and asthma control								
Bahçecioglu et al., 2014[30]	Cross-Sectional	Europe	200	NR	Range, % 20-30: 16.5% 31-40: 30.5% 41-50: 18.5% 51-60: 22.0% 61-70: 12.5%	Adults	NR	NR
Beharry et al., 2015[31]	Cross-Sectional	Central/South America and Caribbean	329	NR	54.36 (14.87)	Adults	None	Reliever inhaler: 67.78%
Ciprandi et al., 2016*[32]	Cross-Sectional	Europe	388	NR	39.7 (16.2)	Adults	VAS ≥ 6, VAS < 6	NR
Ciprandi et al., 2015*[33]	Cross-Sectional	Europe	370	NR	39.7 (16.1)	Adults	None	NR
González-Freire et al., 2020[34]	Cross-Sectional	Europe	373	Intermittent: 51.4% Mild: 7.8% Moderate: 25% Severe: 15.7%	36.88 (14.82)	Adults	NR	No daily controller: 32.2% Low-dose ICS or LTRA: 8.6% Low-to-med dose ICS + LABA or med dose ICS + theophylline/LTRA or high-dose ICS: 46.9% High-dose ICS + LABA ± theophylline, LTRA, OCS, or anti-IgE: 12.1%
Henderson et al., 2013[35]	Cross-Sectional	Oceania	318 doctors 319 patients	NR	NR	Adults	NR	SABA (± others): 54.8% SABA only: 13.2% ICS without LABA: 5.5% ICS + LABA: 49.8% LAMA: 5.2% OCS: 4.3%

Table 1. (Continued)

Study[Reference]	Study Design	Region	N	Asthma Severity	Mean Age (SD) Years	Population	Subgroups	Current Asthma Medication
Studies measuring a statistical correlation between asthma symptoms and asthma control (Continued)								
Janssens et al., 2012[36]	Longitudinal	Europe	60 30 (follow-up)	NR	36.38 (16.41)	NR	Female Male	NR
Price et al., 2014[10]	Cross-Sectional	Europe	8,000 4,689 report baseline treatments	NR	34.7	Adults	NR	None: 7.7% Reliever inhaler only: 30.3% Single-drug preventer inhaler (± reliever): 41.0% Combination preventer inhaler (± reliever): 16.1% Combination preventer inhaler plus oral pill (± reliever): 5%
Simsek et al., 2020[37]	Cross-Sectional	Europe	60	NR	NR	NR	NR	NR
Small et al., 2019[38]	Cross-Sectional	United States	1288	NR	42.7	NR	NR	NR
Tiggelman et al., 2014[39]	Cross-Sectional and longitudinal*	Europe	261	NR	11.9 (1.0)	Adolescents	NR	NR
Tosca et al., 2013†[40]	Cross-Sectional	Europe	150	NR	11.05 (2.12)	Adolescents and children	Case Control: Patients with bronchial obstruction (n = 50) Patients without bronchial obstruction (n = 100)	NR
Tosca et al., 2012†[41]	Cross-Sectional	Europe	703 138 for sub-analysis	Intermittent: 72.54% Mild: 20.12% Moderate: 7.02% Severe: 0.31%	10.29 (8.33-12.58) [median age, IQR]	Adolescents and children	For sub-analysis: FEV_1 < 80% FEV_1 ≥ 80%	Low-dose ICS: 67.87% Med-High dose ICS, LABA use, and OCS all 0% based on exclusions

*Comparison of the demographic and clinical characteristics of the populations in Ciprandi et al., 2016[32] and Ciprandi et al., 2015[33] suggested that the studies shared the same population with the addition of 18 participants added to the 2016 study. †Comparison of the demographics and details in the texts suggested that the patient population in Tosca et al., 2013[40] was the same as the case-control population in Tosca et al., 2012[41] with the addition of 12 participants added to the 2013 study.[41] ‡Though the study design was longitudinal, data comparing asthma control to the perception of asthma symptoms were cross-sectional.
ACT: Asthma Control Test; FDC: fixed dose controller; ICS: inhaled corticosteroid; IQR: interquartile range; LABA = long-acting beta-agonist; LAMA: long-acting muscarinic antagonist; OCS: oral corticosteroid; NR: not reported; SABA: short-acting beta-agonist; SD: standard deviation; VAS: visual analog scale



