Asthma management and control in children, adolescents, and adults in 25 countries: a Global Asthma Network Phase I cross-sectional study

Luis García-Marcos, Chen-Yuan Chiang*, M Innes Asher, Guy B Marks, Asma El Sony, Refiloe Masekela, Karen Bissell, Eamon Ellwood, Philippa Ellwood, Neil Pearce, David P Strachan, Kevin Mortimer†, Eva Morales†, and the Global Asthma Network Phase I Study Group‡*

Summary

Background Asthma is one of the most common non-communicable diseases globally. This study aimed to assess asthma medicine use, management plan availability, and disease control in childhood, adolescence, and adulthood across different country settings.

Methods We used data from the Global Asthma Network Phase I cross-sectional epidemiological study (2015–20). A validated, written questionnaire was distributed via schools to three age groups (children, 6–7 years; adolescents, 13–14 years; and adults, ≥19 years). Eligible adults were the parents or guardians of children and adolescents included in the surveys. In individuals with asthma diagnosed by a doctor, we collated responses on past-year asthma medicines use (type of inhaled or oral medicine, and frequency of use). Questions on asthma symptoms and health visits were used to define past-year symptom severity and extent of asthma control. Income categories for countries based on gross national income per capita followed the 2020 World Bank classification. Proportions (and 95% CI clustered by centre) were used to describe results. Generalised structural equation multilevel models were used to assess factors associated with receiving medicines and having poorly controlled asthma in each age group.

Findings Overall, 453 473 individuals from 63 centres in 25 countries were included, comprising 101 777 children (6445 [6·3%] with asthma diagnosed by a doctor), 157 784 adolescents (12 532 [7·9%]), and 193 912 adults (6677 [3·4%]). Use of asthma medicines varied by symptom severity and country income category. The most used medicines in the previous year were inhaled short-acting β2 agonists (SABA; range across age groups, 29·3–85·3% participants) and inhaled corticosteroids (12·6–51·9%). The proportion of individuals with severe asthma symptoms not taking inhaled corticosteroids (inhaled corticosteroids alone or with long-acting β2 agonists) was high in all age groups (934 [44·8%] of 2085 children, 2011 [60·1%] of 3345 adolescents, and 1142 [55·5%] of 2058 adults), and was significantly higher in middle-to-low-income countries. Oral SABA and theophylline were used across age groups and country income categories, contrary to current guidelines. Asthma management plans were used by 4049 (62·8%) children, 6694 (53·4%) adolescents, and 3168 (47·4%) adults; and 2840 (44·1%) children, 6942 (55·4%) adolescents, and 4081 (61·1%) adults had well controlled asthma. Independently of country income and asthma severity, having an asthma management plan was significantly associated with the use of any type of inhaled medicine (adjusted odds ratio [OR] 2·75 [95% CI 2·40–3·15] for children; 2·45 [2·25–2·67] for adolescents; and 2·75 [2·38–3·16] for adults) or any type of oral medicine (1·86 [1·63–2·12] for children; 1·53 [1·40–1·68] for adolescents; and 1·78 [1·55–2·04] for adults). Poor asthma control was associated with low country income (lower-middle-income and low-income countries *vs* high-income countries, adjusted OR 2·33 [95% CI 1·32–4·14] for children; 3·46 [1·83–6·54] for adolescents; and 4·86 [2·55–9·26] for adults).

Interpretation Asthma management and control is frequently inadequate, particularly in low-resource settings. Strategies should be implemented to improve adherence to asthma treatment guidelines worldwide, with emphasis on access to affordable and quality-assured essential asthma medicines especially in low-income and middle-income countries.

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Introduction

Asthma is one of the most common non-communicable diseases across the life span, affecting more than 350 million children, adolescents, and adults globally.[1,2] The Global Asthma Network (GAN) Phase I cross-sectional study recently provided data on the burden of asthma in children, adolescents, and adults[3,4] and worldwide trends in the burden of asthma symptoms in

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For the Spanish translation of the abstract see Online for appendix 1

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*Joint first authors

†Joint senior authors

‡All members listed in appendix 2 (pp 22–24)

Paediatric Allergy and Pulmonology Units, Virgen de la Arrixaca University Children's Hospital, University of Murcia and IMIB Bio-medical Research Institute, Murcia, Spain (Prof L García-Marcos PhD); **ARADyAL Allergy Network, Murcia, Spain** (Prof L García-Marcos); **International Union Against Tuberculosis and Lung Disease, Paris, France** (Prof C-Y Chiang DrPhilos); **Division of Pulmonary Medicine, Department of Internal Medicine, Wan Fang Hospital, and Division of Pulmonary Medicine, Department of Internal Medicine, School of Medicine, College of Medicine, Taipei Medical University, Taipei, Taiwan** (Prof C-Y Chiang); **Department of Paediatrics: Child and Youth Health** (Prof M I Asher MBChB, E Ellwood DipTch, P Ellwood MPH) **and School of Population Health** (K Bissell DrPH), **Faculty of Medical and Health Sciences, University of Auckland, Auckland, New Zealand; Respiratory and Environmental Epidemiology, University of New South Wales, Sydney, NSW, Australia** (Prof G B Marks PhD); **Epidemiological Laboratory for Public Health, Research and Development, Khartoum, Sudan** (Prof A El Sony PhD); **Inkosi Albert Luthuli Central Hospital** (Prof R Masekela PhD) **and Department of Paediatrics and Child Health**

(Prof R Masekela, Prof K Mortimer PhD), **College of Health Sciences, School of Clinical Medicine, University of KwaZulu-Natal, Durban, South Africa; Department of Medical Statistics, London School of Hygiene & Tropical Medicine, London, UK** (Prof N Pearce PhD); **Population Health Research Institute, St George's, University of London, London, UK** (Prof D P Strachan MD); **Department of Clinical Sciences, Liverpool School of Tropical Medicine, Liverpool, UK** (Prof K Mortimer); **Respiratory Medicine, Liverpool University Hospitals NHS Foundation Trust, Liverpool, UK** (Prof K Mortimer); **Department of Medicine, University of Cambridge, Cambridge, UK** (Prof K Mortimer); **Department of Public Health Sciences, University of Murcia and IMIB Bio-medical Research Institute, Murcia, Spain** (E Morales PhD)

Correspondence to: Prof Luis García-Marcos, Paediatric Allergy and Pulmonology Units, Virgen de la Arrixaca University Children's Hospital, University of Murcia and IMIB Bio-medical Research Institute, 30120 Murcia, Spain
lgmarcos@um.es

See Online for appendix 2

Research in context

Evidence before this study

In a search of PubMed and Web of Science with the terms ("asthma" AND ["control" OR "treatment" OR "management" OR "asthma plan"] AND "income"), for articles in English and Spanish published from July 1, 2011, to July 1, 2021, we retrieved more than 1000 papers; however, none compared asthma treatments or management plans in different age groups or in countries with different gross national incomes. The Global Asthma Network (GAN) is the continuation of the International Study of Asthma and Allergies in Childhood collaboration, and in the past 2 years has published updated prevalence and time trend data for asthma including, for the first time, in adults. However, how asthma is managed worldwide, or to what extent the use of asthma medicines varies in relation to the affluence of countries, was not analysed. Similarly, the extent to which asthma management plans are used or how use of plans varies between more and less affluent countries was not studied. A global overview of asthma control in different age groups and its relation to per capita income was also not provided.

