Respiratory Medicine 227 (2024) 107637

Contents lists available at ScienceDirect

Respiratory Medicine

journal homepage: www.elsevier.com/locate/rmed

Original Research

Asthma patients' and physicians' perspectives on the burden and management of asthma: Post-hoc analysis of APPaRENT 1 and 2 to assess predictors of treatment adherence

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ARTICLE INFO

Keywords:
3–6): Treatment adherence
Inhalation therapy
Physician–patient relations
Patient engagement

ABSTRACT

Introduction: Patient adherence to maintenance medication is critical for improving clinical outcomes in asthma and is a recommended guiding factor for treatment strategy. Previously, the APPaRENT studies assessed patient and physician perspectives on asthma care; here, a post-hoc analysis aimed to identify patient factors associated with good adherence and treatment prescription patterns.

Methods: APPaRENT 1 and 2 were cross-sectional online surveys of 2866 adults with asthma and 1883 physicians across Argentina, Australia, Brazil, Canada, China, France, Italy, Mexico, and the Philippines in 2020–2021. Combined data assessed adherence to maintenance medication, treatment goals, use of asthma action plans, and physician treatment patterns and preferences. Multivariable logistic regression models assessed associations between patient characteristics and both treatment prescription (by physicians) and patient treatment adherence.

Results: Patient and physician assessments of treatment goals and adherence differed, as did reporting of short-acting β_2-agonist (SABA) prescriptions alongside maintenance and reliever therapy (MART). Older age and greater patient-reported severity and reliever use were associated with better adherence. Patient-reported prescription of SABA with MART was associated with household smoking, severe or poorly controlled asthma, and living in China or the Philippines.

Conclusions: Results revealed an important disconnect between patient and physician treatment goals and treatment adherence, suggesting that strategies for improving patient adherence to maintenance medication are needed, focusing on younger patients with milder disease. High reliever use despite good adherence may indicate poor disease control. Personalised care considering patient characteristics alongside physician training in motivational communication and shared decision-making could improve patient management and outcomes.

1. Introduction

Asthma is a chronic inflammatory respiratory disease often managed with reliever inhalers and maintenance therapy consisting of a combination of inhaled corticosteroids (ICSs), long-acting β_2-agonists (LABAs), and long-acting muscarinic-antagonists, depending on disease severity. Reliever inhalers containing a short-acting β_2-agonist (SABA) are also often prescribed. Global Initiative for Asthma (GINA)

Abbreviations: aOR, adjusted odds ratio; CI, confidence interval; GINA, Global Initiative for Asthma; GP, general practitioner; ICS, inhaled corticosteroid; LABA, long-acting β_2-agonist; MART, maintenance and reliever therapy; PRD, proactive regular dosing; SABA, short-acting β_2-agonist; SD, standard deviation.

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https://doi.org/10.1016/j.rmed.2024.107637
Received 19 January 2024; Received in revised form 12 April 2024; Accepted 15 April 2024
Available online 16 April 2024

recommendations suggest two treatment tracks based on choice of reliever therapy [1]. For moderate-to-severe asthma, the preferred Track 1 follows a maintenance and reliever therapy (MART) strategy where ICS/formoterol is taken as both maintenance and reliever therapy. Track 2 recommends a regular ICS dosing strategy, where a SABA reliever is prescribed alongside an ICS-containing maintenance therapy and to which a LABA is added as disease severity increases. Both tracks recommend increasing ICS dose at higher severity levels and additional add-on therapies for patients with severe disease.

GINA recommends that physicians should consider any barriers to patient adherence to daily maintenance medication when selecting Track 1 or Track 2. Where a patient has good adherence to medication (defined as taking the prescribed medication as agreed by the patient and physician [1]), Track 2 treatment provides regular ICS-based maintenance therapy, which is key to control the inflammation that underlies the pathophysiology of asthma. Patient adherence to maintenance therapy is critical for improved outcomes in chronic non-communicable diseases such as asthma [2]; however, poor adherence to medication by some patients can be a challenge to optimal treatment [1,3]. The identification of factors associated with patient adherence versus non-adherence to medication may allow for more targeted intervention to improve clinical outcomes for patients.

Previously, the APPaRENT studies assessed patient and physician perspectives on asthma treatment [4,5]. In APPaRENT 1 (conducted in Australia, Canada, China, and the Philippines, July–August 2020) [4] it was found that the primary treatment goal for patients and physicians was symptom control, with a shift towards greater prioritisation of exacerbation reduction with increased asthma severity. Patients were also found to overestimate their level of asthma control, and physicians prescribed ICS or ICS/LABA with SABA more often than MART regimens, despite GINA recommendations. APPaRENT 2 (conducted in Argentina, Brazil, France, Italy and Mexico, August–November 2021) [5] identified high rates of poor asthma control and SABA use despite symptom control being a priority treatment goal. Regular ICS-based regimens were more often prescribed than MART regimens across physician specialities, and inappropriate prescription of SABA with MART regimens was observed.

The aim of this post-hoc analysis was to assess the patient factors associated with good adherence and with the inappropriate prescription of an additional reliever with MART, as well as patient and physician treatment goals, using combined data from the APPaRENT 1 and APPaRENT 2 surveys.

2. Methods

2.1. Study design and participants

The study pooled individual-level data from the APPaRENT 1 and 2 surveys. These data comprised of patient and physician demographics, patient adherence to maintenance medication, treatment goals, use of asthma action plans, and physician treatment patterns and preferences.

