

Impairment of EQ-5D-5L Domains According to Allergic Rhinitis and Asthma Control: A MASK-air Real-World Study



Bernardo Sousa-Pinto, PhD^{a,b,*}, Gilles Louis, PhD^{c,*}, Jorge Rodrigues, MD^{a,b,d,e}, Antonio Francesco Maria Giuliano, MD^f, Ilaria Baiardini, PhD^{g,h}, Fulvio Braido, MD^{g,h}, Wienczysława Czarlewski, MD^{i,j}, Anna Bedbrook, BSc^{i,k}, Tari Haahtela, MD^l, Arunas Valiulis, MD^{m,n}, Luisa Brussino, MD^{o,p}, Lorenzo Cecchi, MD^q, Alvaro A. Cruz, MD^r, Bilun Gemicioglu, MD^s, Wytse J. Fokkens, MD^t, Juan Carlos Ivancevich, MD^u, Ludger Klimek, MD^{v,w}, Helga Kraxner, MD^x, Piotr Kuna, MD^y, Maciej Kupczyk, MD^y, Violeta Kvedariene, MD^{z,aa}, Désirée Larenas-Linnemann, MD^{bb}, Renaud Louis, MD^{cc,dd}, Rachel Nadif, MD^{ee,ff}, Marek Niedożytko, MD^{gg}, Yoshitaka Okamoto, MD^{hh,ii}, Markus Ollert, MD^{jj,kk,ll}, Nikolaos G. Papadopoulos, MD^{mm}, Vincenzo Patella, MD^{nn,oo,pp}, Ruby Pawankar, MD^{qq}, Nhat Pham-Thi, MD^{rr,ss,tt}, Oliver Pfaar, MD^{uu}, Frederico S. Regateiro, MD^{vv,ww,xx,yy}, Nicolas Roche, MD^{zz,aaa}, Philip W. Rouadi, MD^{bbb,ccc}, Boleslaw Samolinski, MD^{ddd}, Joaquin Sastre, MD^{eee}, Marine Saviouré, MD^{ee,ff}, Nicola Scichilone, MD^{fff}, Aziz Sheikh, MD^{ggg}, Luís Taborda-Barata, MD^{hhh,iii}, Sanna Toppila-Salmi, MD^l, Arzu Yorgancioglu, MD^{jjj}, Mihaela Zidarn, MD^{kkk,lll}, Josep M. Anto, MD^{mmm,nnn,ooo}, Torsten Zuberbier, MD^{ppp,qqq}, G. Walter Canonica, MD^{rrr,sss}, Maria Teresa Ventura, MD^{f,ttt}, João A. Fonseca, MD^{a,b}, Benoit Pétré, MD^c, and Jean Bousquet, MD^{ppp,qqq}

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What is already known about this topic? Asthma and rhinitis are associated with lower quality of life, as assessed by tools such as the EQ-5D-5L (EuroQOL, 5 Domains, 5 Levels) questionnaire. However, the impact of rhinitis or asthma control in each of the different EQ-5D-5L domains has remained unclear.

What does this article add to our knowledge? In this mHealth-based real-world data study, worse rhinitis and asthma control were associated with higher pain/discomfort and greater impairments in the performance of daily activities. Worse rhinitis control was also associated with anxiety/depression, whereas worse asthma control was associated with worse mobility.

How does this study impact current management guidelines? This study points to the importance of an adequate asthma and rhinitis control, as these conditions appear to (distinctly) impact key quality-of-life domains.

BACKGROUND: EQ-5D-5L (EuroQOL, 5 Domains, 5 Levels) is a widely used health-related quality-of-life instrument, comprising 5 domains. However, it is not known how each domain is impacted by rhinitis or asthma control. **OBJECTIVE:** To assess the association between rhinitis or asthma control and the different EQ-5D-5L domains using data from the MASK-air mHealth app.

METHODS: In this cross-sectional study, we assessed data from all MASK-air users (2015-2021; 24 countries). For the levels of each EQ-5D-5L domain, we assessed rhinitis and asthma visual analog scales (VASs) and the combined symptom-medication score (CSMS). We built ordinal multivariable models assessing the adjusted association between VAS/CSMS values and the levels of each EQ-5D-5L domain. Finally, we compared

^aMEDCIDS—Department of Community Medicine, Information and Health Decision Sciences, Faculty of Medicine, University of Porto, Porto, Portugal

^bCINTESIS@RISE—Health Research Network, Faculty of Medicine, University of Porto, Porto, Portugal