Added value of this study

This analysis of the GAN phase I survey reports data on asthma medicine use, asthma management plan availability, and disease control in childhood, adolescence, and adulthood across different country settings. This study is the first global report on the use of asthma medicines and the control of the disease in three age groups, which also investigates the effect of country affluence. Among a large population of individuals with asthma worldwide, the most used medicines were inhaled short-acting β2 agonists (SABA; range across age groups, 29·3–85·3% participants) and inhaled corticosteroids (12·6–51·9%). The proportion of individuals with severe asthma symptoms not taking inhaled corticosteroids was high in all age groups (44·8–60·1%), and was significantly higher in centres in low country income categories. Oral SABA and theophylline were used across age groups and country income categories, contrary to current guidelines. Management plans were used by 47·4–62·8% participants across the age groups. Asthma was well controlled in a higher proportion of adults (61·1%) than children (44·1%) and adolescents (55·4%). Poor asthma control was associated with low country income.

Implications of all the available evidence

Improved asthma control is an urgent need worldwide, particularly in children and in less affluent countries. Improving the availability and affordability of inhaled medicines (particularly those including corticosteroids) in less affluent countries should be a priority. Working towards this aim would help the transition away from oral SABA and theophylline and towards modern, safe, and effective treatments that target the underlying airway inflammation in asthma.

school-aged children,[5] identifying a high prevalence of asthma symptoms. However, information is scarce on the worldwide use of asthma medicines or asthma plans among children, adolescents, and adults, and the extent to which asthma symptoms are controlled.

Most people with asthma can achieve asthma control,[6] although the real-world situation is usually far from this ideal.[7] Inadequate asthma control can be a consequence of several factors, such as doctors not following guidelines or strategies,[8] poor adherence by patients to the recommended treatment regimen[9] (including inhaler technique[10]), poor access to health care, unavailability or unaffordability of essential asthma medicines,[11,12] or a combination of these factors. Many studies have addressed ways of improving adherence in the past two decades.[13,14] Both individual and community-based interventions to improve awareness, adherence, and availability of medicines usually yield good results, as measured by access to medicines, reduced emergency visits and hospitalisations, or improved quality of life.[15] Further, many national and international asthma guidelines or strategies are published and updated regularly.[16] However, despite having the means to control asthma for most people, its burden remains high both in terms of disability-adjusted life-years and deaths.[17]

GAN Phase I, continuing the surveillance work of the International Study of Asthma and Allergies in Childhood (ISAAC),[18] included specific questions on asthma management.[19] Although the GAN methods were not designed to assess adherence to asthma management guidelines, they offer a unique international perspective on the use of asthma medicines and the extent of asthma control. In this study, we did a sub-analysis of the GAN Phase I data to investigate how frequently asthma medicines were used relative to the severity of asthma symptoms, the availability of asthma management plans, and to what extent asthma remained uncontrolled, across different age groups worldwide.

Methods

Study design

The GAN methods built on those of ISAAC and have been published previously.[19] Briefly, GAN Phase I was a cross-sectional epidemiological study performed in centres and countries worldwide between 2015 and 2020. The study used written questionnaires distributed in schools, among three age groups: adolescents aged 13–14 years (self-completed questionnaire), children aged 6–7 years (parental completed questionnaires), and adults aged 19 years or older (parents or guardians of the children and adolescents included in the surveys). GAN centres (as defined by a geographical area; typically cities) performed the fieldwork in the schools of their area. A centre was required to include adolescents to be considered a GAN

centre; inclusion of children or adults in the survey was optional. A random sample of schools in each geographical area was selected to survey at least 1000 childen or adolescents. High participation rates were sought (response rate ≥80% for adolescents and ≥70% for children) and achieved[18] in most centres. Centres with a participation rate lower than 50% for any given age group were excluded from all GAN analyses, as the sample was considered as not minimally representative of the specific centre.

Before starting the study, all centres in GAN Phase I were required to attain approval from their local ethics committee. Consent (either active written consent or passive oral consent, depending on the age group and requirements from the ethics committees) was obtained from all participants.

Procedures

Variables used in the present study relating to asthma management and control came from the written questionnaires (or in some cases online questionnaires; 3·3% in children, 3·7% in adolescents, and 3·2% in adults) completed by adolescents in the school classroom, or by the parents of children at home. The original questionnaire was in English and translation and back-translation for other languages used followed the same methodology as ISAAC.[20]

We defined asthma diagnosed by a doctor on the basis of a positive answer to both of the questions: "Have you (has this child) ever had asthma?" and "Was your (this child's) asthma confirmed by a doctor?" Having an asthma management plan was defined as an affirmative answer to: "Do you (does this child) have a written plan which tells you (him/her) how to look after your (his/her) asthma?"

We distinguished the severity of asthma symptoms and the degree of asthma control in the past 12 months, in individuals with asthma diagnosed by a doctor. Severity of asthma symptoms was defined by three categories on the basis of answers to questions on symptoms. The categories were asymptomatic (no symptoms in the past year according to the question: "Have you [has this child] had wheezing or whistling in the chest in the past 12 months?"); mild current symptoms (less than four attacks of wheeze, less than one night per week with sleep disturbance from wheeze, or no wheezing episode affecting speech in the past 12 months); and severe current symptoms (four or more attacks of wheeze, one or more nights per week with sleep disturbance from wheeze, or at least one wheezing episode affecting speech in the past 12 months).

The GAN steering committee defined the degree of asthma control in the previous 12 months by three categories on the basis of answers to two questions on health visits. One of these questions concerned unscheduled visits to a doctor or to the emergency department due to asthma (none, one to three visits, four to 12 visits, or >12 visits); and the other question concerned hospital admissions due to asthma (none, one admission, two admissions, or more than two admissions). The three categories to define asthma control were: poor control of asthma (uncontrolled asthma), defined as unscheduled visits to the doctor at least four times, attending the emergency department at least four times, or being admitted to hospital at least once for asthma symptoms; partially controlled asthma, defined as unscheduled visits to the doctor less than four times or attending the emergency department less than four times for asthma symptoms, without admittance to hospital; and well controlled asthma, defined by not meeting the criteria for poorly controlled or partially controlled asthma.

We also determined the specific medicines used by respondents. For inhaled medicines, first there was a general question: "Have you (has this child) used any inhaled medicines, for example puffers (or local terminology), to help your (his/her) breathing problems at any time in the past 12 months? (When you [he/she] did not have a cold)". This question was followed by specific questions about the type of inhaled medication and the frequency of use (ie, drug regimen) in the past 12 months ("as needed", "in short courses", or "every day"). The type of inhaled medications asked about were inhaled short-acting β2 agonists (SABA), inhaled long-acting β2 agonists (LABA), inhaled corticosteroids, and combinations of inhaled corticosteroids and LABA. A pertinent list of local brands of each of those medicine categories, decided by the principal investigators for each centre, was included in each question. The same approach was used for oral medicines with a first general question: "Please indicate how often you (this child) used any tablets, capsules, liquids, or other medicines, for example pills (or local terminology) that you (he/she) swallowed to help your (his/her) breathing at any time during the past 12 months? (When you [he/she] did not have a cold)". Oral medicines were categorised into oral corticosteroids, leukotriene receptor antagonists (LTRAs), theophylline, and oral SABA.