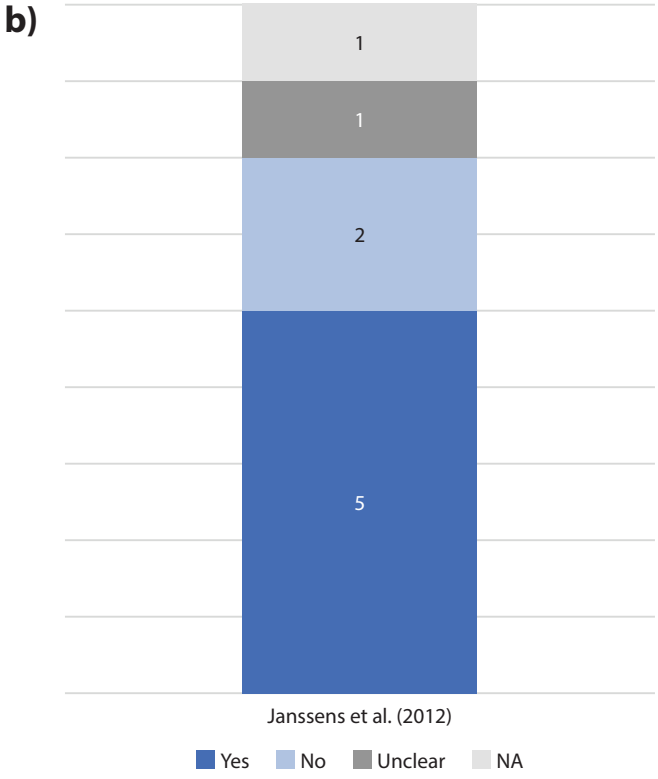


Figure 2. Fulfillment of appraisal checklist criteria by included studies for a) Studies reporting cross-sectional results and b) Study reporting longitudinal results.

Quality of studies

The quality of cross-sectional studies was evaluated according to eight criteria; only three studies fulfilled six or more of these criteria (**Figure 2a**). Two of the cross-sectional studies identified confounding factors,[26,27] one of which reported strategies to adjust for these factors.[26] In three studies that fulfilled ≤ 3 of the eight criteria, all were reported in abstract form only.[28,37,38] The quality of the longitudinal study was appraised against nine criteria; five of these were fulfilled (**Figure 2b**).[36]

As all of the studies used established methods for measuring asthma control - albeit one method was non-validated (the GINA questionnaire) and one was validated (ACT questionnaire) - this would have contributed to a level of consistency between study centers in international studies.

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Table 2. Studies outcomes: Association between perception of symptoms and asthma control.

