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Asthma and rhinitis control in adolescents and young adults: A real-world MASK-air study

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Abstract

Background: In allergic rhinitis and asthma, adolescents and young adult patients are likely to differ from older patients. We compared adolescents, young adults and adults on symptoms, control levels, and medication adherence.

Methods: In a cross-sectional study (2015–2022), we assessed European users of the MASK-air mHealth app of three age groups: adolescents (13–18 years), young adults (18–26 years), and adults (>26 years). We compared them on their reported rhinitis and asthma symptoms, use and adherence to rhinitis and asthma treatment and app adherence. Allergy symptoms and control were assessed by means of visual analogue scales (VASs) on rhinitis or asthma, the combined symptom-medication score (CSMS), and the electronic daily control score for asthma (e-DASTHMA). We built multivariable regression models to compare symptoms or medication accounting for potential differences in demographic characteristics and baseline severity.

Results: We assessed 965 adolescent users (15,252 days), 4595 young adults (58,161 days), and 15,154 adult users (258,796 days). Users of all three age groups displayed similar app adherence. In multivariable models, age groups were not found to

A complete list of the think tank members appears in the 'The MASK-air think tank' section (Appendix Appendix).

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significantly differ in their adherence to rhinitis or asthma medication. These models also found that adolescents reported lower VAS on global allergy, ocular, and asthma symptoms (as well as lower CSMS) than young adults and adults.

Conclusions: Adolescents reported a better rhinitis and asthma control than young adults and adults, even though similar medication adherence levels were observed across age groups. These results pave the way for future studies on understanding how adolescents control their allergic diseases.

KEYWORDS
adherence, adolescents, allergic rhinitis, asthma, digital health, mHealth, real-world data

1 | INTRODUCTION

Adolescence (10–17/18 years of age) is a stage of life characterized by specific health issues that differ from those of childhood or adulthood. Young adulthood (18–26 years) is a newly defined transitional period, which, according to a report from the US Institute of Medicine and the US National Research Council, should be considered as a separate group from adolescence and adulthood (>26 years).[1] The report suggests developing evidence-based practices for young adults for medical and behavioral health.

In allergic diseases, some aspects need to be considered in adolescents or young adults. Asthma in adolescents is often uncontrolled due to several factors including poor adherence to therapy, smoking, and mental health conditions.[2–4] On the other hand, adolescents and young adults may be more prone to using digital health solutions in order to improve self-management. An example of such digital solutions is the MASK-air® app (a DG Santé Good Practice for digitally enabled patient-centered care[5,6]), in which users are requested to report their respiratory allergy symptoms and medication use daily. Differences in app and medication adherence between adolescents, young adults, and adults have never been explored using mHealth tools. Evaluating such differences may be particularly relevant, not only to assess medication adherence with real-world data but also to help understand the role of digital tools in the asthma and allergic rhinitis (AR) management of younger patients.

In this study, the overall aim was to compare adolescent and young adult MASK-air® users with adult users on their AR and asthma symptoms and control levels, as well as on their adherence. In particular, we started by comparing adolescents, young adults, and adults on rhinitis and asthma control and app adherence. Second, in order to assess whether there may be across-age group differences in asthma underreporting, we assessed asthma symptoms in patients with no evidence of asthma, possible asthma, and probable asthma (defined according to previous studies) of the three age groups. Finally, we assessed whether the participants' age group may be associated with differences in allergy medication adherence.

Key message

Using real-world data from a digital health tool, we observed that adolescents reported similar medication adherence, but better rhinitis and asthma control compared with young adults and older adults. These results pave the way for future studies on understanding how adolescents control their allergic diseases.

2 | METHODS

2.1 | Study design

This is a cross-sectional study using MASK-air® data. MASK-air® is a mobile health app freely available on the Google Play and Apple App Stores in 27 countries. MASK-air® has been developed by the Allergic Rhinitis and its Impact on Asthma (ARIA) group and targets adult and adolescent patients with rhinitis and/or asthma.[6] It encompasses a set of visual analogue scales (VASs) assessing the impact of allergy symptoms, which have been assessed on their reliability, validity, and responsiveness.[7] In addition, it encompasses a set of other validated questionnaires, including EQ-5D-5L and the Control of Allergic Rhinitis and Asthma Test.[8]

We compared MASK-air® users of three age groups: (i) adolescents (13–18 years), (ii) young adults (18–26 years), and (iii) adults (>26 years) on demographic characteristics, reported allergy/asthma symptoms, medication use, and adherence to AR and asthma treatment. Although the upper age limit of adolescence may differ, we used 17 years, in accordance with the US Institute of Medicine and the US National Research Council (we performed a sensitivity analysis considering the World Health Organization age group cutoffs).[1]

2.2 | Setting and participants

We included the daily monitoring data provided by European MASK-air® users older than the age of digital consent (which ranges

between 13 and 16 years depending on the country) and with self-reported AR. Participants were either (i) patients followed in clinics who had been enrolled by physicians or (ii) patients who had freely downloaded the app by themselves. We considered data provided between 2015 and 2022.