^cDepartment of Public Health, University of Liège, Liège, Belgium

^dOtorhinolaryngology Department, Centro Hospitalar Universitário de S João, EPE, Porto, Portugal

^eUnit of Anatomy, Department of Biomedicine, Faculty of Medicine, University of Porto, Porto, Portugal

^fDepartment of Internal Medicine 'A. Murri' and Unit of Geriatric Immunology, University of Bari Medical School, Bari, Italy

Abbreviations used

CI- Confidence interval

CSMS- Combined symptom-medication score

EQ-5D-5L- EuroQOL, 5 Domains, 5 Levels

HR-QOL- Health-related quality of life

OR- Odds ratio

RQLQ- Rhinoconjunctivitis Quality-of-Life Questionnaire

SD- Standard deviation

SF-36- 36-Item Short Form Survey

VAS- Visual analog scale

EQ-5D-5L data from users with rhinitis and self-reported asthma with data from users with rhinitis alone.

RESULTS: We assessed 5354 days from 3092 users. We observed an association between worse control of rhinitis or asthma (higher VASs and CSMS) and worse EQ-5D-5L levels. In multivariable models, all VASs and the CSMS were associated with higher levels of pain/discomfort and daily activities. For anxiety/depression, the association was mostly observed for rhinitis-related tools (VAS nose, VAS global, and CSMS), although the presence of self-reported asthma was also associated

with worse anxiety/depression. Worse mobility (“walking around”) was particularly associated with VAS asthma and with the presence of asthma.

CONCLUSIONS: A worse rhinitis control and a worse asthma control are associated with higher EQ-5D-5L levels, particularly regarding pain/discomfort and activity impairment. Worse rhinitis control is associated with worse anxiety/depression, and poor asthma control with worse mobility. © 2023 American Academy of Allergy, Asthma & Immunology (J Allergy Clin Immunol Pract 2023;11:3742-51)

Key words: Allergic rhinitis; Asthma; Mobile health; Quality of life

The EQ-5D-5L (EuroQOL, 5 Domains, 5 Levels) questionnaire is the most widely used generic health-related quality-of-life (HR-QOL) instrument for (1) assessing and comparing the effects of health care interventions and (2) valuing health.¹ Since 2008, this tool has been the preferred measure of HR-QOL in adults by the National Institute for Health and Excellence (UK) for the support of economic evaluation in health.^{2,3} The EQ-5D-5L includes 5 items reflecting the domains of mobility, self-care, activities, pain/discomfort, and anxiety/depression. Patients can

^gRespiratory Clinic, Department of Internal Medicine, University of Genoa, Genoa, Italy

^hIRCCS Ospedale Policlinico San Martino, Genoa, Italy

ⁱMedical Consulting Czarlewski, Levallois, France

^jMASK-air, Montpellier, France

^kARIA, Montpellier, France

^lSkin and Allergy Hospital, Helsinki University Hospital, University of Helsinki, Helsinki, Finland

^mInterdisciplinary Research Group of Human Ecology, Institute of Clinical Medicine and Institute of Health Sciences, Medical Faculty of Vilnius University, Vilnius, Lithuania

ⁿEuropean Academy of Paediatrics, (EAP/UEMS-SP), Brussels, Belgium

^oDepartment of Medical Sciences, University of Torino, Torino, Italy

^pAllergy and Clinical Immunology Unit, Mauriziano Hospital, Torino, Italy

^qSOS Allergology and Clinical Immunology, USL Toscana Centro, Prato, Italy

^rFundação ProAR, Federal University of Bahia and GARD/WHO Planning Group, Salvador, Bahia, Brazil

^sDepartment of Pulmonary Diseases, Istanbul University-Cerrahpaşa, Cerrahpaşa Faculty of Medicine, Istanbul, Turkey

^tDepartment of Otorhinolaryngology, Amsterdam University Medical Centres, Amsterdam, the Netherlands

^uServicio de Alergia e Inmunología, Clínica Santa Isabel, Buenos Aires, Argentina

^vDepartment of Otolaryngology, Head and Neck Surgery, Universitätsmedizin Mainz, Mainz, Germany

^wCenter for Rhinology and Allergology, Wiesbaden, Germany

^xDepartment of Otorhinolaryngology, Head and Neck Surgery, Semmelweis University, Budapest, Hungary

^yDivision of Internal Medicine, Asthma and Allergy, Barlicki University Hospital, Medical University of Lodz, Lodz, Poland

^zInstitute of Clinical Medicine, Clinic of Chest Diseases and Allergology, Faculty of Medicine, Vilnius University, Vilnius, Lithuania