We minimised classification bias by surveying recent symtoms (past year) and reporting asthma diagnosed by a doctor. Restricting responses on asthma diagnosis, symptoms, and management also minimised recall bias.

Income category for each country according to gross national income per capita followed the classification by The World Bank as of June, 2020. As the number of centres in low-income countries (LICs) was small, the categories of LIC and lower-middle-income countries (LMICs) were merged for analyses. The other two categories were upper-middle-income countries (UMICs) and high-income countries (HICs).

The data handling procedures have been described previously.[19] In summary, all centres submitted their datasets and a completed centre report (including sampling frame [schools, classes, and children],

For the **World Bank country income classifications** see https://datahelpdesk.worldbank.org/knowledgebase/articles/906519-world-bank-country-and-lending-groups

partipation rates of schools and children, map of the area surveyed, rate of school rejection to participate and reasons why [if any], type of data entry and checking, how the questionnaire was translated, and dates of data collection)[19] to the GAN Global Centre in Auckland, New Zealand, which performed an initial data check and an assessment of whether the centre had adhered to the GAN methods. Depending on the language used by the centre, the dataset was then sent to a GAN data centre in Murcia, Spain (when the primary language of the centre was Spanish or Portuguese) or London (UK; all other languages), which performed a standardised and coordinated data check. A uniform approach to data processing, checking, and analysis was used, with use of Stata (versions 13–15).

Outcomes and statistical analysis

Sample size was calculated for the prevalence study.[19] Proportions of individuals (and 95% CIs clustered by centre) were used to describe results for all countries or by country income group. The proportion of individuals with asymptomatic, mild, and severe asthma symptoms being treated with each inhaled or oral medication was calculated for each country income category. Generalised multilevel structural equation models with a multinomial link function were used to assess factors associated with receiving asthma medicines or having poorly controlled asthma. First, we calculated odds ratios (ORs) and 95% CIs for the association of inhaled or oral asthma medicine use (and the regimen) with mild and severe asthma symptoms, compared with asymptomatic asthma (reference category). This model was controlled for sex, age, country income category (HICs as the reference), and having an asthma management plan at the first level; for school at the second level; and for centre at the third level. Second, we assessed the association between medicine use and poor asthma control, for which the modelling was the same but included inhaled and oral medicines at the first level and an ordinal link (asthma control coded as 1, good [well controlled]; 2, partial [partially controlled]); and 3, poor [poorly controlled]). Multivariable analyses included individuals with all data on the variables used without imputation.

Role of the funding source

The funders of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report.

Results

Overall, 453 473 individuals (101 777 children, 157 784 adolescents, and 193 912 adults [mean age 38·4 years [SD 7·5]) from 63 centres in 25 countries were included in our analyses (appendix 2 pp 3–4). Of these, 6445 (6·3%) children, 12 532 (7·9%) adolescents, and 6677 (3·4%) adults (mean age 38·9 years [SD 8·3]) had asthma confirmed by a doctor. The population of children with asthma comprised 3582 boys and 2801 girls (62 with sex not specified); the adolescent population with asthma comprised 6408 boys and 5970 girls (154 not specified), and the adult population with asthma comprised 2675 men and 3936 women (66 not specified). The number of individuals overall and those with diagnosed asthma per age group stratified by country income

	High-income countries (n=2863)			Upper-middle-income countries (n=2699)			Lower-middle-income and low-income countries (n=883)		
	Asymptomatic (n=1446)	Mild symptoms (n=746)	Severe symptoms (n=671)	Asymptomatic (n=927)	Mild symptoms (n=641)	Severe symptoms (n=1131)	Asymptomatic (n=406)	Mild symptoms (n=194)	Severe symptoms (n=283)
Inhaled medicine*									
SABA (n=3628)	442 (30·6%)	513 (68·8%)	545 (81·2%)	315 (34·0%)	482 (75·2%)	965 (85·3%)	119 (29·3%)	90 (46·4%)	157 (55·5%)
LABA (n=200)	17 (1·2%)	30 (4·0%)	31 (4·6%)	10 (1·1%)	19 (3·0%)	32 (2·8%)	17 (4·2%)	17 (8·8%)	27 (9·5%)
Corticosteroids (n=2003)	283 (19·6%)	298 (40·0%)	348 (51·9%)	141 (15·2%)	244 (38·1%)	527 (46·6%)	51 (12·6%)	46 (23·7%)	65 (23·0%)
Corticosteroids and LABA† (n=1036)	122 (8·4%)	142 (19·0%)	186 (27·7%)	83 (9·0%)	136 (21·2%)	258 (22·8%)	30 (7·4%)	28 (14·4%)	51 (18·0%)
Any inhaled medicine (n=4088)	527 (36·4%)	550 (73·7%)	588 (87·6%)	384 (41·4%)	533 (83·2%)	1014 (89·7%)	158 (38·9%)	120 (61·9%)	214 (75·6%)
Oral medicine*									
LTRA (n=1243)	115 (8·0%)	134 (18·0%)	162 (24·1%)	128 (13·8%)	203 (31·7%)	369 (32·6%)	34 (8·4%)	33 (17·0%)	65 (23·0%)
Corticosteroids (n=1309)	95 (6·6%)	181 (24·3%)	259 (38·6%)	92 (9·9%)	133 (20·7%)	335 (29·6%)	75 (18·5%)	52 (26·8%)	87 (30·7%)
SABA (n=1573)	162 (11·2%)	188 (25·2%)	232 (34·6%)	151 (16·3%)	208 (32·4%)	468 (41·4%)	38 (9·4%)	46 (23·7%)	80 (28·3%)
Theophylline (n=319)	28 (1·9%)	28 (3·8%)	32 (4·8%)	25 (2·7%)	26 (4·1%)	46 (4·1%)	42 (10·3%)	36 (18·6%)	56 (19·8%)
Any oral medicine (n=3014)	285 (19·7%)	331 (44·4%)	413 (61·5%)	296 (31·9%)	413 (64·4%)	820 (72·5%)	161 (39·7%)	107 (55·2%)	188 (66·4%)
Asthma management plan (n=4049)	756 (52·3%)	435 (58·3%)	473 (70·5%)	597 (64·4%)	447 (69·7%)	818 (72·3%)	214 (52·7%)	112 (57·7%)	197 (69·6%)

Data are n (%) where denominators are the total number in each symptom severity category per income group. Percentages with 95% CIs clustered by centre are provided in appendix 2 (p 5). SABA=short-acting β2 agonist. LABA=long-acting β2 agonist. LTRA=leukotriene receptor antagonist. *Drug therapy groups are not mutually exclusive and participants could be represented in more than one group. †Combined in the same inhaler; patients using LABA and corticosteroids in separate inhalers were included in the corresponding single-agent treatment groups.