We were able to classify all patients reporting MASK-air® data in at least three different months as having "no evidence of asthma," "possible asthma" (i.e., (i) patients not self-reporting asthma and not using asthma medication but with moderate or severe asthma symptoms or (ii) patients self-reporting asthma but not using asthma medication and with mild or no asthma symptoms), or "probable asthma" (i.e., patients self-reporting asthma and using asthma treatment or reporting moderate or severe asthma symptoms) using the clustering methods described previously.[9]

2.3 | Ethics

MASK-air® complies with the General Data Protection Regulation.[10] All data are anonymously introduced by users, and geolocation-related data are subsequently "blurred" using k-anonymity.[11] Users consented to having their data analyzed for scientific purposes in the Terms of Use. The use of MASK-air® data for research purposes has been approved by an independent review board (Köln-Bonn, Germany).[12]

2.4 | Data sources and variables

MASK-air® includes a daily monitoring questionnaire assessing (i) the impact of allergy symptoms through four mandatory VASs on a 0–100 scale (Table S1) and (ii) self-reported daily medication use (available through a scroll list customized for each country and regularly updated).

Symptom and medication data daily provided by patients enable the calculation of two daily combined symptom-medication scores from formulae previously published—the CSMS (allergy combined symptom-medication score)[13] and e-DASTHMA (electronic daily control score for asthma).[14]

The responses to the daily questionnaire allow computation of the adherence to the MASK-air® app and to medication. Adherence to the MASK-air® app was defined as the proportion of days on which the patient used MASK-air® during the period from the day when the app was first used until December 31, 2022. For each drug class, medication adherence was computed as the proportion of reported MASK-air® days on which a medication of that class was used. Of note, medication adherence for each drug class was computed only for patients who reported having used a medication of that class for at least one day. Furthermore, only the weeks in which patients answered to the MASK-air® daily monitoring questionnaire for six or seven days were considered (to avoid adherence to the MASK-air® app distorting the computation of medication adherence). We considered that the patient was adherent to medication in the weeks in which medication use was reported in ≥80% of days.

2.5 | Statistical analysis

We assessed all data provided within the defined time period. When responding to the MASK-air® daily monitoring questionnaire, it is not possible to skip any of the questions, and data are saved to the dataset only after the final answer. This precludes any missing data within each questionnaire. All analyses were performed using the software R.

Categorical variables were described using absolute and relative frequencies, while continuous variables were described using medians and interquartile ranges (IQRs). For comparison between different age groups, effect size measures for differences in proportions and medians were estimated. Effect size measures quantify how large the differences between groups are (larger differences being probably more relevant): values <0.2 indicate non-meaningful differences, between 0.2 and 0.5 small differences, between 0.5 and 0.8 moderate differences, and >0.8 large differences.[15] Given the large volumes of data, *p*-values were not computed for descriptive analyses.

We compared users' demographic characteristics, symptom levels, medication use, app adherence, and medication adherence across the age groups. Sub-analyses on VAS asthma and e-DASTHMA levels were performed in users classified as having "no evidence of asthma," "possible asthma," or "probable asthma."[9] In addition, and across the different age groups, we compared VAS asthma levels and frequency of short-acting beta-agonist (SABA) use in weeks when there was adherence to inhaled corticosteroids (ICS) or ICS + long-acting beta-agonists (LABA) versus those in which adherence was not observed. For these sub-analyses, we assessed both median and maximum (per week or user) VAS and e-DASTHMA values.

In order to assess the association between age group and medication adherence, we built multivariable mixed-effects linear regression models. We built regression models assessing that association in oral H_1-antihistamine, intranasal corticosteroids, azelastine-fluticasone, ICS, and ICS + LABA users. For each medication class, the dependent variable of the model corresponded to the weekly medication adherence. The main independent variable concerned the age group of the patient (adolescent, young adult or adult). We "clustered" weeks by users, by country, and by month of the year, setting these variables as random effects. In addition, results were further adjusted for the following independent variables, which were included in our regression models: number of domains impacted by AR ("baseline impact"), number of different AR reported by the patient ("baseline symptoms"), and patients' sex. Similar multivariable regression models were built in order to assess the association between age group and rhinitis or asthma control (with VAS, CSMS, or e-DASTHMA levels as dependent variables).