The surveys were online, cross-sectional and assessed perspectives on asthma care among physicians and patients with asthma across nine countries. APPaRENT 1 was conducted in 2020 and recruited patients (n = 1216) and physicians (n = 803) from Australia (n = 305; n = 200, respectively), Canada (n = 308; n = 202), China (n = 300; n = 201), and the Philippines (n = 303; n = 200); APPaRENT 2 was conducted in 2021 with patients (n = 1650) and physicians (n = 1080) from Argentina (n = 330; n = 216, respectively), Brazil (n = 330; n = 216), France (n = 330; n = 216), Italy (n = 330; n = 216), and Mexico (n = 330; n = 216) [4,5].

Participants were recruited via high-quality online non-probability panels. Eligible patients were aged ≥18 years with self-reported history of past or current physician-diagnosed asthma, and for APPaRENT 2, self-reported use of an inhaler for ≥6 months. Eligible physicians were primary care physicians and pulmonologists (respirologists/respiratory therapists in Canada; APPaRENT 2 only) with ≥3 years in clinical practice and treating ≥4 patients with asthma per month on average.

Full details of the APPaRENT 1 and APPaRENT 2 survey methodologies have been published previously [4,5]. Copies of the survey questions and response options are provided in the supplementary material. Though both surveys were designed to assess patient and physician perspectives on asthma treatment, the wording of questions differed, which was considered during data combination.

2.2. Study outcomes

The primary study outcome was a binary indicator of patient-reported adherence to ICS, defined as a patient who used ICS-containing maintenance treatment and indicated use of their maintenance inhaler at least once a day. Use of an ICS-containing maintenance inhaler less than once a day was considered non-adherent.

A secondary outcome of the study was to assess rates of prescription of an additional SABA reliever with the MART regimen, defined through patient reporting of being prescribed a quick-relief rescue inhaler alongside MART.

Additional outcomes included patient and physician treatment goals and use and follow-up of asthma action plans. Physician-preferred treatment patterns were also assessed, including physician-reported prescription rates of an additional SABA with MART. Further details regarding the data sources for all outcomes can be found in Supplementary Table 1.

2.3. Statistical analysis

Descriptive statistics were used to summarise patient and physician characteristics. Quantitative data were summarised, with mean and standard deviation (SD) for continuous data, and frequency and proportions for categorical data.

Multivariable logistic regression analysis was conducted to identify patient factors associated with good ICS adherence. From the overall sample of 1993 patients who received maintenance therapy, listwise deletion for missing data resulted in an analytical sample of 1354 patients. This was a result of the inclusion of the reliever use variable because ICS-only users were excluded. The independent variables entering the regression model were selected based on the authors' expertise as potential predictors of patient adherence to ICS and data availability and comparability within and across the APPaRENT surveys. The following variables were included in the regression model: sex, age, education, household smoking status, country, asthma severity, reliever use, and treatment regimen.

A separate multivariable logistic regression analysis using the same analytical sample assessed patient characteristics associated with prescription of SABA with the MART regimen. The independent variables entering the model were again selected based on the authors' expertise as well as data availability and comparability. Variables in the regression model included sex, age, education, household smoking status, country, asthma severity, and perceived asthma control.

The analyses generated adjusted odds ratios (aORs) and 95% confidence intervals (CIs) for the association between each potential predictor variable and patient ICS adherence (primary outcome), or additional SABA prescription with MART (secondary outcome).

To account for the correlation in the data because of respondents participating from the same country, cluster-robust standard errors were estimated using the vce (cluster clustvar) option in Stata with country as the cluster variable. P-values were calculated from likelihood ratio tests. Tests for trend were conducted for ordered categorical exposures. To assess country-specific differences in the association between a potential predictor and ICS adherence, an interaction term (predictor*country) was entered into the regression model and investigated using likelihood ratio tests.

All analyses were conducted in Stata version 18 SE (StataCorp LLC, College Station, TX, USA) [6].

To confirm that the association between frequency of reliever use and asthma severity did not confound the analysis, a test compared the odds ratios for asthma severity with the model excluding reliever use and found no major difference.

A sensitivity analysis was performed for the main outcome of patient adherence to explore the impact of the definition of adherence on the associations with predictors. The outcome definition was changed from self-reported maintenance inhaler use at least once a day to only used more than once a day (APPaRENT 1 response to patient question P16: twice a day or more; APPaRENT 2 response to patient question P9: more than once a day). Patients selecting any other response were classified as non-adherent. The results of the sensitivity analysis did not change substantially (Supplementary Fig. 1).

3. Results

3.1. Population characteristics

Patients A total of 2866 patients across the nine countries completed APPaRENT 1 and APPaRENT 2 surveys. Overall, 41.2% (1181/2866) of patients were male, with a mean (SD) age of 40.6 (14.5) years. Approximately half (52.2%) lived in metropolitan areas and 42.9% in a smoking household (Table 1). Patients self-reported that their asthma was moderate (55.0%), mild (40.2%), or severe (4.8%), with 73% of patients in APPaRENT 2 reporting that this classification came from their physician (Table 1, Supplementary Tables 2 and 3). ICS-based maintenance inhaler to be taken at least once a day was prescribed for 69.5% (1993/2866) of patients, making them relevant for the treatment adherence analyses. With adherence defined as self-reported ICS use at least once a day, 60.5% (1206/1993) of patients reported being adherent to their maintenance inhaler treatment (Table 1, Fig. 1).

Physicians The physician population (n = 1883) had a mean (SD) age of 45.7 (10.2) years, and 61.6% were male. The mean (SD) time in clinical practice was 17.6 (9.1) years; 53.3% practiced in a private clinic or physician's office and 60.4% in a metropolitan area (Table 2, Supplementary Table 4).

Physicians reported that 70.8% of their patients with moderate or severe asthma were adherent to their prescribed maintenance medication (Fig. 1, Supplementary Table 5).