Study[Reference]	Sample Size, N	Symptom Perception assessment	Asthma control assessment	Outcome	Association analysis method	*p*-value
Al-Busaidi and Soriano, 2011[21]	201	Study-specific questionnaire	ACT	• Disparities between adult patients' perception of their asthma control and ACT-measured control. 57% perceived their asthma as well-controlled vs. 43% measured as controlled with ACT score.	Two-sided test	< 0.05
Bereznicki et al. 2017[22]	1960	B-IPQ	ACT	• Overestimation of asthma control was apparent in 45.9% of respondents. Patients whose perception of asthma was better than their asthma control level were also more likely to experience more symptoms	Independent sample t-test	< 0.0001
Bosnic-Antcevich et al. 2018[23]	200	Study-specific questionnaire	GINA-defined	• 66.5% of patients perceived their asthma to be well controlled when only 11.5% were controlled • 49.0% of uncontrolled patients perceived asthma control despite normal activities being affected by symptoms	Chi-squared test	< 0.001
Forno et al. 2018[24]	59	Patient-perceived quantitative impact of FEV_1	Clinic FEV_1	• 56% of patients providing an accurate estimate, 18% under-estimating, and 26% over-estimating their lung function. • Patients who overestimated their FEV_1 had a lower mean FEV_1 measures than those who accurately estimated their FEV_1; (89.2% vs. 95.2%)	Chi-squared test	0.037
Janssens et al. 2012[25]	94	ASC	ACT	• Patients with poorly controlled asthma had a lower perception of asthma control compared to those with well-controlled asthma	Chi-squared test	< 0.01
Kritikos et al. 2019[26]	4274	Study-specific questionnaire	GINA-defined	• 28.9% of patients accurately perceived their asthma as controlled; 71.1% inaccurately reported controlled asthma • 67.4% of patients correctly perceived their asthma as uncontrolled	Chi-squared test	0.010
Ozoh et al. 2019[27]	405	ACT – symptom question	ACT	• In patients with uncontrolled asthma, 12.6% perceived their asthma as poorly or not at all controlled; 87.4% inaccurately reported their asthma as somewhat, well, or completely controlled • No patients who perceived their asthma as poorly controlled or uncontrolled met GINA criteria for well-controlled asthma	Chi-squared test	< 0.001
Silva et al. 2020[28]	149	IPQ	ACQ	• Patients with worse perception of illness reported worse clinical control compared to those with better illness perception	NR	0.001
Varsano et al. 2020[29]	69	Study-specific questionnaire	ACT	• 20% of patients with uncontrolled asthma (ACT score < 20) perceived themselves as having good asthma control in last 3 months • Patients with uncontrolled asthma (ACT score < 20) had a significantly poorer perception of asthma control compared to patients with well-controlled asthma (ACT score ≥ 20)	Independent sample t-test	< 0.001

ACQ: Asthma Control Questionnaire, ACT: Asthma Control Test, ASC: Asthma Symptom Control, B-IPQ: Brief Illness Perception Questionnaire, BSQ: Body Sensations Questionnaire, FEV_1: forced expiratory volume, GINA: Global Initiative for Asthma, IPQ: Illness Perception Questionnaire, NR: not reported

Study outcomes

Association between perception of symptoms and asthma control

Nine studies measured the association between patients' perception of symptoms and asthma control (**Table 2**). Of these, six studies reported the association between asthma control (GINA criteria or ACT score) and patient perception assessed by the ACT symptoms question or study-specific questions;[21,23,25-27,29] two studies compared asthma control (using the Asthma Control Questionnaire [ACQ] or ACT) to the illness perception questionnaire (IPQ);[22,28] and one compared an objective measure of pulmonary function to patient estimates of pulmonary function.[24] Despite a range of measures being used, eight of the nine studies showed a discordance between patients perceived symptoms and level of asthma control or lung function, and among these studies, patients more frequently overestimated their asthma control than they underestimated their asthma control.[21-27,29] Two studies showed that some patients overestimated their asthma control even when reporting higher levels of symptoms.[22,25]

One study showed concordance between symptoms perception and asthma control, Silva et al reported that patients who had a worse perception of illness had a higher ACQ score than those with better illness perception (2.4 ± 1 vs. 1.6 ± 1, respectively; P = 0.001), indicating that patients who had a worse perception of illness reported worse clinical control.[28]

Correlation between perception of symptoms and asthma control

Thirteen studies reported correlations between patients' perception of symptoms and asthma control (**Table 3**; **Figure 3**). The magnitude of the coefficient determined the strength of the correlation between worsening (or increased) symptoms and worse asthma control, irrespective of the negative or positive direction, and numerically ranged from 0.12 to 0.74 across 10 studies.[10,30,32,33,35-37,39-41] Although all studies reported a statistically significant correlation between perception of symptoms and asthma control, most studies (n = 8), using a conventional approach to interpreting a correlation coefficient,[43] showed only a weak or moderate correlation between these measures,[30,32,33,36,37,39-41] (**Table 3**).