3 | RESULTS

3.1 | Demographic characteristics

We assessed 965 adolescents (15,252 days), 4595 young adults (58,161 days), and 15,154 adults (258,796 days) (Table 1; Table S2 and Figure S1). The average number of MASK-air® days reported per user ranged from 12.7 (young adults) to 15.8 (adolescents) and 17.1 (adults). Similar results were observed in a sensitivity analysis considering the World Health Organization definition for adolescence (Table S3).

3.2 | Adherence to the MASK-air app

Adherence to the app was similar in the three groups (Table 2). The frequency of users reporting MASK-air® data for at least 6 days a week ranged from 18.8% (young adults) to 22.2% (adolescents), with no trend between age groups.

3.3 | Symptoms and medication use

Visual analogue scales global allergy symptoms, VAS nose, and CSMS displayed similar median values in the three age groups (Table 1). On the other hand, median VAS asthma, VAS eye, and e-DASTHMA levels meaningfully increased from adolescents to young and older adults (effect sizes ranged from 0.33 to 0.75). However, this trend was not seen when comparing user-maximum VAS levels. In multivariable models, age groups showed significant differences in VAS global allergy symptoms, eye and asthma and CSMS. (Table 3).

The frequency of AR medication use was similar in the three age groups (effect sizes <0.2) (Table 1). The percentage of days using asthma medication was not meaningfully different in adults (23.7%) versus adolescents or young adults (17.3%) (effect size = 0.16). Nevertheless, the percentage of days using ICS + LABA was higher for adults (15.1%) than for adolescents (5.2%; effect size = 0.34) and young adults (8.1%; effect size = 0.22).

3.4 | Assessment of VAS asthma and e-DASTHMA in patients with probable, possible and no evidence of asthma

We were able to classify 4256 users as having "no evidence of asthma," "possible asthma," or "probable asthma," with the proportions of users within each classification being similar in the three age groups (Table 4).

For VAS asthma and e-DASTHMA median maximal values, there were no major changes when comparing age groups. On the other hand, for overall median values, particularly for patients with probable asthma, there was a trend to have increased values for both VAS asthma and e-DASTHMA in more advanced age groups.

3.5 | Adherence to medication

In AR, adherence (≥80%) to oral H_1-antihistamines ranged from 35.5% (young adults) to 40.8% (adolescents), with no trend according to age groups (Table S4). Adherence was slightly lower for intranasal corticosteroids (27.4% to 34.9%), with no trend according to age groups. For azelastine-fluticasone, adherence was lower in adolescents (21.1%) than in young adults (41.2%; effect size = 0.44) and adults (31.1%; effect size = 0.23).

In asthma, adherence to ICS was similar in the three age groups (33.9 to 43.6%) (Table 4). On the other hand, adherence to ICS + LABA increased from 28.2% in adolescents to 38.3% in young adults and 64.1% in adults older than 27 years (small and moderate effect sizes). We observed that, for all age groups, VAS asthma and SABA use were higher in weeks with adherence to ICS or ICS-LABA than in weeks in which no adherence was observed (Table 5).

In multivariable models, age groups were not found to be significantly associated with adherence in users of any medication class (Table 6).

4 | DISCUSSION

This is the first mHealth real-world data study to assess differences in asthma and AR symptoms and adherence to treatment in adolescents, young adults, and older adults. Moreover, although several studies have been carried out in adolescent patients with asthma, the group of "young adults" has, to our knowledge, never been considered. In this study, we found that different age groups did not display meaningful differences in allergy medication adherence and that adolescents reported better disease control by comparison to adults.

4.1 | Interpretation of the data

Several studies assessed medication adherence among children or adolescents. Nonadherence in pediatric asthma is a significant issue, with reported adherence rates as low as 24%–30% in adolescents (e.g., reported adherence to ICS ranges from 25 to 35%).[16,17] In an observational cohort study of forty 15- to 18-year-old asthmatic children who were prescribed fluticasone/salmeterol, the median treatment adherence was 43%.[18] Adolescents with asthma have poor adherence, independently of the asthma control grade.[19] Time-based trends among ICS adherence rates published between 1985 and 2012 showed no systematic improvements in intervention effectiveness. In a scoping review, it was shown that many adolescents adapt ICS use according to asthma symptoms, by reducing or eliminating controller medication in the absence of symptoms.[20] The levels of medication adherence reported in those studies were not very different from those observed in this study on adolescents. However, previous studies have not compared adherence in adolescents and other age groups. Of note, the possibility that the actual use of the MASK-air® app has promoted medication adherence is a

TABLE 1 Characteristics of MASK-air® adolescent, young adult, and adult users.