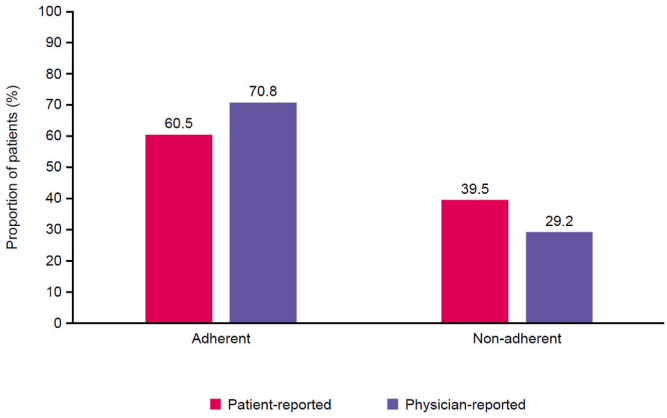

Fig. 1. Patient adherence to maintenance medication as reported by patients and physicians. For patient self-reported adherence, reporting of using a maintenance inhaler ≥once a day was considered adherent and <once a day as non-adherent.
Data collected from: APPaRENT 1 patient question P16; APPaRENT 1 physician question H15; APPaRENT 2 patient question P9; APPaRENT 2 physician question H15. Owing to the incompatibility between questions H14 in both physician surveys, physician-reported patient adherence could only be combined for patients with moderate/severe asthma (H15).

3.2. Patient adherence to maintenance medication

Among the potential predictors assessed, findings from the multivariable logistic regression analysis showed that older age (≥50 years: aOR = 2.7 [95% CI 1.6, 4.6], p < 0.001) compared with ages 18–29 years, greater disease severity (moderate: aOR = 1.7 [95% CI 1.3, 2.2]; severe: aOR = 8.7 [95% CI 2.3, 33.7], p < 0.001) compared with mild disease, and greater reliever use (once a day: aOR = 7.3 [95% CI 3.3, 16.1]; more than once a day: aOR = 9.6 [95% CI 4.0, 22.7], p < 0.001)

Table 1
Patient demographics.

Characteristic	Overall Patients (N = 2866)
Sex,[a] n (%)	
Male	1181 (41.2)
Female	1685 (58.8)
Age,[b] mean years (SD)	40.6 (14.5)
Age[b] category, years, n (%)	
18–29	660 (23.0)
30–39	941 (32.8)
40–49	536 (18.7)
≥50	729 (25.4)
Self-reported asthma severity,[c] n (%)	
Mild	1153 (40.2)
Moderate	1576 (55.0)
Severe	137 (4.8)
Education,[d] n (%)	
High school or less	676 (23.6)
College/university	1805 (63.1)
Postgraduate degree	380 (13.3)
Location of residence,[e] n (%)	
Large city/metropolitan area	1494 (52.2)
Suburb	512 (17.9)
Small city	421 (14.7)
Town	210 (7.3)
Rural area	228 (8.0)
Household smoking status,[f] n (%)	
No	1636 (57.1)
Yes	1230 (42.9)
Adherent to regular controller inhaler,[g] n (%)	
No	787 (39.5)
Yes	1206 (60.5)

SD, standard deviation.
Data collected from: APPaRENT 1 patient questions [a]PD1, [b]PD2, [c]P3, [d]PD3, [e]PD5, [f]P12, [g]P16; APPaRENT 2 patient questions [a]PD1, [b]PD2, [c]P1, [d]PD3, [e]PD4, [f]P7, [g]P9.

Table 2
Physician demographics.

Characteristic	Overall Physicians (N = 1883)
Sex,[a] n (%)	
Male	1160 (61.6)
Female	723 (38.4)
Age,[b] mean years (SD)	45.7 (10.2)
Age[b] category, years, n (%)	
18–29	28 (1.5)
30–39	579 (30.8)
40–49	641 (34.1)
≥50	634 (33.7)
Years in clinical practice,[c] mean (SD)	17.6 (9.1)
Treatment setting,[d] n (%)	
Government-sponsored clinic or doctor's office	254 (13.7)
Government-sponsored hospital	451 (24.3)
Private clinic or doctor's office	989 (53.3)
Private hospital or hospital-based facility	109 (5.9)
Multiple facilities	54 (2.9)
Location of treatment facility,[e] n (%)	
Large city/metropolitan area	1137 (60.4)
Suburb/small city/town	679 (36.1)
Rural area/remote (hard to reach) location	67 (3.6)

SD, standard deviation.
Data collected from: APPaRENT 1 physician questions [a]HD1A, [b]HD1, [c]HS4, [d]HD5, [e]HD6; APPaRENT 2 physician questions [a]HD1, [b]HD2, [c]HS4, [d]HD3, [e]HD4.

compared with reliever use less than once a week, were associated with increased odds of ICS adherence. For patients aged ≥50 years, the adjusted odds of ICS adherence were around 2.5 times those for patients aged 30–39 years, and for patients with severe disease, the adjusted odds of ICS adherence were around 5 times those for patients with moderate disease (Fig. 2). Compared with regular ICS dosing (also referred to as proactive regular dosing [PRD]), the odds of adherence to ICS for patients receiving MART were 32% lower, although this was not statistically significant (odds ratio 0.68 for MART, using PRD as a reference [95% CI 0.39, 1.18]; p = 0.169 in the Wald test; p = 0.016 in the likelihood ratio test).

3.3. Patient and physician treatment preferences

Treatment goals Across the three patient-reported asthma severities, patients ranked exacerbation reduction as the most important treatment goal (mild: 60.8%, moderate: 64.9%, severe: 58.6%).