^{aa}Department of Pathology, Institute of Biomedical Sciences, Faculty of Medicine, Vilnius University, Vilnius, Lithuania

^{bb}Center of Excellence in Asthma and Allergy, Médica Sur Clinical Foundation and Hospital, México City, Mexico

^{cc}Department of Pulmonary Medicine, CHU Liège, Liège, Belgium

^{dd}GIGA I3 Research Group, University of Liège, Liège, Belgium

^{ee}Université Paris-Saclay, UVSQ, Univ. Paris-Sud, Villejuif, France

^{ff}Inserm, Equipe d'Epidémiologie Respiratoire Intégrative, CESP, Villejuif, France

^{gg}Department of Allergology, Medical University of Gdańsk, Gdansk, Poland

^{hh}Chiba Rosai Hospital, Chiba, Japan

ⁱⁱChiba University Hospital, Chiba, Japan

^{jj}Department of Infection and Immunity, Luxembourg Institute of Health, Esch-sur-Alzette, Luxembourg

^{kk}Department of Dermatology and Allergy Centre, Odense University Hospital, Odense, Denmark

^{ll}Odense Research Center for Anaphylaxis (ORCA), Odense, Denmark

^{mm}Allergy Department, 2nd Pediatric Clinic, University of Athens, Athens, Greece

ⁿⁿDivision of Allergy and Clinical Immunology, Department of Medicine, “Santa Maria della Speranza” Hospital, Battipaglia, Salerno, Italy

^{oo}Agency of Health ASL, Salerno, Italy

^{pp}Postgraduate Programme in Allergy and Clinical Immunology, University of Naples Federico II, Naples, Italy

^{qq}Department of Pediatrics, Nippon Medical School, Tokyo, Japan

^{rr}Ecole Polytechnique de Palaiseau, Palaiseau, France

^{ss}IRBA (Institut de Recherche Bio-Médicale des Armées), Brétigny sur Orge, France

^{tt}Université Paris Cité, Paris, France

^{uu}Section of Rhinology and Allergy, Department of Otorhinolaryngology, Head and Neck Surgery, University Hospital Marburg, Philipps-Universität Marburg, Marburg, Germany

^{vv}Allergy and Clinical Immunology Unit, Centro Hospitalar e Universitário de Coimbra, Coimbra, Portugal

^{ww}Center for Innovative Biomedicine and Biotechnology (CIBB), Faculty of Medicine, University of Coimbra, Coimbra, Portugal

^{xx}Institute of Immunology, Faculty of Medicine, University of Coimbra, Coimbra, Portugal

^{yy}UBIAir - Clinical & Experimental Lung Centre and CICS-UBI Health Sciences Research Centre, University of Beira Interior, Covilhã, Portugal

^{zz}Pneumologie, AP-HP Centre Université de Paris Cité, Hôpital Cochin, Paris, France

^{aaa}UMR 1016, Institut Cochin, Paris, France

^{bbb}Department of Otolaryngology-Head and Neck Surgery, Eye and Ear University Hospital, Beirut, Lebanon

^{ccc}Department of Otorhinolaryngology-Head and Neck Surgery, Dar Al Shifa Hospital, Salimiya, Kuwait

^{ddd}Department of Prevention of Environmental Hazards, Allergology and Immunology, Medical University of Warsaw, Warsaw, Poland

^{eee}Allergy Service, Fundacion Jimenez Diaz, Autonoma University of Madrid, CIBERES-ISCI, Madrid, Spain

^{fff}PROMISE Department, University of Palermo, Palermo, Italy

^{ggg}Usher Institute, the University of Edinburgh, Edinburgh, United Kingdom

^{hhh}Department of Immunoallergology, Cova da Beira University Hospital Centre, Covilhã, Portugal

ⁱⁱⁱUBIAir—Clinical & Experimental Lung Centre and CICS-UBI Health Sciences Research Centre, University of Beira Interior, Covilhã, Portugal

rate their status for each domain using a 5-level scale (no/slight/moderate/severe/extreme problems). The EQ-5D-5L also contains one visual analog scale (VAS) for patients to self-assess their overall health status from 0 (worst imaginable health) to 100 (best possible health).