	Days from patients aged 13–17 years (*N* = 15,252)	Days from patients aged 18–26 years (*N* = 58,161)	Days from patients aged 27–64 years (*N* = 258,796)	Effect sizes[a]		
				13–17 vs 18–26 years	13–17 vs 27–64 years	18–26 vs 27–64 years
N users (average days per user)	965 (15.8)	4595 (12.7)	15,154 (17.1)			
Females—*N* (%)	7613 (49.9)	32,765 (56.3)	132,915 (48.4)	0.13	0.03	0.16
Age—mean (SD)	15.7 (1.2)	22.0 (2.7)	42.0 (9.4)	–	–	–
VAS global allergy symptoms						
Users' median—median (IQR)	11 (29)	14 (33)	11 (27)	0.16	0	0.16
Users' maximum—median (IQR)	56 (46)	62 (44)	59 (47)	0.18	0.09	0.09
VAS nose						
Users' median—median (IQR)	11 (30)	14 (35)	12 (27)	0.16	0.06	0.10
Users' maximum—median (IQR)	63 (47)	66 (51)	59 (53)	0.08	0.11	0.19
VAS eyes						
Users' median—median (IQR)	1 (11)	3 (18)	5 (18)	0.61	0.75	0.33
Users' maximum—median (IQR)	36 (61)	33 (58)	36 (57)	0.07	0	0.07
VAS asthma						
Users' median—median (IQR)	2 (12)	4 (20)	8 (24)	0.43	0.69	0.43
Users' maximum—median (IQR)	35 (54)	38 (57)	42 (55)	0.07	0.18	0.10
CSMS						
Users' median—median (IQR)	8.0 (16.4)	10.1 (20.8)	9.7 (18.6)	0.19	0.16	0.03
Users' maximum—median (IQR)	36.7 (29.6)	39.1 (29.2)	38.8 (32.2)	0.11	0.09	0.01
e-DASTHMA						
Users' median—median (IQR)	3.5 (12.7)	6.9 (16.4)	11.7 (18.1)	0.42	0.83	0.51
Users' maximum—median (IQR)	24.5 (33.0)	25.9 (34.5)	28.2 (33.1)	0.06	0.15	0.09
Total days reporting rhinitis medication—*N* (%)	6701 (43.9)	27,430 (47.2)	125,323 (48.4)	0.07	0.09	0.02
OAH monotherapy	3224 (21.1)	13,869 (23.8)	55,224 (21.3)	0.06	0.01	0.06
INCS monotherapy	1160 (7.6)	5068 (8.7)	26,927 (10.4)	0.04	0.10	0.06
AzeFlu monotherapy	529 (3.5)	3440 (5.9)	13,534 (5.2)	0.11	0.08	0.03
OAH + INCS	693 (4.5)	3785 (6.5)	18,790 (7.3)	0.09	0.12	0.03
AzeFlu + other rhinitis medication	569 (3.7)	2778 (4.8)	12,265 (4.7)	0.05	0.05	0.01
Allergen immunotherapy—*N* (%)	1255 (8.2)	6807 (11.7)	27,608 (10.7)	0.12	0.09	0.03
Self-reported asthma—*N* (%)	6122 (40.1)	20,810 (35.8)	106,377 (41.1)	0.09	0.02	0.11

(Continues)

TABLE 1 (Continued)

	Days from patients aged 13–17 years (*N* = 15,252)	Days from patients aged 18–26 years (*N* = 58,161)	Days from patients aged 27–64 years (*N* = 258,796)	Effect sizes[a]		
				13–17 vs 18–26 years	13–17 vs 27–64 years	18–26 vs 27–64 years
Total days reporting asthma medication—*N* (%)[b]	2638 (17.3)	10,046 (17.3)	61,257 (23.7)	0	0.16	0.16
SABA	240 (1.6)	1239 (2.1)	8717 (3.4)	0.04	0.12	0.08
ICS	951 (6.2)	2619 (4.5)	17,012 (6.6)	0.08	0.02	0.09
ICS + LABA	799 (5.2)	4731 (8.1)	39,071 (15.1)	0.12	0.34	0.22
LAMA or biologics	19 (0.1)	422 (0.7)	3658 (1.4)	0.10	0.17	0.07
Conjunctivitis—*N* (%)	10,840 (72.0)	37,142 (67.4)	182,962 (72.5)	0.10	0.01	0.11
Baseline symptoms—median (IQR)	5 (3)	5 (4)	5 (4)	0	0	0
Baseline impact—median (IQR)	1 (3)	2 (3)	2 (3)	0.42	0.42	0