Physicians ranked symptom control as the most important treatment goal for patients with physician-diagnosed mild (63.5%) and moderate (55.7%) asthma. For severe asthma, there was equal preference for reducing exacerbations (50.9%) and achieving symptom control (49.1%).

MART treatment patterns APPaRENT 2 asked physicians to report their speciality, allowing differences in prescribing patterns to be examined. The majority of internal medicine (70%) and general practitioner (GP)/family medicine physicians (71%) did not select the recommended treatment regimen (ICS/formoterol) when asked for their preferred initial MART therapy; 56% of pulmonologists/chest physicians reported ICS/formoterol as their preferred initial MART therapy (Fig. 3).

The majority of patients receiving MART also reported being prescribed SABA reliever; the proportion ranged across countries (71.2–96.9%), being highest (>90%) in China, the Philippines, and

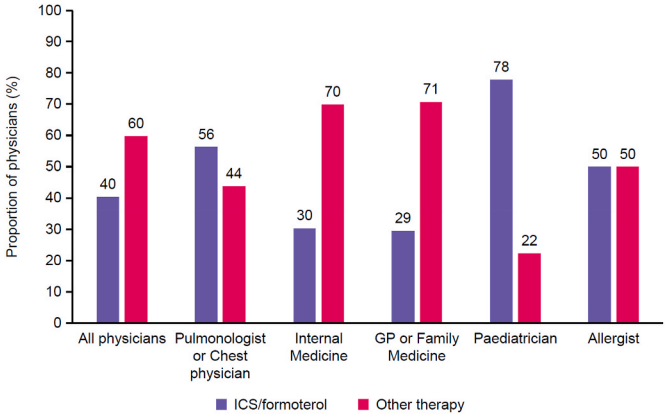

Fig. 3. MART therapy preferences among physicians, by speciality.
Data collected from: APPaRENT 2 physician question H29. Response options included under "Other therapy" were ICS/LABA, ICS/LABA + inhaled SABA, and ICS/formoterol + inhaled SABA. GP, general practitioner; ICS, inhaled corticosteroid; LABA, long-acting β_2-agonist; MART, maintenance and reliever therapy; SABA, short-acting β_2-agonist.

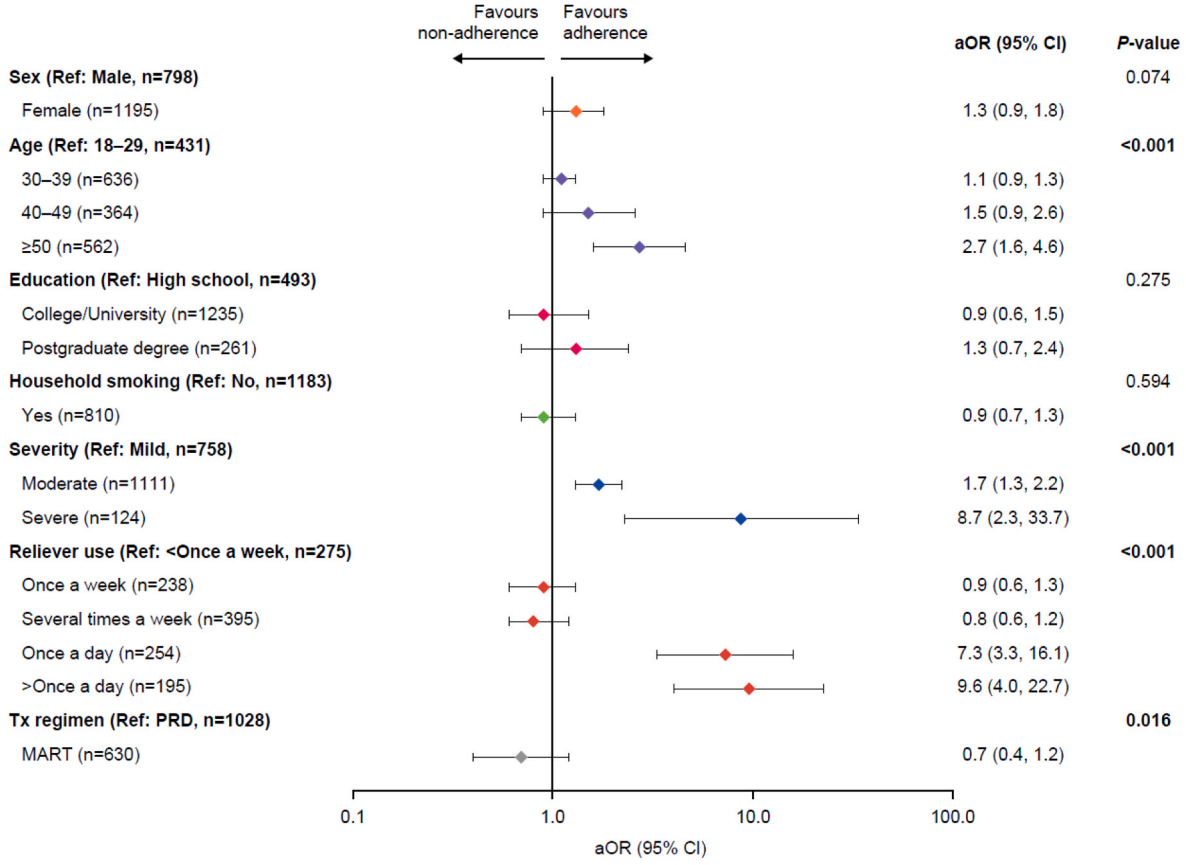

Fig. 2. Multivariable logistic regression of the association between adherence (defined as use of ICS-based maintenance treatment ≥once per day) and patient characteristics.
Data collected from: APPaRENT 1 patient questions P16, PD1, PD2, PD3, P12, P3, P17, P14; APPaRENT 2 patient questions P9, PD1, PD2, PD3, P7, P1, P10, P8. P-values were calculated from likelihood ratio tests. aOR, adjusted odds ratio; CI, confidence interval; ICS, inhaled corticosteroid; MART, maintenance and reliever therapy; PRD, proactive regular dosing; Ref, reference; Tx, treatment.