Table 1: **Children receiving inhaled and oral asthma medicines according to symptom severity stratified by country income group**

	High-income countries (n=5304)			Upper-middle-income countries (n=5200)			Lower-middle-income and low-income countries (n=2028)		
	Asymptomatic (n=3105)	Mild symptoms (n=1066)	Severe symptoms (n=1133)	Asymptomatic (n=2782)	Mild Symptoms (n=930)	Severe symptoms (n=1488)	Asymptomatic (n=958)	Mild Symptoms (n=346)	Severe symptoms (n=724)
Inhaled medicine*									
SABA (n=5477)	1102 (35·5%)	711 (66·7%)	893 (78·8%)	611 (22·0%)	446 (48·0%)	919 (61·8%)	194 (20·3%)	134 (38·7%)	467 (64·5%)
LABA (n=1634)	290 (9·3%)	135 (12·7%)	244 (21·5%)	223 (8·0%)	109 (11·7%)	294 (19·8%)	64 (6·7%)	32 (9·2%)	243 (33·6%)
Corticosteroids (n=2367)	444 (14·3%)	258 (24·2%)	415 (36·6%)	253 (9·1%)	163 (17·5%)	423 (28·4%)	89 (9·3%)	53 (15·3%)	269 (37·2%)
Corticosteroids and LABA† (n=2074)	396 (12·8%)	250 (23·5%)	392 (34·6%)	220 (7·9%)	141 (15·2%)	316 (21·2%)	72 (7·5%)	37 (10·7%)	250 (34·5%)
Any inhaled medicine (n=6818)	1203 (38·7%)	811 (76·1%)	982 (86·7%)	927 (33·3%)	585 (62·9%)	1161 (78·0%)	339 (35·4%)	216 (62·4%)	594 (82·0%)
Oral medicine*									
LTRA (n=1477)	256 (8·2%)	126 (11·8%)	207 (18·3%)	191 (6·9%)	159 (17·1%)	358 (24·1%)	73 (7·6%)	31 (9·0%)	76 (10·5%)
Corticosteroids (n=1206)	171 (5·5%)	86 (8·1%)	213 (18·8%)	154 (5·5%)	74 (8·0%)	315 (21·2%)	70 (7·3%)	26 (7·5%)	97 (13·4%)
SABA (n=2175)	372 (12·0%)	251 (23·5%)	420 (37·1%)	247 (8·9%)	164 (17·6%)	482 (32·4%)	59 (6·2%)	58 (16·8%)	122 (16·9%)
Theophylline (n=774)	139 (4·5%)	47 (4·4%)	123 (10·9%)	118 (4·2%)	52 (5·6%)	160 (10·8%)	42 (4·4%)	32 (9·2%)	61 (8·4%)
Any oral medicine (n=4255)	496 (16·0%)	315 (29·5%)	540 (47·7%)	569 (20·5%)	397 (42·7%)	953 (64·0%)	313 (32·7%)	175 (50·6%)	497 (68·6%)
Asthma management plan (n=6694)	1237 (39·8%)	535 (50·2%)	666 (58·8%)	1547 (56·6%)	520 (55·9%)	999 (67·1%)	516 (53·9%)	186 (53·8%)	461 (63·7%)

Data are n (%) where denominators are the total number in each symptom severity category per income group. Percentages with 95% CIs clustered by centre are provided in appendix 2 (p 6). SABA=short-acting β2 agonist. LABA=long-acting β2 agonist. LTRA=leukotriene receptor antagonist. *Drug therapy groups are not mutually exclusive and participants could be represented in more than one group. †Combined in the same inhaler; patients using LABA and corticosteroids in separate inhalers were included in the corresponding single-agent treatment groups.

Table 2: **Adolescents receiving inhaled and oral asthma medicines according to symptom severity stratified by country income group**

category, country, and centre are shown in appendix 2 (pp 3–4). The distribution of symptom severity in the previous year by age group and income region is also shown (appendix 2 p 20). Overall, 2085 (32·4%) children, 3345 (26·7%) adolescents, and 2058 (30·8%) adults had severe asthma symptoms. The proportion of adolescents with severe symptoms increased as country income category decreased. The proportion of individuals with asymptomatic asthma was highest in HICs for all age groups.

Well controlled asthma was defined in 2840 (44·1%) children, 6942 (55·4%) adolescents, and 4081 (61·1%) adults (appendix 2 p 20). In all age groups, there was a notable trend that asthma control worsened in lower country income categories. The number of children with poorly controlled asthma was 571 (19·9%) of 2863 in HICs, 704 (26·1%) of 2699 in UMICs, and 354 (40·1%) of 883 in LMICs and LICs. The corresponding numbers for adolescents were 794 (15·0%) of 5304 in HICs, 1360 (26·2%) of 5200 in UMICs, and 645 (31·8%) of 2028 in LMICs and LICs; and for adults, 235 (8·6%) of 2724 in HICs, 389 (15·1%) of 2575 in UMICs, and 442 (32·1%) of 1378 in LMICs and LICs.

We determined the proportions of individuals receiving inhaled and oral medicines in the previous year, and the drug regimen used, according to the severity of symptoms and country income category (tables 1–3, appendix 2 pp 5–13). The most frequently used medicines across the three age groups were inhaled SABA (29·3–85·3% of participants with asthma) and inhaled corticosteroids (12·6–51·9%). Overall, we observed a significant trend that inhaled or oral medicines were used by an increasing proportion of individuals as the severity of symptoms increased for all age groups.

The proportion of individuals with severe asthma symptoms not using a corticosteroid-containing inhaler (inhaled corticosteroids alone or with LABA) in the previous year was high in all age groups (934 [44·8%] of 2085 children, 2011 [60·1%] of 3345 adolescents, and 1142 [55·5%] of 2058 adults). This proportion was significantly higher in children and adults in LMICs and LICs versus HICs (appendix 2 p 21). In LMICs and LICs, 185 (65·4%) of 283 children, 405 (55·9%) of 724 adolescents, and 315 (65·1%) of 484 adults with severe asthma symptoms were not using a corticosteroid-containing inhaler. Among individuals using a corticosteroid-containing inhaler for all asthma severities, high proportions took the medication as needed, and some individuals were taking the medicine in short courses (appendix 2 pp 8, 10, 12). Additionally, a high proportion of adolescents (781 [23·3%] of 3345) and adults (379 [18·4%] of 2058) with severe asthma symptoms reported taking LABA in a separate inhaler across all country income categories (tables 2–3), although most of them also reported using ICS in a separate inhaler (628 [80·4%] of 781 adolescents; 197 [52·0%] of 379 adults). Taking medicines as needed was the most frequent regimen for all inhaled medicines across all age groups, asthma severities, and country income groups (appendix 2 pp 8, 10, 12).