Abbreviations: AzeFlu, Azelastine-fluticasone; CSMS, Combined symptom-medication score; e-DASTHMA, Electronic daily control score for asthma; ICS, Inhaled corticosteroids; INCS, Intranasal corticosteroids; IQR, Interquartile range; LABA, Long-acting beta-agonists; LAMA, Long-acting muscarinic antagonists; OAH, Oral antihistamines; SABA, Short-acting beta-agonists; SD, Standard-deviation; VAS, Visual analogue scale.

[a]The effect sizes quantify how large the differences are between groups. Values <0.2 indicate non-meaningful differences (cells in white), between 0.2 and 0.5 small differences (cells in yellow), between 0.5 and 0.8 moderate differences (cells in orange), and >0.8 large differences (cells in red).

[b]In patients with self-reported asthma.

TABLE 2 Adherence to the MASK-air® app among adolescent, young adult, and adult users.

				Effect sizes[a]		
	Patients aged 13–17 years (*N* = 965)	Patients aged 18–26 years (*N* = 4595)	Patients aged 27–64 years (*N* = 15,154)	13–17 vs 18–26 years	13–17 vs 27–64 years	18–26 vs 27–64 years
MASK-air® adherence (%)—median (IQR)	0.3 (0.9)	0.3 (1.0)	0.3 (1.0)	0	0	0
N full weeks	709	2593	13,919	–	–	–
Users reporting at least one full week—*N* (%)	138 (14.3)	557 (12.1)	2024 (13.4)	0.07	0.03	0.04
N weeks with up to one missing day	1043	3865	19,280	–	–	–
Users reporting at least 1 week with up to one missing day—*N* (%)	214 (22.2)	865 (18.8)	2875 (19.0)	0.08	0.08	0.01
N months with up to four missing days	103	358	2197			
Users reporting at least 1 month with up to four missing days—*N* (%)	36 (3.7)	131 (2.9)	560 (3.7)	0.04	0	0.04

Abbreviation: IQR, Interquartile range.

[a]The effect sizes quantify how large the differences are between groups. Values <0.2 indicate non-meaningful differences, between 0.2 and 0.5 small differences, between 0.5 and 0.8 moderate differences, and >0.8 large differences.

TABLE 3 Results of multivariable models assessing the association between the age group (and other independent variables) and rhinitis and asthma control.

Country	VAS global allergy symptoms	VAS nose	VAS eye	CSMS	VAS asthma[a]	e-DASTHMA[a]
Age group						
Adolescents	–[b]	–[b]	–[b]	–[b]	–[b]	–[b]
Young adults	1.5 (0.5; 2.4) [0.002]	0.7 (−2.3; 1.7) [0.135]	2.2 (1.4; 3.0) [<0.001]	1.2 (0.5; 1.8) [<0.001]	2.0 (0.9; 4.7) [<0.001]	0.3 (−0.4; 1.0) [0.399]
Adults	1.0 (0.1; 2.1) [0.047]	−1.0 (−2.1; 0.1) [0.080]	3.2 (2.3; 4.2) [<0.001]	1.4 (0.7; 2.1) [<0.001]	3.3 (1.9; 4.7) [<0.001]	0.7 (−0.2; 1.6) [0.125]
Male gender	−7.1 (−7.8; −6.3) [<0.001]	−6.2 (−7.0; −5.5) [<0.001]	−4.6 (−5.3; −3.9) [<0.001]	−5.2 (−5.7; −4.7) [<0.001]	−5.1 (−6.4; −3.9) [<0.001]	−3.7 (−4.5; −2.9) [<0.001]
Baseline impact	1.5 (1.2; 1.9) [<0.001]	1.4 (1.1; 1.7) [<0.001]	0.2 (−0.1; 0.5) [0.135]	1.1 (0.8; 1.3) [<0.001]	2.0 (1.5; 2.5) [<0.001]	1.3 (0.9; 1.6) [<0.001]
Baseline symptoms	−0.5 (−0.7; −0.4) [<0.001]	−0.6 (−0.8; −0.4) [<0.001]	0.9 (0.8; 1.1) [<0.001]	−0.2 (−0.3; −0.1) [0.002]	−0.9 (−1.2; −0.6) [<0.001]	−0.6 (−0.8; −0.4) [<0.001]

Note: Results are expressed as regression coefficients (95% confidence intervals) [*p*-value].