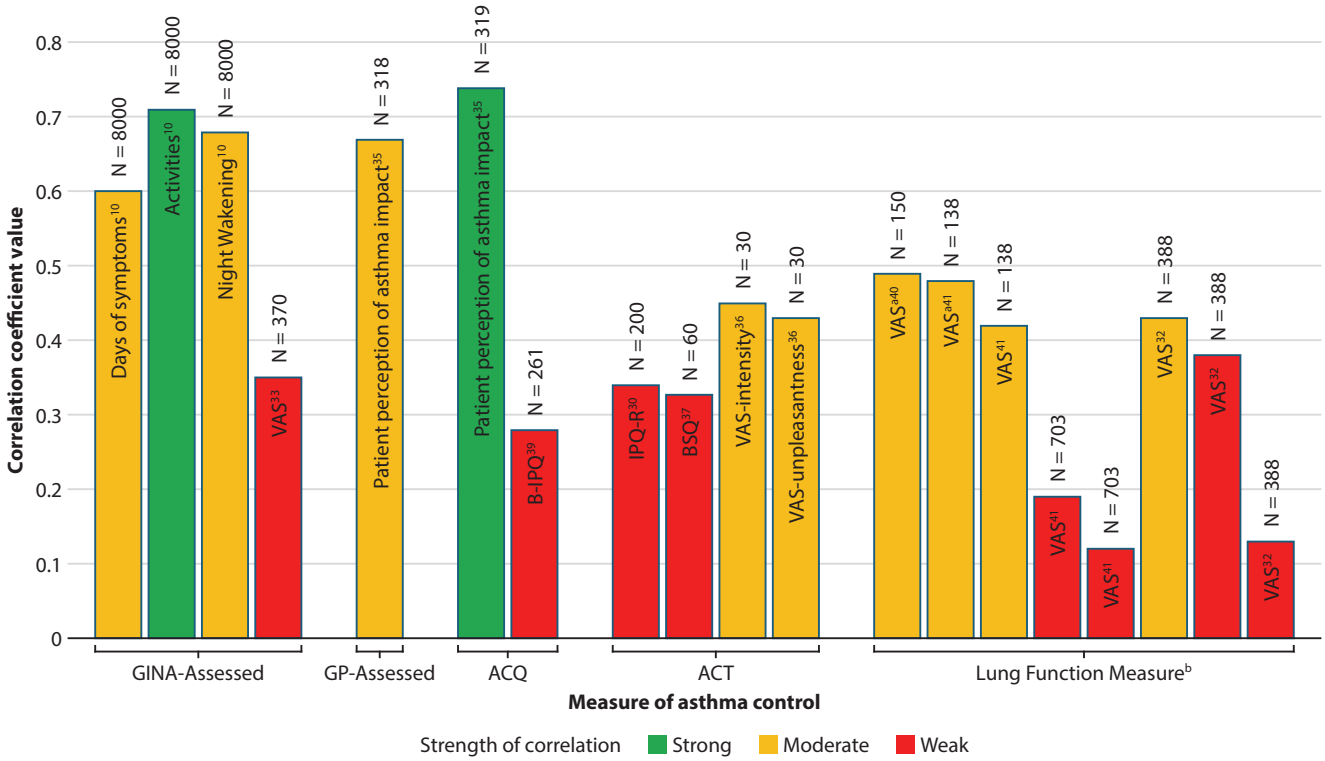

Figure 3. Correlation between asthma control and perception of symptoms

[a]Correlation coefficient for the case-control sub-analysis population (see **Table 3**). [b]Lung function measures included FEV_1, FEF, FVC and FEV_1/FVC. Method of assessing symptom perception shown inside each bar; VAS refers to perception of symptoms/breathlessness unless stated. Study reference shown as superscript number inside bar. Correlation values of 0.00-0.09 denote a negligible correlation, values of 0.10-0.39 denote a weak correlation (shown in red), values of 0.4 and 0.69 denote a moderate correlation (shown in orange), values of 0.70 to 0.89 denote a strong correlation (shown in green) and values of 0.90-1.00 denote a very strong correlation, based on a conventional approach to interpreting values.[43]

ACQ: Asthma Control Questionnaire; ACT: Asthma Control test; B-IPQ: Brief Illness Perception Questionnaire; BSQ: Body Sensations Questionnaire; FEF: Forced expiratory flow; FEV_1: Forced expiratory volume in 1 sec; FVC: Forced vital capacity; GINA: Global Initiative for Asthma; GP: General practitioner; IPQ-R: Illness Perception Questionnaire – Revised; Pt: Patient; VAS: Visual analogue scale

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Table 3. Studies outcomes: Correlation between perception of symptoms and asthma control.