The use of oral SABA was high among individuals with severe asthma symptoms, with 780 (37·4%) of 2085 children, 1024 (30·6%) of 3345 adolescents, and 571 (37·8%) of 2058 adults reporting their use. In

	High-income countries (n=2724)			Upper-middle-income countries (n=2575)			Lower-middle-income and low-income countries (n=1378)		
	Asymptomatic (n=1412)	Mild symptoms (n=677)	Severe symptoms (n=635)	Asymptomatic (n=1085)	Mild symptoms (n=551)	Severe symptoms (n=939)	Asymptomatic (n=618)	Mild symptoms (n=276)	Severe symptoms (n=484)
Inhaled medicine*									
SABA (n=3030)	314 (22·2%)	391 (57·8%)	471 (74·2%)	262 (24·1%)	366 (66·4%)	727 (77·4%)	112 (18·1%)	109 (39·5%)	278 (57·4%)
LABA (n=718)	39 (2·8%)	53 (7·8%)	80 (12·6%)	47 (4·3%)	128 (23·2%)	230 (24·5%)	49 (7·9%)	23 (8·3%)	69 (14·3%)
Corticosteroids (n=1118)	134 (9·5%)	189 (27·9%)	230 (36·2%)	51 (4·7%)	70 (12·7%)	282 (30·0%)	51 (8·3%)	28 (10·1%)	83 (17·1%)
Corticosteroids and LABA† (n=1280)	151 (10·7%)	199 (29·4%)	284 (44·7%)	52 (4·8%)	79 (14·3%)	223 (23·7%)	76 (12·3%)	65 (23·6%)	151 (31·2%)
Any inhaled medicine (n=3646)	350 (24·8%)	439 (64·8%)	534 (84·1%)	333 (30·7%)	409 (74·2%)	823 (87·6%)	178 (28·8%)	185 (67·0%)	395 (81·6%)
Oral medicine*									
LTRA (n=520)	71 (5·0%)	46 (6·8%)	80 (12·6%)	47 (4·3%)	46 (8·3%)	192 (20·4%)	10 (1·6%)	4 (1·4%)	24 (5·0%)
Corticosteroids (n=602)	59 (4·2%)	62 (9·2%)	114 (18·0%)	49 (4·5%)	40 (7·3%)	231 (24·6%)	12 (1·9%)	5 (1·8%)	30 (6·2%)
SABA (n=1004)	101 (7·2%)	127 (18·8%)	185 (29·1%)	83 (7·6%)	64 (11·6%)	316 (33·7%)	29 (4·7%)	29 (10·5%)	70 (14·5%)
Theophylline (n=307)	47 (3·3%)	40 (5·9%)	68 (10·7%)	18 (1·7%)	27 (4·9%)	78 (8·3%)	1 (0·2%)	5 (1·8%)	23 (4·8%)
Any oral medicine (n=2226)	177 (12·5%)	227 (33·5%)	320 (50·4%)	159 (14·7%)	195 (35·4%)	613 (65·3%)	133 (21·5%)	125 (45·3%)	277 (57·2%)
Asthma management plan (n=3168)	461 (32·6%)	270 (39·9%)	321 (50·6%)	521 (48·0%)	276 (50·1%)	651 (69·3%)	217 (35·1%)	128 (46·4%)	323 (66·7%)

Data are n (%) where denominators are the total number in each symptom severity category per income group. Percentages with 95% CIs clustered by centre are provided in appendix 2 (p 7). SABA=short-acting β2 agonist. LABA=long-acting β2 agonist. LTRA=leukotriene receptor antagonist. *Drug therapy groups are not mutually exclusive and participants could be represented in more than one group. †Combined in the same inhaler; patients using LABA and corticosteroids in separate inhalers were included in the corresponding single-agent treatment groups.

Table 3: **Adults receiving inhaled and oral asthma medicines according to symptom severity stratified by country income group**

children with severe asthma, oral SABA was used in 232 (34·6%) of 671 in HICs, 468 (41·4%) of 1131 in UMICs, and 80 (28·3%) of 283 in LMICs and LICs (tables 1–3). The use of theophylline was also reported frequently in children from LMICs and LICs (42 [10·3%] of 406 who were asymptomatic, 36 [18·6%] of 194 with mild symptoms, and 56 [19·8%] of 283 with severe symptoms; table 1). Excluding the use of LTRAs in children, taking medicines "as needed" was the most frequently used regimen for all oral medicines across all age groups, asthma severities, and country income groups (appendix 2 pp 9, 11, 13).

We assessed how asthma medicine use was associated with the severity of asthma symptoms, having an asthma management plan, and country income category (table 4). Of all medicines, inhaled SABA was most likely to be used in mild and severe asthma in all age groups. In individuals with mild asthma, the adjusted OR for the use of inhaled SABA was 6·02 (5·16–7·04) in children, 3·55 (3·18–3·97) in adolescents, and 4·32 (3·71–5·03) in adults. In individuals with severe asthma, the corresponding values were 9·11 (7·80–10·6) in children, 6·31 (5·68–7·01) in adolescents, and 9·08 (7·79–10·6) in adults. Use of inhaled corticosteroids and inhaled SABA generally showed inverse associations with residence in LMICs and LICs (*vs* HICs), with adjusted ORs for inhaled corticosteroid use in LMICs and LICs of 0·44 (0·26–0·75) in children, 0·59 (0·32–1·09) in adolescents, and 0·33 (0·18–0·62) in adults. The corresponding values for inhaled SABA were 0·45 (0·26–0·78) in children, 0·46 (0·23–0·92) in adolescents, and 0·59 (0·26–1·36) in adults.

In all age groups, having an asthma management plan became more frequent as the severity of asthma symptoms increased in all country income categories (tables 1–3). However, many participants with asthma reported not having a management plan, with plans being reported in 4049 (62·8%) of 6445 children, 6694 (53·4%) of 12 532 adolescents, and 3168 (47·4%) of 6677 adults overall. In those with severe symptoms, these proportions increased to 1488 (71·4%) of 2085 children, 2126 (63·6%) of 3345 adolescents, and 1295 (62·9%) of 2058 adults. Independent of the severity of symptoms, having an asthma management plan was significantly associated with receiving any type of inhaled medicine (adjusted OR 2·75 [95% CI 2·40–3·15] for children; 2·45 [2·25–2·67] for adolescents; and 2·75 [2·38–3·16] for adults) or any type of oral medicine (1·86 [1·63–2·12] for children; 1·53 [1·40–1·68] for adolescents; and 1·78 [1·55–2·04] for adults; table 4). The medicines most strongly associated with having an asthma management plan were inhaled SABA in children (2·31 [2·03-2·62]) and adolescents (2·26 [2·07–2·47]), and inhaled corticosteroids combined with LABA in adults (2·28 [1·95–2·67]). Additionally, in all age groups, having a management plan was most strongly associated with a daily regimen for all medicines, except for oral corticosteroids in adolescents and theophylline in adults, for which the strongest association was with the short-courses regimen (appendix 2 pp 14–16).

Poor asthma control was significantly associated with having severe symptoms (*vs* asymptomatic asthma, OR 6·48 [95% CI 5·61–7·47] for children; 3·82 [3·46–4·21] for adolescents; and 5·70 [4·88–6·66] for