Abbreviations: CSMS, Combined symptom-medication score; e-DASTHMA, Electronic daily control score for asthma; VAS, Visual analogue scale.

[a]Data for patients self-reporting asthma.

[b]Reference category.

TABLE 4 Visual analogue scale (VAS) asthma and e-DASTHMA levels in patients with no evidence of asthma, possible asthma and probable asthma depending on the age group.

	Days from patients aged 13–17 years	Days from patients aged 18–26 years	Days from patients aged 27–64 years	Effect sizes[a]		
				13–17 vs 18–26 years	13–17 vs 27–64 years	18–26 vs 27–64 years
No evidence of asthma						
Members—*N* (%)	110 (40.7)	356 (41.7)	1039 (33.2)			
VAS asthma						
Users' median—median (IQR)	0 (0)	0 (0)	0 (0)	0	0	0
Users' maximum—median (IQR)	1 (6)	3 (8)	5 (9)	0.60	0.93	0.38
e-DASTHMA						
Users' median—median (IQR)	0 (0)	0 (0)	0 (0)	0	0	0
Users' maximum—median (IQR)	0.6 (3.5)	1.7 (4.6)	2.9 (5.2)	0.60	0.93	0.38
Possible asthma						
Members—*N* (%)	76 (28.1)	216 (25.3)	889 (28.4)			
VAS asthma						
Users' median—median (IQR)	0 (6)	1 (8)	1 (8)	0.96	0.96	0
Users' maximum—median (IQR)	37 (41)	36 (38)	45 (39)	0.03	0.27	0.34
e-DASTHMA						
Users' median—median (IQR)	0 (3.5)	0.6 (4.6)	0.6 (4.6)	0.95	0.95	0
Users' maximum—median (IQR)	21.7 (23.6)	21.3 (21.9)	26.5 (22.5)	0.02	0.27	0.32
Probable asthma						
Members—*N* (%)	84 (31.1)	281 (32.9)	1205 (38.5)			
VAS asthma						
Users' median—median (IQR)	1 (9)	2 (17)	8 (23)	0.43	0.83	0.69
Users' maximum—median (IQR)	59 (38)	59 (42)	62 (42)	0	0.12	0.10
e-DASTHMA						
Users' median—median (IQR)	2.9 (4.3)	7.2 (15.2)	11.8 (17.5)	0.53	0.96	0.40
Users' maximum—median (IQR)	38.3 (23.9)	39.7 (25.6)	41.7 (25.9)	0.08	0.19	0.10

Abbreviations: e-DASTHMA, Electronic daily control score for asthma; IQR—Interquartile range.

[a]The effect sizes quantify how large the differences are between groups. Values <0.2 indicate non-meaningful differences (cells in white), between 0.2 and 0.5 small differences (cells in yellow), between 0.5 and 0.8 moderate differences (cells in orange), and >0.8 large differences (cells in red).

hypothesis that cannot be excluded, but which can only be assessed by future studies (as we had no information on medication adherence prior to the start of MASK-air® use).

Adherence to AR medication has not been well-studied. Existing studies estimate adherence to be at around 30% in specialists' surgeries.[21–23] However, no study has ever specifically investigated adolescents.

Curiously, adherence to the MASK-air® app was similar across age groups. Therefore, we observed neither (i) higher MASK-air® adherence among adolescents due to a potentially higher digital proficiency among the latter nor (ii) lower MASK-air® adherence among adolescents due to potentially less compliant behaviors.

Even though no meaningful differences were observed in medication (or app) adherence when comparing age groups, adolescents reported lower VAS asthma, VAS eye, and e-DASTHMA levels. Overall, this finding may suggest that patients of all age groups use allergy medications according to their symptoms, with adolescents achieving better levels of control with the same levels of adherence. Another explanation may be related to the fact that, being a digital tool, physicians may recommend MASK-air® more often to adolescents (and young adults) than to older adults (and that there may be a larger overrepresentation of more severe patients among adult MASK-air® users than among adolescents).

Finally, in the "no evidence of asthma" group, median VAS asthma and e-DASTHMA were similar in adolescents and in the remaining age groups, while maximum values were lower. This suggests that the underreporting or underdiagnosis of asthma may not be more common in adolescents than in other age groups. Furthermore, in patients with "possible asthma" and "probable asthma," there was no evidence suggesting that adolescents had a worse disease control.