In the context of respiratory allergic diseases, a recent meta-analysis has found that patients with uncontrolled asthma have lower EQ-5D-5L levels.⁴ However, for asthma, the EQ-5D-5L has been reported as a less sensitive measure than asthma-specific questionnaires,⁵ as (1) it does not react very sensitively to small changes in asthma control⁶ and (2) its VAS is less sensitive than the Asthma Control Questionnaire-6 for assessing asthma control.⁷ In rhinitis, the EQ-5D-5L has also been used (eg, for the estimation of utilities).⁸

Although the EQ-5D-5L has been applied to patients with asthma and rhinitis, the association between each individual EQ-

5D-5L domain and the daily control of asthma or rhinitis is unclear. Such an association may be explored using observational studies with real-world data, which play an increasing role in healthcare decisions. Real-world data relate to patient health status and/or to the delivery of health care and are routinely collected from a variety of sources including mHealth apps.⁹ Among these mHealth apps, MASK-air allows for an assessment of the association between allergy control and EQ-5D-5L.¹⁰ In fact, this mHealth app for digitally-enabled, patient-centered care in rhinitis and asthma multimorbidity allows patients to daily report their global allergy, nasal, ocular, and asthma symptoms (by means of VASs)¹¹ and to answer to the EQ-5D-5L.¹ mHealth apps may also enable the clarification of another understudied question, namely, whether patients with rhinitis alone compared with those with rhinitis and asthma differ in the EQ-5D-5L domains. Rhinitis and asthma are often

^{jjj}Department of Pulmonary Diseases, Celal Bayar University, Faculty of Medicine, Manisa, Turkey

^{kkk}University Clinic of Respiratory and Allergic Diseases, Golnik, Slovenia

^{lll}University of Ljubljana, Faculty of Medicine, Ljubljana, Slovenia

^{mmm}ISGlobal, Barcelona Institute for Global Health, Barcelona, Spain

ⁿⁿⁿUniversitat Pompeu Fabra (UPF), Barcelona, Spain

^{ooo}CIBER Epidemiología y Salud Pública (CIBERESP), Barcelona, Spain

^{ppp}Fraunhofer Institute for Translational Medicine and Pharmacology ITMP, Allergology and Immunology, Berlin, Germany

^{qqq}Institute of Allergology, Charité—Universitätsmedizin Berlin, Corporate Member of Freie Universität Berlin and Humboldt-Universität zu Berlin, Berlin, Germany

^{rrr}Department of Biomedical Sciences, Humanitas University, Pieve Emanuele, Milan, Italy

^{sss}IRCCS Humanitas Research Hospital, Rozzano, Milan, Italy

^{ttt}Institute of Sciences of Food Production, National Research Council (ISPA-CNR), Bari, Italy

*These authors contributed equally to the paper.

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Corresponding author: Jean Bousquet, MD, Fraunhofer Institute for Translational Medicine and Pharmacology (ITMP), Immunology and Allergology, Paul-Ehrlich-Haus, Hindenburgdamm 30, Haus II, 12203 Berlin, Germany. E-mail: jean.bousquet@orange.fr.

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comorbid in the same patient, and the relative impact of EQ-5D-5L domains attributed to each disease is unknown. Moreover, it appears that rhinitis alone and rhinitis and asthma represent 2 distinct phenotypes with different control levels of nasal symptoms.¹²

This study aimed to assess the association between rhinitis or asthma control and the different domains of EQ-5D-5L using data from MASK-air, an mHealth tool.

METHODS

Study design

This cross-sectional study assessed all MASK-air days on which the EQ-5D-5L questionnaire was reported. We compared rhinitis and asthma control across the different domains of the EQ-5D-5L questionnaire. We computed median rhinitis and asthma VAS and combined symptom-medication score (CSMS) values across different levels of each EQ-5D-5L domain. In addition, we built multivariable models assessing the adjusted association between VAS/CSMS values and each EQ-5D-5L domain. Finally, we compared data from users with rhinitis and self-reported asthma with data from users with rhinitis alone.

Settings and participants

MASK-air has been launched in 27 countries (www.mask-air.com). It has been freely available on the Google Play and Apple App Stores since 2015. In this study, we included data from MASK-air users from May 21, 2015 to December 2021. The users (1) had a self-reported diagnosis of allergic rhinitis and (2) ranged in age from 16 to 90 years (or lower than 16 years in countries with a lower age of digital consent).^{13,14}

Ethics

MASK-air has a CE1 marking. It follows the General Data Protection Regulation.¹⁵ An independent review board was not required for this specific study as (1) the use of MASK-air secondary data has been approved by an independent review board (Bohn-Köln),¹⁶ (2) all data were anonymized before the study using k-anonymity, and (3) users agreed to the analysis of their data for research purposes in the terms of use (translated into all languages and customized according to the legislation of each country).