Study[Reference]	Observation period	Sample size	Symptom perception	Asthma control	Correlation analysis method	Correlation coefficient (*r*)	Strength of correlation[e]	*p*-value
Bahçecioglu & Akyl 2014[30]	2012–13	200	IPQ-R[a] (symptom)	ACT	Pearson	–0.34	Weak	0.001
Beharry et al. 2015[31]	2013	329	Chest pain	Caribbean guidelines (originally developed in collaboration with GINA)[38]	Spearman	NR	N/a	< 0.008
			Tightness					< 0.004
			Cough					< 0.02
Ciprandi et al. 2016[32]	NR	388	VAS (perception of asthma symptoms)	FEV_1	Spearman	0.43	Moderate	0.001
				FVC		0.38	Weak	< 0.001
				FEV_1/FVC		0.13	Weak	0.01
Ciprandi et al. 2015[33]	NR	370	VAS (perception of asthma symptoms)	ACT	Spearman	ACT vs. VAS: 0.35	Weak	< 0.001
				GINA				
González-Freire et al. 2020[34]	NR	373	SGRQ (symptoms sub score)	ACT	Spearman	Regression co-efficient: 16.81 (95% CI: 12.57–21.05)	NR	< 0.001
				GINA				
Henderson et al. 2013[35]	2011–12	318	Patient perception of asthma impact	GP perception	Pearson	0.67	Moderate	NR
		319	Patient perception of asthma impact	ACQ		0.74	Strong	
Janssens et al. 2012[36]	NR	60	VAS, intensity[a]	ACT	Pearson	–0.45	Moderate	< 0.05
		30 (follow-up)	VAS, unpleasantness[a]			–0.43	Moderate	< 0.05

Table 3. (Continued)

Study[Reference]	Observation period	Sample size	Symptom perception	Asthma control	Correlation analysis method	Correlation coefficient (*r*)	Strength of correlation[e]	*p*-value
Price et al. 2014[10]	2012	8,000	Number of days with symptoms	GINA	Pearson	0.60	Moderate	0.001
			Normal activities affected			0.71	Strong	
			Night-time awakening			0.68	Moderate	
Simsek et al. 2020 (Abstract)[37]	NR	60	BSQ[a]	ACT	Pearson	–0.327	Weak	0.011
Small et al. 2019 (Abstract)[38]	2016–18	1,288	Study-specific	GINA	Spearman	NR	N/a	NR
Tiggelman et al. 2014[39]	2011–13	261	B-IPQ[a] (symptom)	ACQ	Pearson	–0.28	Weak	–0.001
Tosca et al. 2013[40]	NR	150	VAS (perception of breathlessness)	FEV_1	Spearman	0.49	Moderate	0.0001
Tosca et al. 2012[41]	2009–11	703 (case-control sub-analysis population: 138)	VAS (perception of breathlessness)	FEV_1	Spearman	0.19 (0.48)[d]	Weak (Moderate)[d]	< 0.0001 (< 0.0001)[d]
				FEF		0.12 (0.42)[d]	Weak (Moderate)[d]	0.0011 (< 0.0001)[d]

[a]These studies report negative correlation values because they used measures of perception where a higher score represents an increase of asthma symptoms. [b]This publication appears to report the same population as Ciprandi et al. 2015,[33] with an additional 18 patients. [c]This publication appears to report results from the case-control sub-analysis population of the Tosca et al. 2012 study,[41] plus 12 other participants. [d]Data in parentheses are for the case-control sub-analysis population (these 138 patients were included within the overall population of 703). [e]correlation values of 0.00-0.09 denote a negligible correlation, values of 0.10-0.39 denote a weak correlation, values of 0.4 and 0.69 denote a moderate correlation, values of 0.70 to 0.89 denote a strong correlation and values of 0.90-1.00 denote a very strong correlation, based on a conventional approach to interpreting values.[43]

ACQ: Asthma Control Questionnaire, ACT: Asthma Control Test, ASC: Asthma Symptom Control, B-IPQ: Brief Illness Perception Questionnaire, BSQ: Body Sensations Questionnaire, FEF: forced expiratory flow, FEV_1: forced expiratory volume, FVC: forced vital capacity, GINA: Global Initiative for Asthma, IPQ: Illness Perception Questionnaire, IPQ-R: Illness Perception Questionnaire – Revised, NR: not reported, SGRQ: St. George Respiratory Questionnaire, VAS: visual analogue scale.