	Severity of symptoms: mild*	Severity of symptoms: severe*	Asthma management plan†	GNI: upper-middle-income countries‡	GNI: lower-middle-income and low-income countries‡
Children					
Inhaled medicine					
SABA	6·02 (5·16–7·04)	9·11 (7·80–10·6)	2·31 (2·03–2·62)	1·05 (0·65–1·68)	0·45 (0·26–0·78)
LABA	2·86 (1·89–4·32)	3·40 (2·28–5·07)	0·97 (0·70–1·33)	0·15 (0·02–1·06)	2·61 (0·38–17·9)
Corticosteroids	3·04 (2·61–3·55)	4·11 (3·54–4·75)	2·25 (1·96–2·57)	0·68 (0·43–1·07)	0·44 (0·26–0·75)
Corticosteroids and LABA	2·71 (2·23–3·30)	3·33 (2·77–4·01)	2·17 (1·82–2·58)	1·02 (0·62–1·70)	0·97 (0·54–1·76)
Any inhaled medicine	6·36 (5·40–7·48)	13·8 (11·5–16·5)	2·75 (2·40–3·15)	1·18 (0·80–1·76)	0·74 (0·46–1·18)
Oral medicine					
LTRA	2·69 (2·22–3·26)	3·73 (3·11–4·47)	2·01 (1·68–2·39)	2·71 (0·68–10·9)	0·34 (0·07–1·77)
SABA	2·76 (2·31–3·28)	4·64 (3·93–5·48)	1·45 (1·25–1·69)	1·49 (0·43–5·16)	0·36 (0·09–1·51)
Corticosteroids	3·20 (2·64–3·87)	5·81 (4·84–6·98)	1·46 (1·24–1·72)	0·74 (0·15–3·50)	0·18 (0·03–1·13)
Theophylline	1·71 (1·22–2·39)	2·45 (1·78–3·36)	1·41 (1·05–1·88)	1·69 (0·44–6·50)	2·49 (0·51–12·0)
Any oral medicine	3·74 (3·21–4·36)	6·89 (5·91–8·04)	1·86 (1·63–2·12)	2·22 (1·39–3·54)	2·27 (1·32–3·90)
Adolescents					
Inhaled medicine					
SABA	3·55 (3·18–3·97)	6·31 (5·68–7·01)	2·26 (2·07–2·47)	0·58 (0·31–1·08)	0·46 (0·23–0·92)
LABA	1·46 (1·24–1·72)	3·22 (2·81–3·68)	1·54 (1·36–1·75)	1·02 (0·51–2·02)	0·98 (0·46–2·11)
Corticosteroids	1·89 (1·65–2·17)	3·82 (3·39–4·30)	2·00 (1·79–2·23)	0·58 (0·33–1·01)	0·59 (0·32–1·09)
Corticosteroids and LABA	2·00 (1·73–2·31)	3·62 (3·19–4·10)	1·88 (1·68–2·11)	0·51 (0·30–0·84)	0·57 (0·32–1·01)
Any inhaled medicine	4·08 (3·66–4·56)	7·96 (7·12–8·89)	2·45 (2·25–2·67)	0·64 (0·46–0·89)	0·86 (0·59–1·24)
Oral medicine					
LTRA	1·90 (1·62–2·24)	3·31 (2·88–3·81)	1·64 (1·44–1·87)	1·02 (0·30–3·42)	0·28 (0·07–1·11)
SABA	2·27 (1·98–2·61)	4·45 (3·94–5·02)	1·62 (1·45–1·81)	0·66 (0·16–2·71)	0·25 (0·05–1·22)
Corticosteroids	1·44 (1·19–1·74)	4·07 (3·51–4·72)	1·56 (1·35–1·79)	0·88 (0·26–3·06)	0·47 (0·11–1·89)
Theophylline	1·25 (1·00–1·56)	2·78 (2·33–3·32)	1·34 (1·13–1·58)	1·11 (0·33–3·70)	0·41 (0·10–1·71)
Any oral medicine	2·45 (2·19–2·75)	5·71 (5·16–6·33)	1·53 (1·40–1·68)	1·40 (1·04–1·90)	2·91 (2·07–4·10)
Adults					
Inhaled medicine					
SABA	4·32 (3·71–5·03)	9·08 (7·79–10·6)	2·24 (1·96–2·55)	0·86 (0·41–1·80)	0·59 (0·26–1·36)
LABA	2·57 (1·97–3·37)	5·08 (3·96–6·53)	2·17 (1·75–2·69)	1·08 (0·38–3·09)	1·14 (0·35–3·68)
Corticosteroids	2·83 (2·30–3·48)	4·84 (4·02–5·83)	2·05 (1·74–2·42)	0·51 (0·30–0·88)	0·33 (0·18–0·62)
Corticosteroids and LABA	2·68 (2·21–3·24)	4·88 (4·07–5·85)	2·28 (1·95–2·67)	0·28 (0·14–0·53)	0·54 (0·26–1·11)
Any inhaled medicine	5·89 (5·02–6·91)	16·0 (13·4–19·1)	2·75 (2·38–3·16)	0·99 (0·47–2·07)	0·96 (0·42–2·17)
Oral medicine					
LTRA	1·82 (1·34–2·48)	3·82 (2·97–4·93)	2·07 (1·63–2·63)	1·47 (0·28–7·63)	0·15 (0·02–1·09)
SABA	2·85 (2·27–3·58)	5·61 (4·60–6·85)	1·70 (1·43–2·03)	1·51 (0·26–8·84)	0·45 (0·06–3·24)
Corticosteroids	2·30 (1·70–3·11)	5·83 (4·54–7·49)	2·15 (1·70–2·70)	1·08 (0·18–6·44)	0·25 (0·03–1·95)
Theophylline	2·67 (1·82–3·90)	4·33 (3·10–6·06)	1·66 (1·24–2·22)	0·99 (0·22–4·50)	0·18 (0·03–1·17)
Any oral medicine	3·88 (3·27–4·60)	9·06 (7·69–10·7)	1·78 (1·55–2·04)	2·15 (1·13–4·09)	2·35 (1·15–4·83)

Data are odds ratio (95% CI). Associations were adjusted for sex, age, country income category (high-income countries as the reference), and having an asthma management plan at the first level, school at the second level, and centre at the third level of the model. SABA=short-acting β2 agonist. LABA=long-acting β2 agonist. LTRA=leukotriene receptor antagonist. GNI=gross national income. Reference categories: *asymptomatic asthma; †no asthma management plan; ‡high-income countries.

Table 4: **Factors associated with receiving asthma medicines among children, adolescents, and adults in multilevel analysis**

adults; table 5). Poor asthma control was also associated with the lower country income categories (2·33 [1·32–4·14] for children; 3·46 [1·83–6·54] for adolescents; and 4·86 [2·55–9·26] for adults). In all age groups, poor asthma control was associated with receiving any type of medicine except for inhaled corticosteroids combined with LABA in adolescents, theophylline in all age groups, and oral corticosteroids in adults, independent of the severity of symptoms and country income group. Regarding regimens for inhaled drugs, the strongest associations with poor asthma control were with inhaled SABA taken in short courses or daily in children and adolescents; and with daily inhaled SABA and LABA in adults (appendix 2 pp 17–19). With respect to oral medicines, oral corticosteroids taken in short courses in children and adults, and oral corticosteroids taken at any