Independent variables and outcomes

The MASK-air app comprises a daily monitoring questionnaire assessing (1) the impact of asthma and rhinitis symptoms (ie, self-reported asthma and rhinitis control) on a daily basis by means of 0 to 100 VASs (with a higher score corresponding to a higher impact of allergy symptoms/poorer allergy control) (Table E1, available in this article's Online Repository at www.jaci-inpractice.org), and (2) the daily use of asthma and rhinitis medications (available from country-specific lists with prescribed and over-the-counter medications).¹⁰ Data from daily-reported symptoms and medication use allow for the computation of the Allergic Rhinitis and Its Impact on Asthma-European Academy of Allergy and Clinical Immunology CSMS (a 0-100 score assessing allergy control, taking into account both reported allergy symptoms and medication use), according to the following formula:¹⁷

$$[(0.037 \times \text{VAS global symptoms}) + (0.033 \times \text{VAS eyes}) + (0.020 \times \text{VAS nose}) + (0.027 \times \text{VAS asthma}) + (0.450 \text{ if intranasal MP azelastine-fluticasone is used}) + (0.424 \text{ if nasal steroids are used}) + (0.243 \text{ if asthma medication is used}) + (0.380 \text{ if other rhinitis relief medication is used})] \times 7.577$$

A MASK-air VAS value of 0 is indicative of full allergy control, whereas values of 1-20 point to good control, 21-35 to medium control, and 36-100 to poor control.¹⁸ On the other hand, for the CSMS, values of 0-15.8 correspond to good allergy control, 15.8-35.3 to medium control, and 35.3-100 to poor control.¹⁷

The full EQ-5D-5L questionnaire was included in the third iteration of MASK-air as an optional questionnaire (May 2016), not mandatory within the daily monitoring questionnaire (Table E1, available in this article's Online Repository at www.jaci-inpractice.org).¹

Sample size

Data from all users meeting the inclusion criteria were included. No sample size calculation was performed.

Biases

There are potential information biases related to the self-reported nature of the data collection. There may be an over-representation of users with moderate-to-severe allergy¹⁹ and of younger individuals.

Data analysis

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. All analyses were performed using the R software (version 4.0.0; R Foundation for Statistical Computing, Vienna, Austria).

Categorical variables were described using absolute and relative frequencies. Continuous variables were described using medians and quartiles or means and standard deviations (SDs). For each EQ-5D-5L domain, we assessed median VAS and CSMS levels per EQ-5D-5L level (given the low number of observations on the EQ-5D-5L levels 4 or 5, we analyzed them together). For analyses involving VAS asthma, only the data from users' self-reported asthma were considered. As aging is associated with increased morbidity, we performed sensitivity analyses restricted to MASK-air users aged less than 65 years.

To further assess the association between rhinitis or asthma control and EQ-5D-5L levels, we built ordinal hierarchical (mixed-effects) regression models,²⁰ with each EQ-5D-5L domain as the dependent variable. For each EQ-5D-5L domain, we built 5 multivariable models, with each of the VAS/CSMS (VAS global allergy symptoms, VAS nose, VAS eye, VAS asthma, and CSMS) as an independent variable. We also adjusted for the patients' age, gender, number of baseline symptoms affected by respiratory allergy, number of baseline domains affected by respiratory allergy, self-reported presence of asthma, use of rhinitis or asthma medication, use of allergen immunotherapy, and the other domains of the EQ-5D-5L (ie, those not being considered as the dependent variable in each model). The identification of the user was included in the models as a random effect (ie, observations were "clustered" by a MASK-air user). In our main models, the VASs or the CSMS were included as continuous variables.

Finally, we compared patients with rhinitis alone with those with rhinitis + self-reported asthma. In particular, for each EQ-5D-5L domain, we compared the frequency of observations of each level in users with rhinitis alone versus those with rhinitis + asthma. Frequencies were compared by the computation of effect sizes based on standardized differences in accordance with Cohen.²¹ We considered clinically meaningful effect sizes as those higher than 0.2. We considered effect sizes of 0.2-0.5 to indicate small differences, 0.5-0.8 to indicate medium differences, and >0.8 to indicate large

TABLE I. Demographic and clinical characteristics associated with included MASK-air observations and respective users