Argentina, and lowest in France (71.2%). Physician reporting of prescribing an additional SABA reliever with MART varied greatly between countries (27.0–95.1%), being the highest in China and lowest in Italy (Supplementary Table 6).

Multivariable logistic regression assessed associations between patient characteristics and being prescribed MART with an additional SABA. Living in a smoking household compared with a non-smoking household (aOR = 3.0 [95% CI 2.4, 3.7], p < 0.001) and reporting having severe versus mild asthma (aOR = 2.7 [95% CI 1.0, 7.0], p = 0.201) or reporting asthma that was somewhat or poorly controlled versus well controlled (somewhat controlled: aOR = 2.2 [95% CI 1.6, 3.1]; poorly/not at all controlled: aOR = 3.3 [95% CI 1.0, 11.0], p = 0.005) was associated with MART plus additional SABA prescription. Compared with living in Australia (the reference country), living in China or the Philippines was also associated with higher MART plus additional SABA prescription, whereas living in Canada, France, or Italy was associated with lower prescription of MART plus additional SABA compared with Australia (Fig. 4).

Asthma action plans From the APPaRENT 2 survey, 68.4% (1128/1650) of patients reported that an asthma action plan was discussed with their physician. Of these patients, 72.2% (814/1128) reported that their physician very often (42.3%) or sometimes (29.9%) followed up on the progress of the plan, with 17.2% reporting that their physician always followed up (Supplementary Table 7). Country-level differences were observed: for example, 86.1% of patients in Argentina reported discussing an asthma action plan with their doctor compared with 37.3% of patients in France.

The majority of physicians (80.3%; 867/1080) reported always (43.9%) or often (36.4%) providing an action plan, with 14.3% doing so sometimes and 3.4% rarely. Physicians reported consistent results, with 91.7% in Argentina always or often providing patients with an asthma action plan, compared with 57.9% in France. Of the physicians who provided action plans, 6.6% (70/1058) and 51.5% (545/1058) thought that their patients always and often adhered to their plans, respectively.

3.4. Treatment patterns and preferences

Across the countries surveyed in APPaRENT 2, the top three factors influencing patient outcomes when prescribing maintenance medication were asthma exacerbations (74.9%), asthma control (70.8%), and symptom severity (68.0%) (Table 3). Previous poor adherence to treatment was considered by 12.9% (139/1080) of physicians overall. Adherence was most often considered in Italy (20.4%) compared with other countries (8.8–13.0%) (Supplementary Table 8).

Across all countries, 10.3% of physicians reported prescribing ICS/LABA with as-needed SABA to ≥60% of their patients with moderate asthma, and 1.9% prescribed the MART regimen (Table 4).