	Overall population	HICs	UMICs	LMICs and LICs
Children				
Severity of symptoms*				
Mild	2·55 (2·22–2·93)	2·76 (2·24–3·40)	2·42 (1·93–3·03)	2·17 (1·53–3·07)
Severe	6·48 (5·61–7·47)	7·72 (6·10–9·76)	5·83 (4·69–7·24)	5·55 (3·91–7·89)
Country income category†				
UMIC	0·92 (0·56–1·52)	..	..	..
LMIC and LIC	2·33 (1·32–4·14)	..	..	..
Asthma management plan‡	1·16 (1·03–1·30)	1·01 (0·85–1·21)	1·15 (0·95–1·39)	1·56 (1·17–2·08)
Inhaled medicine§				
SABA	2·01 (1·76–2·30)	2·03 (1·63–2·51)	1·99 (1·61–2·45)	2·13 (1·52–2·97)
LABA	1·02 (1·02–1·31)	1·24 (0·76–2·01)	1·05 (0·61–1·82)	0·77 (0·41–1·42)
Corticosteroids	1·16 (1·02–1·31)	1·10 (0·91–1·33)	1·35 (1·12–1·62)	0·81 (0·54–1·24)
Corticosteroids and LABA	1·24 (1·07–1·43)	1·20 (0·96–1·52)	1·31 (0·96–1·44)	1·08 (0·67–1·74)
Oral medicine§				
LTRA	1·18 (1·02–1·37)	1·22 (0·95–1·56)	1·18 (0·96–1·44)	1·02 (0·60–1·75)
Corticosteroids	1·80 (1·57–2·08)	2·14 (1·73–2·65)	1·44 (1·16–1·79)	2·24 (1·47–3·42)
SABA	1·61 (1·40–1·84)	1·60 (1·29–1·98)	1·79 (1·47–2·17)	1·10 (0·66–1·84)
Theophylline	0·97 (0·75–1·27)	0·97 (0·60–1·57)	1·06 (0·69–1·63)	0·85 (0·49–1·49)
Adolescents				
Severity of symptoms*				
Mild	1·65 (1·49–1·83)	1·56 (1·33–1·83)	1·79 (1·52–2·10)	1·59 (1·22–2·08)
Severe	3·82 (3·46–4·21)	3·80 (3·24–4·46)	3·88 (3·35–4·48)	4·03 (3·15–5·15)
Country income category†				
UMIC	2·33 (1·30–4·16)	..	..	..
LMIC and LIC	3·46 (1·83–6·54)	..	..	..
Asthma management plan‡	1·32 (1·21–1·43)	1·38 (1·21–1·57)	1·25 (1·10–1·41)	1·35 (1·10–1·64)
Inhaled medicine§				
SABA	1·95 (1·77–2·15)	2·29 (1·95–2·69)	1·65 (1·43–1·92)	2·13 (1·67–2·72)
LABA	1·17 (1·00–1·36)	1·18 (0·93–1·51)	1·32 (1·03–1·70)	0·98 (0·67–1·43)
Corticosteroids	1·30 (1·14–1·48)	1·15 (0·94–1·39)	1·57 (1·27–1·93)	1·17 (0·85–1·63)
Corticosteroids and LABA	0·93 (0·81–1·07)	1·02 (0·84–1·25)	0·77 (0·61–0·97)	0·95 (0·67–1·34)
Oral medicine§				
LTRA	1·18 (1·02–1·36)	1·37 (1·08–1·74)	1·04 (0·84–1·28)	1·51 (1·01–2·28)
Corticosteroids	1·38 (1·17–1·63)	1·68 (1·28–1·22)	1·22 (0·96–1·56)	1·41 (0·94–2·10)
SABA	1·39 (1·24–1·57)	1·53 (1·28–1·82)	1·28 (1·05–1·57)	1·38 (0·99–1·93)
Theophylline	1·14 (0·91–1·41)	0·77 (0·52–1·31)	1·34 (0·96–1·88)	1·15 (0·72–1·83)

(Table 5 continues on next page)

administration frequency in adolescents showed the strongest associations with poor asthma control (appendix 2 pp 17–19). Notably, in all age groups, oral SABA use (in various regimens depending on the age group and country income group) was also associated with poor asthma control. Having an asthma management plan was weakly associated with poor asthma control, and among children and adults this finding seemed to be driven by data from LMICs and LICs (table 5).

Discussion

To our knowledge, this study is the first to collect individual-level data on asthma treatment in children, adolescents, and adults living under different economic circumstances worldwide. The results provide a description of the use of medications reported by individuals with diagnosed asthma, how these medicines relate to the severity of symptoms or use of asthma management plans, and factors that are related to asthma control. However, due to the cross-sectional nature of this study, the direction of causality of associations cannot be established.

This study reveals several important factors related to the use of asthma medicines. Firstly, as asthma symptoms increased in severity, the proportion of individuals taking any type of inhaled or oral asthma medicine increased. This finding has four possible hypothetical interpretations: asthma medicines are used because of asthma symptoms; asthma medicines are a potential marker of the severity of symptoms; asthma medicines make asthma symptoms worse (unlikely); or, contrary to self-reporting, the medicines are not taken by the patient so symptoms persist. Due to the cross-sectional nature of the study, the information we had on the severity of asthma symptoms was simultaneous to that of medicine use; thus we could not assess the change in severity resulting from the use of asthma medicines. We could only assess the severity of symptoms correlated with reported treatment and thus interpret it as a composite measure of underlying disease and effectiveness of treatment.

Secondly, the use of oral SABA was widespread, with 37·4% children, 30·6% adolescents, and 37·8% adults with severe asthma symptoms reporting their use. This use of oral SABA was despite their low efficacy[21] and increased adverse effects[22] compared with the inhaled preparation; the fact that oral SABA are not recommended by current guidelines;[23] and WHO's reluctance to include them in the list of essential medicines.[24] Oral SABA was used in similar proportions of individuals with severe asthma symptoms between country income categories, except for adolescents and adults in LMICs and LICs, in whom the proportions taking oral SABA were the lowest across the age and country income groups (16·9% and 14·5%, respectively).

Thirdly, theophylline use was widespread, especially in children from LMICs and LICs (where oral SABA are less commonly used than in higher income regions), with rates of use approaching 20% in children with mild and severe asthma symptoms. This is despite recommendations against theophylline use.[23] The use of oral medicines, either oral SABA or theophylline, might be a consequence of unavailability or unaffordability of inhaled asthma medicines in some countries.[25] Among children and adolescents, we observed a significant association between use of any oral medication and being in UMICs or LMICs and LICs. However, in HICs, where availability of inhaled medicines should not be a consideration, theophylline was being used in about one in ten adolescents and adults with severe symptoms, indicating other influences beyond economic factors.

Fourthly, a high proportion of people with asthma and reporting severe symptoms were not taking inhaled

corticosteroids with or without LABA. This proportion tended to be greater as country income group decreased, probably due to difficult access to these medicines in LMICs and LICs.[26] The use of inhaled corticosteroids (with or without LABA) on an as needed basis in all age groups, independent of the severity of symptoms, which is not the ideal regimen for all types of asthma, was the most used regimen. This regimen is recommended by The Global Initiative for Asthma in mild asthma; however, this is not the way the medicines should be used in severe asthma, for which a continuous regimen is recommended.[23] Additionally, a high proportion of children with severe symptoms took oral corticosteroids in the previous year. As the highest proportion (38·6%) was in HICs, it does not seem that unavailability or unaffordability of inhaled corticosteroids is the explanation, although some specific populations in HICs can face this barrier. One explanation could be that oral corticosteroids were needed for acute treatment of asthma attacks, given that around a third of children with severe asthma symptoms in the previous year needed oral corticosteroids (appendix 2 p 5).

Finally, independent of the severity of symptoms or of having an asthma management plan, country income category was also important: the chances of receiving inhaled corticosteroids in UMICs or in LMICs and LICs were 32–67% lower (across the age groups) than in HICs. This finding is possibly explained by the lack of availability and affordability.[11]

Although widely recommended by asthma management guidelines and strategies,[23] the use of asthma management plans was not widespread in individuals with severe asthma (28–37% without a plan across the age groups), which was generally consistent across country income categories. As symptoms increased in severity, asthma management plans were used more frequently, which could be explained by reverse causality. Asthma management plans were associated with receiving any type of inhaled or oral asthma medicine independent of severity or country income category. Importantly, this association was strongest with the daily regimen of inhaled corticosteroids both in adolescents and children. It is possible that asthma management plans had been given to patients but forgotten.