Variable	All participants	Rhinitis alone	Rhinitis and asthma
No. of observations	5354	2935	2419
No. of users	3092	1196	1896
Females, n (%)	3489 (65.2)*	1868 (63.6)	1621 (67.0)
Age (y), mean (SD)	37.6 (13.2)	36.2 (13.1)	39.3 (13.2)
VAS global, median (P25-P75)	31 (9-61)	29 (7-59)	35 (11-62)
Full control [0], n (%)	611 (11.4)	421 (14.3)	190 (7.9)
Good control [1-20], n (%)	1481 (27.7)	800 (27.3)	681 (28.2)
Medium control [21-35], n (%)	796 (14.9)	436 (14.9)	360 (14.9)
Poor control [36-100], n (%)	2465 (46.0)	1278 (43.5)	1187 (49.1)
VAS eyes, median (P25-P75)	12 (1-46)	10 (0-42)	15 (3-49)
Full control [0], n (%)	1292 (24.1)	823 (28.0)	469 (19.4)
Good control [1-20], n (%)	1822 (34.0)	927 (31.6)	895 (37.0)
Medium control [21-35], n (%)	596 (11.1)	325 (11.1)	271 (11.2)
Poor control [36-100], n (%)	1644 (30.7)	860 (29.3)	784 (32.4)
VAS nose, median (P25-P75)	31 (9-61)	29 (7-60)	33 (11-62)
Full control [0], n (%)	647 (12.1)	428 (14.6)	219 (9.1)
Good control [1-20], n (%)	1474 (27.5)	783 (26.7)	691 (28.6)
Medium control [21-35], n (%)	807 (15.1)	438 (14.9)	369 (15.3)
Poor control [36-100], n (%)	2426 (45.3)	1286 (43.8)	1140 (47.1)
VAS asthma†, median (P25-P75)	18 (3-51)	—	18 (3-51)
Full control [0], n (%)	402 (16.6)	—	402 (16.6)
Good control [1-20], n (%)	873 (36.1)	—	873 (36.1)
Medium control [21-35], n (%)	278 (11.5)	—	278 (11.5)
Poor control [36-100], n (%)	866 (35.8)	—	866 (35.8)
CSMS, median (P25-P75)	22.5 (8.0-43.2)	19.0 (5.8-38.8)	26.0 (11.1-49.2)
Good control [0-15.8], n (%)	2096 (39.1)	1301 (44.3)	795 (32.9)
Medium control [15.8-35.3], n (%)	1439 (26.9)	788 (26.8)	651 (26.9)
Poor control [35.3-100], n (%)	1818 (34.0)	846 (28.8)	972 (40.2)
Baseline impact of AR‡, median (P25-P75)	2 (1-3)	2 (1-3)	2 (1-4)
Baseline symptoms§, median (P25-P75)	5 (4-7)	5 (4-6)	6 (4-7)
Self-reported asthma, n (%)	2419 (45.2)*	—	2419 (100)
Self-reported conjunctivitis, n (%)	4291 (80.1)*	2274 (77.5)	2017 (83.4)
Medication for AR, n (%)	2893 (54.0)	1384 (47.2)	1509 (62.4)
No medication	2461 (46.0)	1551 (52.8)	910 (37.6)
Single medication	1603 (29.9)	829 (28.2)	774 (32.0)
Comedication	1290 (24.1)	555 (18.9)	735 (30.4)
Medication for asthma†, n (%)	1267 (23.7)	—	1267 (23.7)
No medication	1178 (48.7)	—	1178 (48.7)
Single medication	747 (30.9)	—	747 (30.9)
Comedication	431 (17.8)	—	431 (17.8)
Immunotherapy, n (%)	1286 (24.3)	730 (24.9)	556 (23.0)

AR, Allergic rhinitis; CSMS, combined symptom-medication score; P25-P75, percentile 25-percentile 75; SD, standard deviation; VAS, visual analog scale (scale of 0-100, with higher values indicating poorer control).

*n (%) users: females: 2037 (58.4%), self-reported asthma: 1196 (34.3%), and self-reported conjunctivitis: 2283 (65.4%).

†Data from users with self-reported asthma.

‡Computed based on the number of different ways in which allergy symptoms affect the users at baseline.

§Computed based on the number of reported allergy symptoms at baseline.

differences.²¹ In addition, we compared the regression coefficients observed for self-reported asthma in the aforementioned models.