One study reported demonstrated that poor asthma control was closely related to the symptoms domain of SGRQ (non-standardized regression coefficient (95% CI): 16.81 (12.57 to 21.05), $p < 0.001$).[34]

Discussion

This rapid review aimed to evaluate and quantify the relationship between patients' perception of symptoms and asthma control. Across the 22 studies included in the review, a broad and heterogenous collection of outcome measures were used and made quantitative analysis challenging. Despite this, the overall results clearly demonstrated that studies measuring association outcomes showed a discordance between patients' perceptions of their symptoms and asthma control, particularly noted in patients with poorly controlled asthma, suggesting that patients have a tendency to underperceive their symptoms and/or overestimate their level of asthma control. In studies that measured the statistical correlation between patient perceptions and asthma control, although there was clear evidence of a statistically significant correlation between these two measures, the strength of correlation coefficients varied widely and most studies demonstrated only a weak or moderate correlation between these parameters. This highlights an uncertainty in the consistency of the correlation data and the ability to identify patients who are most likely to misperceive their asthma control.

In clinical practice, the assessment of asthma control (including symptom control and future risk of exacerbations) underpins the long-term goals of asthma management, and patient self-monitoring of symptoms is a key component of asthma self-management.[1] It has been estimated that between 50% and 75% of patients with asthma have mild asthma,[44] and some argue that leaving the decision to patients of when to take their ICS-containing medication may lead to undertreatment with ICS.[45] Patients could be under-perceivers, normal perceivers or over-perceivers of their asthma symptoms - in a study of 113 patients with stable asthma, 15% over-estimated their symptoms and 26% under-estimated their symptoms, this latter group being those at risk of undertreatment with ICS.[46] Healthcare professionals may also under-estimate patients' symptoms, either directly or indirectly if symptoms are under-reported by the patients themselves,[47] which may lead to an inappropriate optimization of treatment through a step-up approach to achieve good asthma control. In a questionnaire-based study of physicians (n = 183) and patients with asthma (not treated with anti-inflammatory medications, n = 856), 66% of patients and 43% of physicians rated the control of asthma symptoms as adequate to good when all were deemed to have uncontrolled asthma according to the asthma guidelines current at the time.[48] In the APPaRENT surveys, both patients and physicians prioritized asthma symptom control over exacerbation reduction and most physicians favoured a regular ICS plus as-needed SABA dosing treatment strategy.[49,50] Regular ICS-based maintenance treatment, as well as increasing levels of asthma control, results in improvements in airway responsiveness, markers of inflammation, lung function and health-related quality of life, as well as in reduced i.e. more appropriate SABA reliever use.[51-55] Previous studies have reported discrepancies between asthma symptoms and level of airway obstruction and markers of inflammation, highlighting the risk of ongoing airway obstruction or underlying inflammation, even in patients with mild asthma.[56,57] In accordance with this, data from a pharmacokinetic/pharmacodynamic modelling study that demonstrated, at ICS doses recommended for mild asthma, only a scenario of regular dosing with high adherence provided sustained bronchoprotective efficacy, whereas for scenarios that reflected poor adherence (50%) or as-needed ICS dosing regimens, reduced levels of bronchoprotection were observed.[58]