4.2 | Limitations and strengths

This study has some limitations. First, the age of digital consent is not the same in all assessed countries. This may possibly explain

TABLE 5 Visual analogue scale (VAS) levels and short-acting beta-agonist (SABA) use in weeks with adherence and weeks with no adherence to inhaled corticosteroids (ICS) or ICS + long-acting beta-agonists (LABA) in MASK-air® users of different age groups.

				Effect sizes[a]		
	Patients aged 13–17 years	Patients aged 18–26 years	Patients aged 27–64 years	13–17 vs 18–26 years	13–17 vs 27–64 years	18–26 vs 27–64 years
A. ICS users						
All weeks						
Weekly median VAS asthma—median (IQR)	2 (8)	0 (5)	6 (21)	0.95	0.60	0.95
Weekly maximum VAS asthma—median (IQR)	7 (17)	6 (23)	15 (31)	0.10	0.49	0.56
Days using SABA (%)	1.6	2.7	7.3	0.08	0.29	0.22
Weeks with no medication adherence						
Weekly median VAS asthma—median (IQR)	0 (6)	0 (3)	5 (19)	0	0.95	0.95
Weekly maximum VAS asthma—median (IQR)	5 (12)	5 (24)	13 (29)	0	0.55	0.55
Days using SABA (%)	0.8	1.0	5.1	0.02	0.28	0.26
Weeks with medication adherence						
Weekly median VAS asthma—median (IQR)	6 (18)	3 (10)	7 (26)	0.43	0.10	0.50
Weekly maximum VAS asthma—median (IQR)	15 (30)	7 (21)	16 (36)	0.55	0.05	0.55
Days using SABA (%)	3.2	4.5	10.1	0.07	0.29	0.22
B. ICS-LABA users						
All weeks						
Weekly median VAS asthma—median (IQR)	2 (7)	5 (23)	9 (20)	0.53	0.72	0.37
Weekly maximum VAS asthma—median (IQR)	11 (21)	17 (44)	19 (31)	0.31	0.49	0.09
Days using SABA (%)	2.9	7.3	9.6	0.20	0.29	0.08
Weeks with no medication adherence						
Weekly median VAS asthma—median (IQR)	0 (5)	3 (21)	8 (18)	0.95	0.95	0.56
Weekly maximum VAS asthma—median (IQR)	7 (20)	16 (42)	19 (29)	0.49	0.77	0.14
Days using SABA (%)	1.7	7.6	5.8	0.30	0.22	0.07
Weeks with medication adherence						
Weekly median VAS asthma—median (IQR)	6 (14)	7 (25)	10 (21)	0.10	0.35	0.25
Weekly maximum VAS asthma—median (IQR)	18 (20)	21 (46)	19 (31)	0.14	0.08	0.06
Days using SABA (%)	6.2	6.9	11.7	0.03	0.19	0.17

Abbreviation: IQR, Interquartile range.

[a]The effect sizes quantify how large the differences are between groups. Values <0.2 indicate non-meaningful differences (cells in white), between 0.2 and 0.5 small differences (cells in yellow), between 0.5 and 0.8 moderate differences (cells in orange), and >0.8 large differences (cells in red).

TABLE 6 Results of multivariable models assessing the association between the age group (and other independent variables) and weekly percent adherence.

Country	Oral antihistamines	Intranasal steroids	Azelastine-fluticasone	ICS	ICS + LABA
Age group					
Adolescents	_[a]	_[a]	_[a]	_[a]	_[a]
Young adults	−0.7 (−6.1; 4.7) [0.793]	−1.5 (−9.7; 6.8) [0.729]	−3.4 (−12.2; 5.4) [0.451]	−4.1 (−23.1; 14.9) [0.671]	−4.1 (−12.1; 3.8) [0.306]
Adults	0.1 (−5.4; 5.5) [0.989]	−1.2 (−9.1; 6.8) [0.773]	−7.2 (−16.8; 2.4) [0.141]	−11.8 (−29.1; 5.5) [0.183]	3.0 (−6.4; 12.4) [0.534]
Male gender	−3.5 (−6.2; −0.8) [0.012]	−1.1 (−5.0; 2.8) [0.580]	3.2 (−2.5; 8.9) [0.277]	−7.4 (−15.5; 0.7) [0.074]	−0.2 (−6.1; 5.8) [0.955]
Baseline impact	0.5 (−0.6; 1.6) [0.364]	1.6 (0.1; 3.1) [0.039]	1.7 (−0.5; 3.9) [0.137]	−0.5 (−3.7; 2.7) [0.751]	−1.3 (−3.5; 1.0) [0.280]
Baseline symptoms	−0.4 (−1.0; 0.3) [0.302]	−1.2 (−2.2; −0.3) [0.010]	−2.4 (−3.8; −1.0) [<0.001]	−0.3 (−2.4; 1.9) [0.811]	−0.1 (−1.5; 1.4) [0.928]

Note: Results are expressed as regression coefficients (95% confidence intervals) [*p*-value].