RESULTS

Participants

We assessed 5354 days of MASK-air use from 3092 different users (Figure E1, available in this article's Online Repository at

www.jaci-inpractice.org). Patients had a mean age of 37.6 years (SD = 13.3 years), and 65.2% were women (Table I). The frequency of observations from each country is given in Table E2 in this article's Online Repository at www.jaci-inpractice.org. The median value for VAS global allergy symptoms was 31 (percentiles 25-75 = 9-61). VAS nose presented a median of 31 (percentiles 25-75 = 9-61), followed by VAS eye with a median of 12 (percentiles 25-75 = 1-46). For VAS asthma, only users

TABLE II. Frequency of observations by the EQ-5D-5L level for each domain

EQ-5D-5L level	All observations	Rhinitis alone	Rhinitis and asthma	Effect size*
Anxiety/depression, n (%)				
1	2981 (55.7)	1830 (62.4)	1151 (47.5)	0.30
2	1534 (28.7)	761 (25.9)	773 (31.9)	0.13
3	570 (10.6)	238 (8.1)	332 (13.7)	0.18
4/5	269 (5.0)	106 (3.6)	165 (6.8)	0.15
Daily activities, n (%)				
1	3404 (63.6)	2016 (68.7)	1388 (57.4)	0.23
2	1277 (23.9)	647 (22.0)	630 (26.0)	0.09
3	520 (9.7)	202 (6.9)	318 (13.1)	0.21
4/5	153 (2.9)	70 (2.4)	83 (3.4)	0.06
Mobility, n (%)				
1	4257 (79.5)	2544 (86.7)	1713 (70.8)	0.39
2	637 (11.9)	252 (8.6)	385 (15.9)	0.23
3	335 (6.3)	92 (3.1)	243 (10.0)	0.29
4/5	124 (2.3)	46 (1.6)	78 (3.2)	0.11
Pain/discomfort, n (%)				
1	2255 (42.4)	1360 (46.3)	895 (37.0)	0.19
2	1939 (36.2)	1065 (36.3)	875 (36.2)	0
3	868 (16.2)	381 (13.0)	487 (20.1)	0.19
4/5	292 (5.5)	130 (4.4)	162 (6.7)	0.10
Self-care, n (%)				
1	5023 (93.8)	2789 (95.0)	2234 (92.4)	0.11
2	220 (4.1)	108 (3.7)	112 (4.6)	0.05
3	73 (1.4)	25 (0.9)	48 (2.0)	0.10
4/5	38 (0.7)	13 (0.4)	25 (1.0)	0.07

EQ-5D-5L, EuroQOL, 5 Domains, 5 Levels.

*Effect size measure for the comparison between rhinitis alone and rhinitis + self-reported asthma: nonmeaningful (<0.20), small (0.20-0.49), moderate (0.50-0.79), and high (≥0.80) standardized differences.

with self-reported asthma were assessed, and the median value was 18 (percentiles 25-75 = 3-51). The median CSMS was of 22.5 (percentiles 25-75 = 8.0-43.2).

VAS and CSMS levels in different EQ-5D-5L domains

The frequency of observations by the EQ-5D-5L level is available in Table II and ranged from 38 to 5023. We compared VAS and CSMS levels according to the EQ-5D-5L level for the different domains (Figure 1). We observed a gradual increase of median VAS or CSMS values associated with increasing EQ-5D-5L levels in the domains of “activities,” “mobility,” and “pain/discomfort.” For the “anxiety/depression” domain, we observed an increase of median VAS or CSMS values from levels 1 to 3 and then a plateau for levels 3 and 4/5. These patterns were not observed for the “self-care” domain. The analyses in patients younger than 65 years revealed similar results (Figure E2, available in this article’s Online Repository at www.jaci-inpractice.org).

Multivariable models assessing the association between rhinitis or asthma symptoms and EQ-5D-5L domains