Our review highlights the importance of identifying patients who may be at risk of misperceiving their asthma symptoms and for understanding any associated reasons. This may be due to patients accepting some level of symptoms as normal, and regarding their asthma as controlled when in fact they are experiencing frequent symptoms and regularly use their reliever medication.[7,50] Following a comprehensive survey of patients in the UK (n = 1083), Fletcher et al. suggested that patients' low expectations of achieving asthma control and discrepancies between perceived control and actual symptoms could reflect misunderstandings about the term asthma control, with patients focusing on their response to symptoms rather than considering their future risk of asthma attacks.[7] Similar findings were shown by Bidad et al. who conducted qualitative interviews with 42 patients from primary and secondary care settings, and reported that most patients adopted a symptom response model rather than a symptom prevention model of asthma control.[59] For many participants, their own tolerance level of symptoms was higher than the ACT criteria, suggesting they tolerated their symptoms as part of living with asthma. Ongoing education is critical to enable patients and/or carers to recognize the key characteristics of poorly controlled asthma, specifically targeted at patients who misperceive their asthma symptoms. Future research could help identify patient groups most at risk of symptoms misperception. Healthcare professionals (HCPs) should identify any barriers to patients understanding their asthma and treatment, address concerns and help patients have clear expectations about asthma control and how to achieve this through effective self-management.[7,59] The use of validated asthma control assessment tools could facilitate the assessment of asthma control, and would benefit from HCPs and patients working together to strive for a consistent approach when assessing control in the clinic and at home.[11,14] The ACT and ACQ are two currently available, validated tools for assessing asthma control;[60] however, both include a question about inhaled SABA use and therefore are not suitable for assessing patients on GINA track 1 where ICS-formoterol is the recommended reliever. The four GINA questions to assess asthma control also do not include the use of as-needed ICS formoterol.[1] This raises the question if new tools or biomarkers for identifying early or predicting patients with uncontrolled asthma are required and would be a worthy topic of future research.

Some potential limitations should be considered when interpreting the findings of this literature review. As this was a rapid literature review, not all available published evidence may have been included (e.g., statistical correlations in post-hoc analyses or exploratory outcomes). Studies included in the rapid review were limited to those studies that had perception relative to control as a primary or secondary objective; therefore, some studies reporting the outcomes of interest incidentally may have been excluded. Nevertheless, articles excluded from our analysis as they did not include a statistical measure provide qualitative corroboration of our findings by also reporting a discordance between patients' perceptions of their symptoms and asthma control.[8,61-63] The review cut-off date was two years prior to this publication and therefore does not consider more recent studies on this topic, although recent studies also report a discordance between asthma control and patient symptoms perceptions.[11,14] Furthermore, we included one study in abstract form,[28] that is now available as a full publication,[64] but this did not change the outcome of our conclusions. Another limitation is that we did not consider the degree to which patient perceptions of symptoms and disease control align with physician perceptions; lack of correlation in this respect may contribute to the risk of poor treatment decisions.

The heterogeneity of measures used to assess symptom perception across included studies should also be highlighted. The most frequently used measures were study-specific questionnaires (n = 6) and VAS (n = 5). VAS has been reported to be a valid method for predicting concurrent and future asthma control, including in cross-sectional studies.[33,65] On the other hand, measuring symptom perception using the ACT symptom question is likely to result in multiplicity, since it also contributes to the asthma control measure; only one study explicitly reported symptom perception being derived from ACT. The other least frequent measures of symptom perception were IPQ (n = 3), BSQ (n = 1) and TAS (n = 1), all of which are used for chronic diseases in general rather than being asthma-specific. A further limitation is that all but one of the studies we identified presented the outcome measures of interest cross-sectionally, whereas longitudinal studies might be expected to provide evidence on future asthma control.

Conclusions

This rapid review showed that many patients with asthma tend to underestimate their symptoms and overestimate their level of asthma control. Although more frequent or worse symptoms were shown to be correlated with worsening asthma control, there was wide variation in reported correlation strengths with most studies reporting a weak or moderate correlation. Research to further understand the reasons for patient symptom misperceptions are warranted and additional education to improve the understanding and use of currently available validated assessment tools would be beneficial.

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Conflict of interest

The authors declare the following conflicts of interest during the last three years in relation to this article: SN and SM are employees of GSK. CB, JM and PM are employees of MDM Inc, which was contracted by GSK to conduct the rapid review. AY, HJ and HN have no competing interests to declare.

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Author contributions

- HN, AY, HAJ, JM, CB, PM, SN contributed to the data analysis or data interpretation.
- All authors contributed to the study conception, study design, study execution, acquisition of data, writing, editing and review of the manuscript.
- All authors approved the final version of the manuscript.

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