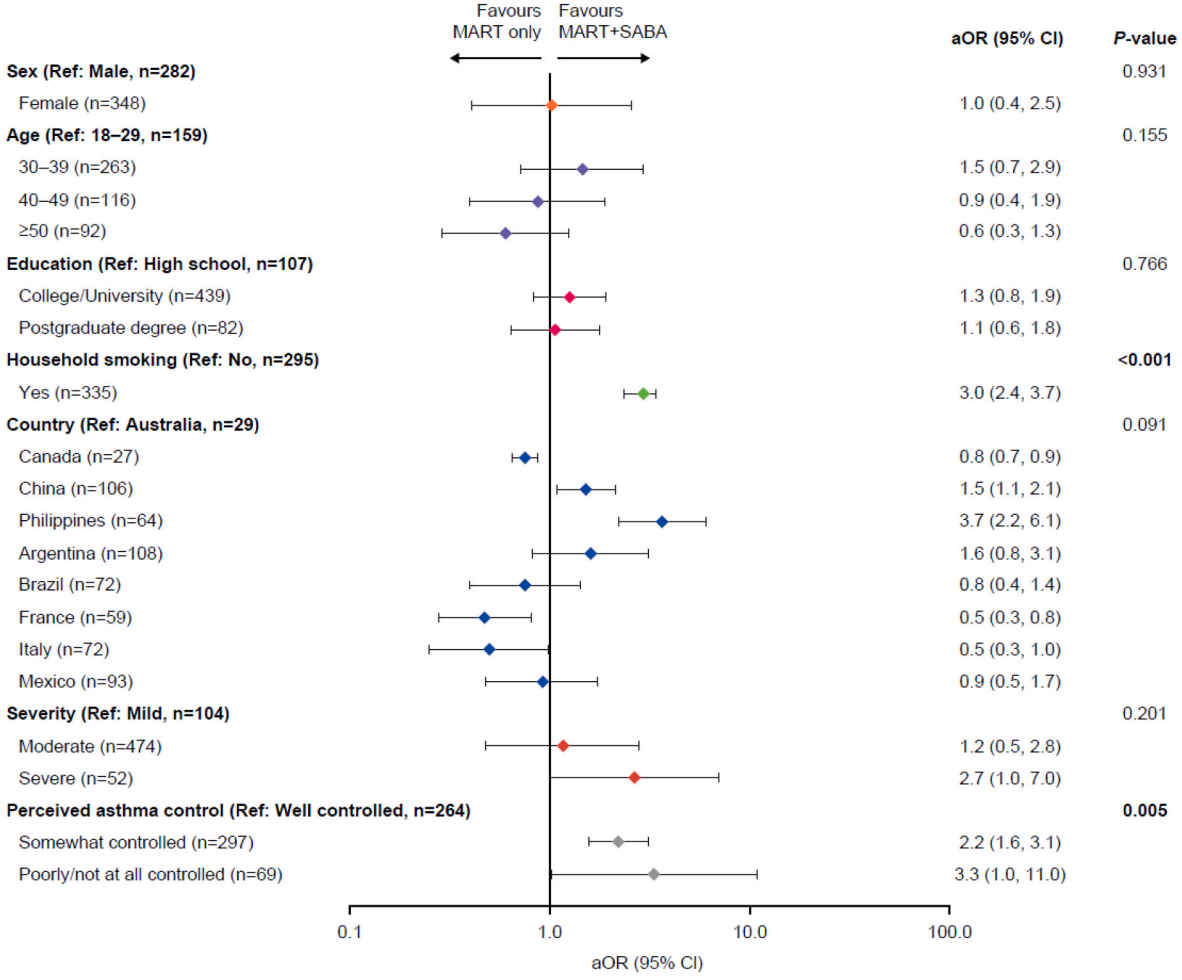

Fig. 4. Multivariable logistic regression of the association between patients being prescribed MART with an additional SABA and patient characteristics.
Data collected from: APPaRENT 1 patient questions P30, PD1, PD2, PD3, P12, P3, P10e; APPaRENT 2 patient questions P29, PD1, PD2, PD3, P7, P1, P6e. P-values were calculated from likelihood ratio tests. aOR, adjusted odds ratio; CI, confidence interval; MART, maintenance and reliever therapy; Ref, reference; SABA, short-acting β_2-agonist.

Table 3
Factors influencing physician treatment choices.

Response, n (%)	All Countries (N = 1080)
Asthma control	765 (70.8)
Asthma exacerbations	809 (74.9)
Symptom severity	734 (68.0)
Whether the patients has comorbidities	150 (13.9)
Whether the patient has any lung function impairment	231 (21.4)
Whether the patient has previous poor adherence	139 (12.9)
Patient device preference	149 (13.8)
Price or cost to the patient	143 (13.2)
Flexibility to change the dose	64 (5.9)
Age of the patient	53 (4.9)

Data collected from: APPaRENT 2 physician question H27a.

3.5. Sensitivity analysis

Analysis with a more stringent definition of adherence, where patients were classified as adherent to maintenance medication only if they reported using their maintenance inhaler more than once a day, gave generally consistent results (Supplementary Fig. 1).

4. Discussion

By combining data from the APPaRENT 1 and 2 surveys, this post-hoc analysis presents a global view of patient and physician perspectives on asthma management. The study calls for improved rates of adherence to regular ICS-based maintenance therapy, which can help to explain the poor levels of asthma control identified previously [4,5]. Adherence was found to be relatively high (60.5–70.8%) compared with published reports, which range from 22% to 63% [7,8], although the values reported here may be overestimates because adherence was self-reported by patients and physicians. To achieve optimal disease control with maintenance treatment, patient adherence should be as close to 100% as possible.

Adherence to maintenance medication was found to be associated with older age and more severe disease; therefore, younger patients and those with milder disease may be at higher risk of poor adherence. Resources for clinical interventions to improve adherence would be best focused on these populations. Poor adherence to maintenance medication in patients with mild asthma is a known phenomenon, with patients more often relying on reliever inhalers for symptom control rather than their maintenance medication needed to treat the underlying inflammation and prevent future exacerbations [9]. For the association between adherence and age, however, the evidence is conflicting, which may reflect the complex and multifactorial nature of adherence [10–12]. Additionally, better adherence was associated with higher reliever use, a seemingly counterintuitive finding. This could reflect a patient population with uncontrolled disease despite adherence to maintenance treatment who may require step-up to increased doses or add-on therapies [13,14].

Despite the known low rates of patient adherence to maintenance medication in chronic conditions and this being a factor in choice of GINA treatment track [1,15,16], only 13.0% of physicians considered previous poor adherence when prescribing initial treatment. In clinical practice, shared decision-making between patients and physicians as well as motivational communication to assess and address adherence should be prioritised. These methods have been shown to improve both adherence and clinical outcomes in patients [17,18]. More effective use of asthma action plans, shown in this study to be variably implemented and followed up across different countries, may also increase patient adherence. There is a known disparity between the recommendation to provide an asthma action plan and physicians implementing these in practice, a finding reflected here [19]. Providing patient-centred action plans and regularly following up on progress has been previously shown to increase adherence [19,20]. Additionally, patient education to increase disease knowledge has also been shown to improve adherence rates and asthma control [9]. However, to effectively change behaviour, strengthening patient motivation and confidence is needed; this could be achieved through more motivational communication training for physicians [9]. The gaps observed between patient and physician views on adherence and goal setting need to be bridged to optimize treatment; this could be achieved through more personalised care and improved patient–physician communication. Physicians generally reported higher treatment adherence than patients (70.8% vs 60.5%), indicating a disconnect in perceptions. Treatment goals also differed between patients and physicians, with patients prioritising reduction of exacerbations (60.8% and 64.9%, for mild and moderate asthma, respectively) and physicians prioritising symptom control (63.5% and 55.7%, for mild and moderate asthma, respectively). This disconnect may contribute to poor adherence if patients are not seeing the progress they expect, so personalised clinical approaches and shared decision-making between patients and physicians may improve adherence [18,21]. Interestingly, this differs from the results of the individual APPaRENT surveys, where the majority of both patients and physicians reported that asthma/-symptom control was the most important treatment goal, particularly for mild/moderate asthma. This highlights the advantages of larger datasets to fully capture patient and physician perspectives overall, and how these perspectives change in different populations.