Well controlled asthma as defined for this study was only achieved in 44·1% of children, 55·4% of adolescents, and 61·1% of adults. The proportion of individuals with controlled asthma was highest in HICs and lowest in LMICs and LICs across all age groups. The low availability and affordability of asthma medicines in LMICs and LICs[27] might be an explanation for these differences. Poor asthma control was associated with LMICs and LICs when controlling for symptom severities, treatments, and use of an asthma management plan. Poor asthma control was also associated with increased use of most types of medicine across the age groups; however, two aspects should be considered. Firstly, the association was markedly stronger with the use of inhaled SABA versus other medicines (particularly with the daily regimen); and secondly, there was no association of poor asthma control with the use of inhaled corticosteroids and LABA. These observations might reflect low use of controller medicine and overuse of inhaled SABA when airway inflammation is out of control.[28] The use of oral SABA and oral corticosteroids was also associated with poor asthma control, probably indicating the need for rescue treatment when control worsened. Factors such as indoor or outdoor pollution (which might differ with country income level) or climate change (which might have differential effects according to country income level) might have a role in asthma control, although these are beyond the scope of this study.

The GAN study has limitations and strengths that have been extensively described.[5] The main strengths are the inclusion of many children, adolescents, and adults with asthma, whose disease has been confirmed by a doctor; and the information on asthma medicines, management plans, and disease control obtained from different parts of the world with varying socioeconomic situations. However, not all parts of the world or country incomes are well represented, due to the characteristics of the GAN Phase I study being centre investigator driven.

	Overall population	HICs	UMICs	LMICs and LICs
(Continued from previous page)				
Adults				
Severity of symptoms*				
Mild	1·88 (1·60–2·22)	2·06 (1·60–2·66)	2·21 (1·66–2·95)	1·18 (0·85–1·65)
Severe	5·70 (4·88–6·66)	5·60 (4·31–7·27)	6·40 (4·90–8·35)	4·27 (3·13–5·83)
Country income category†				
UMIC	1·43 (0·80–2·55)	..	..	..
LMIC and LIC	4·86 (2·55–9·26)	..	..	..
Asthma management plan‡	1·24 (1·09–1·41)	1·01 (0·81–1·25)	1·17 (0·95–1·44)	1·70 (1·31–2·21)
Inhaled medicine§				
SABA	1·71 (1·48–1·98)	1·19 (0·93–1·52)	2·22 (1·73–2·85)	2·09 (1·54–2·83)
LABA	1·80 (1·46–2·21)	1·50 (1·03–2·19)	2·28 (1·71–3·06)	1·25 (0·61–2·55)
Corticosteroids	1·34 (1·13–1·60)	1·42 (1·08–1·87)	1·66 (1·27–2·16)	0·84 (0·45–1·58)
Corticosteroids and LABA	1·24 (1·06–1·46)	1·51 (1·17–1·95)	1·40 (1·06–1·84)	1·01 (0·70–1·47)
Oral medicine§				
LTRA	1·37 (1·08–1·74)	0·96 (0·60–1·54)	1·64 (1·21–2·23)	1·23 (0·52–2·92)
Corticosteroids	1·23 (0·98–1·55)	2·56 (1·73–3·78)	0·85 (0·63–1·15)	0·96 (0·39–2·36)
SABA	1·84 (1·55–2·20)	2·31 (1·73–3·08)	1·81 (1·39–2·35)	1·80 (1·10–2·95)
Theophylline	1·31 (0·97–1·75)	0·68 (0·40–1·16)	1·60 (1·04–2·47)	4·12 (1·34–12·7)

Data are odds ratio (95% CI). Associations were adjusted for sex, age, country income category (high-income countries as the reference), and having an asthma management plan at the first level, school at the second level, and centre at the third level of the model. HIC=high-income country. UMIC=upper-middle-income country. LMIC=lower-middle-income country. LIC=low-income country. SABA=short-acting β2 agonist. LABA=long-acting β2 agonist. LTRA=leukotriene receptor antagonist. Reference categories: *asymptomatic asthma; †high-income countries; ‡no asthma management plan; §not receiving the specific medication.

Table 5: **Factors associated with poor control of asthma among children, adolescents, and adults in multilevel analysis**

Although recall bias is always an issue in cross-sectional epidemiological studies, this issue might have been minimised in the study population of patients with asthma (or their parents or guardians), who are probably quite aware of symptoms, medicines, or markers of poor disease control. The cross-sectional nature of this study means we cannot draw conclusions about how effectively individuals with asthma are managed and reverse causality might explain many results. Nonetheless, there is clear scope for improvement in asthma management overall given the low levels of asthma control that were reported (and despite the fact that some cases cannot be controlled even when managed correctly). A 2018 *Lancet* Commission recommended a biomarker-driven management approach.[29] The extent to which this approach could improve the situation remains to be elucidated. Nevertheless, access to essential medicines should be secured, particularly in low-resource settings where they are frequently unavailable and unaffordable.[30]

In conclusion, improved asthma control is an urgent need worldwide, particularly in children and in less affluent countries. Improving the availability and affordability of inhaled medicines in less affluent countries should be a priority.

Contributors

MIA, KB, C-YC, AES, PE, LG-M, GBM, NP, DPS, RM, and KM conceived the study. EE, PE, LG-M, and EM curated data. LG-M and EM did the formal analysis. LG-M, EM, DPS and NP accessed and verified the underlying data. LG-M led the investigation. MIA, C-YC, PE, LG-M, NP, and DPS designed the methodology. MIA, EE, and PE were project administrators. MIA provided resources to secure employment of the staff at the data centre in Auckland. LG-M, MIA, C-YC, KB, AES, NP, and DPS supervised the study. PE validated the data included from centres. EE, PE, RM, and KM were responsible for data visualisation. LG-M wrote the original draft. MIA, KB, C-YC, AES, EE, PE, EM, KM, NP, DPS, GBM, RM, KM, and the Global Asthma Network Phase I Study Group reviewed and edited the manuscript. The Global Asthma Network Phase I Study Group contributed original data to the analyses. All authors had access to all the data in the study and had final responsibility for the decision to submit for publication.

Declaration of interests

KM reports receiving advisory board fees from AstraZeneca, outside the submitted work. GBM reports grants and non-financial support from AstraZeneca and grants from GlaxoSmithKline Australia and Novartis Australia, outside the submitted work. RM reports receiving consulting fees from AstraZeneca and Merck Sharpe & Dohme (Organon) and honoraria for educational events organised by AstraZeneca. All other authors declare no competing interests.

Data sharing

The study protocol including a recommended informed consent form and statistical analysis plan are in the public domain (http://globalasthmanetwork.org/surveillance/manual/manual.php). The GAN Phase I data, including deidentified individual participant data, will be made available on the Global Asthma Network website (http://www.globalasthmanetwork.org/) within 12 months of all GAN Phase I analyses being published. Access will require a formal request, a written proposal (to be submitted to info@globalasthmanetwork.org), and a signed data access agreement.

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