Abbreviation: ICS, Inhaled corticosteroids; LABA, Long-acting beta-agonists.

[a]Reference category.

differences in the country distribution of adolescent versus adult MASK-air® users. Another limitation may concern baseline severity differences among participants of the different age groups (associated with the overall limitation that participants of different age groups may come from different populations). This may be so if, given the trend for a higher digital proficiency among adolescents, (i) physicians tend to recommend the use of MASK-air® more frequently to adolescents than to adults and (ii) a higher proportion of adolescents started to use MASK-air® after finding it online. Unfortunately, due to anonymization procedures, it is not possible to know how each patient started to use MASK-air®. Overall, we cannot exclude potential selection bias for any of the age groups compared with the general population on healthcare access, disease severity, or motivation.

The analysis was not performed on patients from allergy clinics with a physician-confirmed diagnosis, as that type of study would have had a limited number of patients and would have mostly included patients under treatment and with more severe disease. We have, however, found MASK-air® asthma classification to be consistent with a physician assessment of asthma in a subset of patients.[9]

Another limitation is that patients do not answer to MASK-air® every day, resulting in some variability in app usage patterns. However, overall, patients are more likely to answer to the MASK-air® daily monitoring questionnaire on the days when they have more severe symptoms. Therefore, the reported weeks are not necessarily representative of all yearly weeks (given that patients tend to use more medication when feeling worse, there may have been an overestimation of medication adherence in this study). However, we believe this to be a non-differential bias across age groups.

This study also has important strengths. We assessed real-world data provided by a large number of patients, helping to understand patients' behavior toward allergy control in a real-world context. In addition, we assessed adherence by applying multivariable models adjusting for patients' demographic characteristics and baseline severity. Finally, the MASK-air® VASs, CSMS, and e-DASTHMA display high validity, reliability, and responsiveness.[7,13,14]

5 | CONCLUSION

Although digital observational studies are only hypothesis-generating and need to be confirmed by appropriate studies, the current study found a similar adherence to medication reported by adolescents, young adults, and older adults. However, adolescents reported better symptom control for several outcomes in AR and asthma. These results suggest that adherence to medication may not be so different in adolescents compared with patients of other age groups. In addition, we did not observe worse allergy control or higher risk of asthma underdiagnosis/underreporting in adolescents compared with patients of the remaining age groups. The results pave the way for future studies on understanding how adolescents control their allergic diseases.

AUTHOR CONTRIBUTIONS

Bernardo Sousa-Pinto carried out the analyses and drafted the initial manuscript. Jean Bousquet and Nhan Pham-Thi conceptualized and designed the study, drafted the initial manuscript, and critically reviewed and revised the manuscript. Arunas Valiulis, Erik Melén and Josep M. Antó conceptualized and designed the study, and critically reviewed and revised the manuscript. Gerard H. Koppelman, Nikolaos G. Papadopoulos, Mika Makela, Tari Haahtela, Matteo Bonini, Fulvio Braido, Luisa Brussino, Alvaro A. Cruz, Alessandro Fiocchi, Mattia Giovannini, Bilun Gemicioglu, Marek Kulus, Piotr Kuna, Maciej Kupczyk, Violeta Kvedariene, Désirée E. Larenas-Linnemann, Renaud Louis, Mario Morais-Almeida, Marek Niedoszytko, Markus Ollert, Oliver Pfaar, Frederico S. Regateiro, Graham Roberts, Boleslaw Samolinski, Marine Savouré, Luís Taborda-Barata, Sanna Toppila-Salmi, Maria Teresa Ventura, Marta Vazquez-Ortiz, Rafael José Vieira, João A. Fonseca, Arzu Yorgancioglu and Torsten Zuberbier participated in data collection and critically reviewed and revised the manuscript. All authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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APPENDIX

The MASK-air think tank: Members of the MASK-air think tank include:

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