The paucity of understanding around prescribing/taking medication correctly needs to be addressed with education to prevent inappropriate SABA reliever use. When prescribing MART, 60.7% of physicians reported prescribing additional SABA whereas 80.5% of patients reported receiving MART plus SABA. Some of this discrepancy may be explained by patient use of over-the-counter SABA, which is available without prescription in all countries surveyed in the APPaRENT studies except Canada and France. However, in both APPaRENT surveys, patients were specifically asked if they were prescribed MART. The largest disparity between patient- and physician-reported use of SABA with MART was in Argentina, where 93.5% of patients noted receiving an additional SABA

Table 4
Physician treatment patterns.

Response	N	0–20%, n (%)	21–40%, n (%)	41–60%, n (%)	61–80%, n (%)	81–100%, n (%)
Inhaled SABA only (e.g. salbutamol)	1363	1168 (85.7)	128 (9.5)	50 (3.7)	12 (0.9)	5 (0.4)
Low-dose ICS without inhaled SABA therapy	1330	1216 (91.4)	86 (6.5)	18 (1.4)	7 (0.5)	3 (0.2)
Low-dose ICS with inhaled SABA therapy	1500	1033 (68.9)	309 (20.6)	92 (6.1)	43 (2.9)	23 (1.5)
ICS/formoterol fixed-dose combination as needed (MART)	1398	1062 (76.0)	228 (16.3)	72 (5.2)	22 (1.6)	14 (1.0)
ICS/formoterol as MART with inhaled SABA	878	680 (77.5)	144 (16.4)	38 (4.3)	7 (0.8)	9 (1.0)
ICS/formoterol as MART without inhaled SABA	804	685 (85.2)	71 (8.8)	33 (4.1)	8 (1.0)	7 (0.9)
ICS/LABA: ICS/LABA combined fixed-dose combination with inhaled SABA	1553	907 (58.4)	328 (21.1)	157 (10.1)	92 (5.9)	69 (4.4)
ICS/LABA: ICS/LABA combined fixed-dose combination without inhaled SABA	1319	1020 (77.3)	167 (12.7)	58 (4.4)	34 (2.6)	40 (3.0)
Theophylline	975	955 (98.0)	14 (1.4)	3 (0.3)	3 (0.3)	0 (0.0)
Not receiving any prescribed therapy	803	799 (99.5)	1 (0.1)	3 (0.4)	0 (0.0)	0 (0.0)

ICS, inhaled corticosteroid; LABA, long-acting β_2-agonist; MART, maintenance and reliever therapy; SABA, short-acting β_2-agonist.
Data collected from: APPaRENT 1 physician question H12; APPaRENT 2 physician question H11.

whereas only 34.5% of physicians reported such prescribing. As described previously, most patients who were prescribed SABA with MART in APPaRENT 2 reported that this was at their own request (66.6%) [5]. Physicians may therefore be unwilling to forego prescribing the additional reliever alongside the MART regimen. Strengthening physician communication skills, particularly in motivational communication, could empower physicians to better manage patient expectations and anxiety around reliever inhalers more effectively [22]. Pulmonologists were most likely to prescribe MART correctly, but around 70% of GPs and internal medicine physicians reported preferences for ICS/LABA or additional SABA prescription when selecting a MART therapy. Since additional SABA was most often prescribed at the wish of patients, physician training on how to manage and respond to inappropriate and potentially harmful patient requests may be needed for non-respiratory specialists. Also, as the asthma treatment landscape shifts and recommendations evolve, better education of primary care physicians to maximise their understanding of the latest national and international guidelines, and the importance of following these guidelines, may be of benefit. It is important to note that the insights into SABA prescribing here are restricted by the questions asked: APPaRENT 1 queried physicians directly about prescribing habits ("*When you prescribe ICS/LABA as MART for asthma, how often do you also prescribe a short-acting beta agonist or short-acting bronchodilator as a reliever?*"), whereas APPaRENT 2 asked physicians to choose between ICS/LABA or ICS/formoterol with or without SABA as a preferred initial treatment ("*Which of the following is your preferred initial MART therapy for patients you treat?*").

Living in a household with smokers and patient-reported severe asthma or somewhat or poorly/not controlled asthma were associated with additional SABA prescription with MART. Participants from China and the Philippines were more likely to be prescribed an additional SABA than in other countries. MART became the preferred treatment regimen recommended by GINA in 2019. APPaRENT 1 took place in 2020 and APPaRENT 2 in 2021, meaning by this time physicians may not have started to implement the strategy on a large scale. This may represent a snapshot in time of early MART implementation when the regimen was less understood than now, but it may also offer a guide to countries where more physician education would be valuable. Living in a household with a smoker may contribute to additional SABA prescription, as exposure to cigarette smoke may worsen symptom control [23]. Additional SABA being prescribed to patients with severe and poorly controlled asthma on MART may also reflect physicians' reluctance to leave patients with high symptom burden without a more established reliever.

There was no statistically significant difference in adherence between patients using PRD and MART regimens, owing to variability within the data; however, the odds of adherence were 32% lower with MART compared with PRD. Since the PRD regimen is recommended by GINA when patient adherence to medication is high, the population using PRD might be more likely to be adherent. Additionally, the over-reliance on SABA with MART identified here may contribute to lower adherence to the MART regimen if patients are using a SABA reliever in place of an ICS/formoterol maintenance/reliever inhaler. This suggests that there could be misunderstandings around the intended implementation of MART by both patients and physicians, which could be addressed through physician training in motivational communication to improve patient education and optimize implementation. It is also possible that adherence to PRD may be higher if patients feel that this is an easier or more established regimen to follow than MART.

Even in a future where adherence is optimised for all patients, personalised care that thoroughly considers patient characteristics will continue to be of benefit to inform optimal selection of ICS doses and molecules. For example, the association found between adherence and higher reliever use in this study highlights the existence of patients with poorly controlled asthma not receiving the most appropriate treatment for their disease severity. Assessment of reliever use alongside adherence to maintenance medication may therefore aid physicians in identifying patients who require treatment step-up. In addition to the identified disconnect between treatment goals for patients and physicians, this reinforces the need to consider a broad range of patient characteristics, perspectives, and preferences, including those identified in the APPaRENT studies, to inform future asthma management decisions.

Limitations of this study include those inherent to survey methodology, such as selection and recall bias, particularly as disease severity and patient adherence were self-reported. The limited number of survey responses and recruitment of participants from online panels restricts the generalisability of the findings. As the measure of adherence used here was a binary variable derived from questions in the APPaRENT surveys relating to frequency of maintenance inhaler use, domains such as intentional/unintentional non-adherence could not be captured; however, regardless of the reasons for non-adherence, the consequences for asthma control would be the same. Also, the reported adherence to MART treatment is likely to be an overestimate, because patients use the same inhaler for both maintenance and symptom relief. No quality-of-life treatment goal was given as an option in either APPaRENT survey, which has been identified as an important patient outcome [24,25], and so patient and physician perspectives on this outcome could not be assessed. Future studies should examine both patient and physician perspectives on this. Additionally, data on the types of healthcare provider patients received their prescriptions from were not collected, nor was the type of healthcare and insurance coverage available in each country examined; this information may be useful in future studies to understand how medication access varies. Finally, the MART regimen was relatively recently adopted as the preferred treatment strategy by GINA when the APPaRENT 1 and 2 surveys took place. Differences in the awareness and use of MART between countries may be explained by the timing of MART approval and changing recommendations in various regions. Answers to the survey questions would likely differ if the studies were repeated now.

The strengths of this post-hoc analysis include that data were obtained from nine countries across five continents, capturing a holistic view of asthma treatment practices, perceptions, and outcomes from both patient and physician perspectives. Although adherence was defined as use of ICS-based maintenance therapy at least once per day, when a more stringent definition of more than once per day was set to reflect regimens dosed more than once daily, the same trends were observed in the associations with each patient characteristic.

5. Conclusions

There is a need for refined clinical strategies to improve patient adherence to regular ICS-based maintenance therapy. These efforts should focus on younger patients and those with milder disease and may include implementation and follow-up of asthma action plans, as well as physician training in motivational communication and shared decision-making. Physicians should assess rates of reliever use as well as adherence to maintenance therapy to identify patients with poorly controlled disease despite current medication. More personalised care considering patient characteristics and perspectives is likely to improve adherence and clinical outcomes for patients.

Funding

This work was directly supported by GSK (Study IDs: 212911 and 214325).

Ethical approval

No ethical approval was required for this study as no human participants were recruited or animals used.

Data availability statement

GSK makes available anonymised individual participant data and associated documents from interventional clinical studies which evaluate medicines, upon approval of proposals submitted to https://www.gsk-studyregister.com/en/. To access data for other types of GSK sponsored research, for study documents without patient-level data, and for clinical studies not listed, please submit an enquiry via the website.

CRediT authorship contribution statement

Giorgio Walter Canonica: Writing – review & editing, Writing – original draft, Validation, Conceptualization. **Christian Domingo:** Writing – review & editing, Writing – original draft, Validation, Conceptualization. **Kim L. Lavoie:** Writing – review & editing, Writing – original draft, Validation, Conceptualization. **Amrit Kaliasethi:** Writing – review & editing, Writing – original draft, Methodology, Formal analysis, Conceptualization. **Shireen Quli Khan:** Writing – review & editing, Writing – original draft, Validation, Supervision, Conceptualization. **Anurita Majumdar:** Writing – review & editing, Writing – original draft, Validation, Supervision, Conceptualization. **Sourabh Fulmali:** Writing – review & editing, Writing – original draft, Validation, Supervision, Conceptualization.

Declaration of competing interest

Giorgio Walter Canonica reports having received research grants as well as being a lecturer or having received advisory board fees from A. Menarini, Alk-Abello, Allergy Therapeutics, AstraZeneca, Chiesi Farmaceutici, Firma, Genentech, Guidotti-Malesci, GSK, Hal Allergy, Mylan, Novartis, Regeneron, Roche, Sanofi-Aventis, Sanofi-Genzyme, Stallergenes Greer, Valeas, and OM Pharma, outside the submitted work.

Christian Domingo has received funding for travel or speaker fees from ALK, Almirall, AstraZeneca, Boehringer Ingelheim, Chiesi, GSK, Menarini, Novartis, Stallergenes, Takeda, and Pfizer, and declares no specific conflicts of interest to report regarding this paper.

Kim L. Lavoie reports investigator-initiated research support and speaking fees from AbbVie, consulting fees and speaking fees from Astellas, Boehringer Ingelheim, GSK, X-Factor, Respiplus, and Novartis, consulting fees from Janssen, Sojecci Inc., and AstraZeneca, and speaking fees from Bayer and Mundipharma, outside the submitted work.

Amrit Kaliasethi is an employee of Fishawack Communications Ltd, part of Avalere Health.

Shireen Quli Khan, Anurita Majumdar, and Sourabh Fulmali are full-time employees of GSK and hold shares in GSK.

Acknowledgements

Editorial support (in the form of writing assistance, including preparation of the draft manuscript under the direction and guidance of the authors, collating and incorporating authors' comments for each draft, assembling tables and figures, grammatical editing, and referencing) was provided by Catherine Widnall, PhD, of Fishawack Communications Ltd, part of Avalere Health, and was funded by GSK.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.rmed.2024.107637.

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