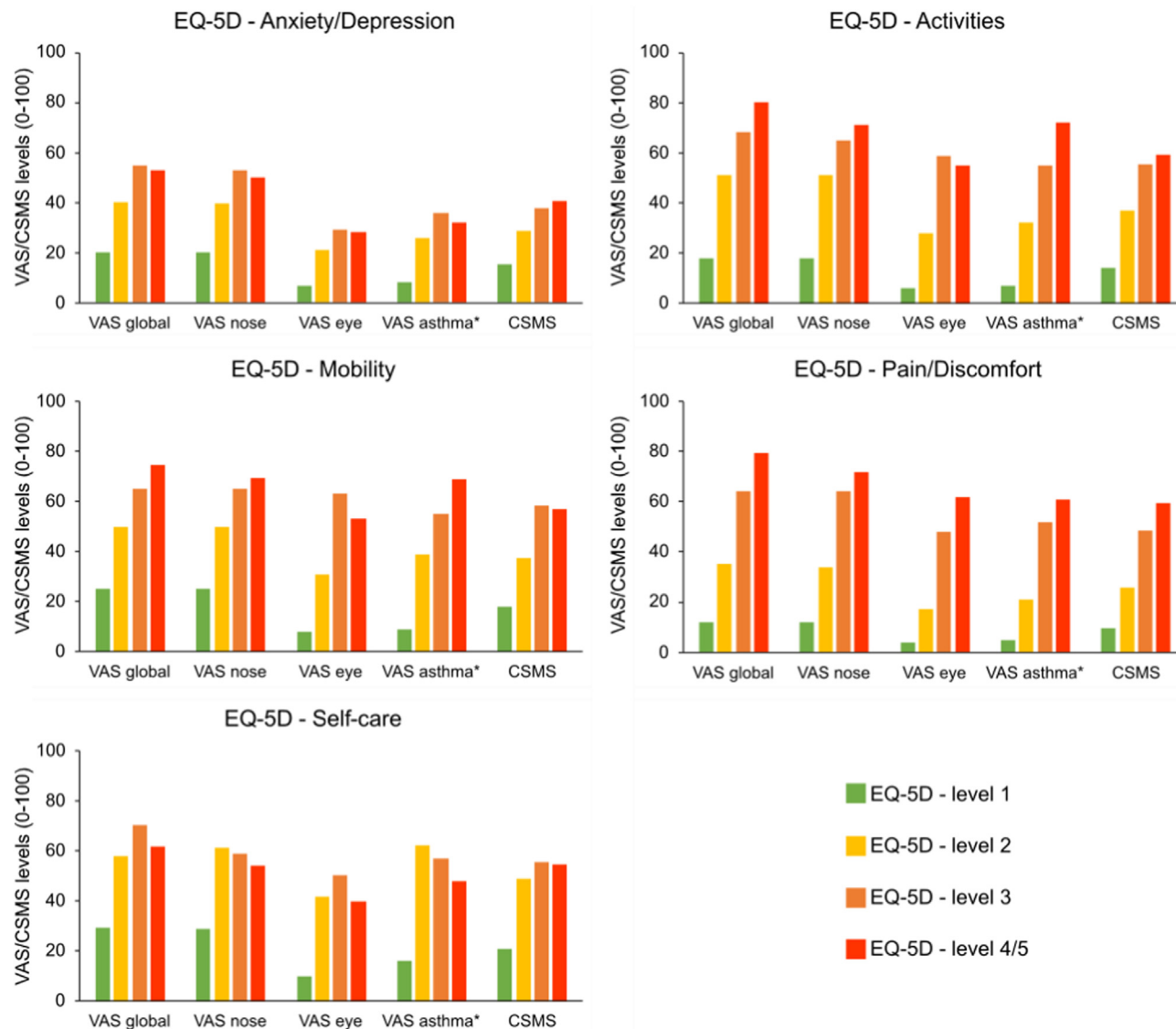
In multivariable models, for all VASs and for the CSMS, a worse allergy control was significantly associated with higher pain/discomfort (odds ratio [OR] range = 1.27-1.73) and impairment in performing daily activities (OR range = 1.28-2.36) (Table III; Figure 2; Tables E3 and E4, available in this

article’s Online Repository at www.jaci-inpractice.org). Higher levels of anxiety/depression were associated with higher VAS global (OR = 1.05; 95% confidence interval [CI] = 1.01; 1.09; $P = .017$) and VAS nose (OR = 1.04; 95% CI = 1.00; 1.08; $P = .028$), but not with VAS eye, VAS asthma, or the CSMS (Table E5, available in this article’s Online Repository at www.jaci-inpractice.org). Worse mobility was only associated with VAS asthma (OR = 1.25; 95% CI = 1.13; 1.38; $P < .001$) (Table E6, available in this article’s Online Repository at www.jaci-inpractice.org). Less consistent results were observed for self-care, with significant results having only been observed for VAS eye (OR = 1.25; 95% CI = 1.08; 1.44; $P = .003$) and for the CSMS (OR = 1.46; 95% CI = 1.15; 1.85) (Table E7, available in this article’s Online Repository at www.jaci-inpractice.org). Overall, the observed effect sizes (OR) were larger for pain/discomfort and daily activities than for anxiety/depression or mobility.

Comparison between rhinitis alone and rhinitis + self-reported asthma

Compared with patients with rhinitis alone, patients with rhinitis + asthma displayed a higher frequency of observations in high EQ-5D-5L levels, particularly in the domains of mobility, daily activities, and anxiety/depression (Table II). Meaningful differences were not observed for pain/discomfort or self-care.

In multivariable models, the presence of self-reported asthma was consistently significantly associated with higher EQ-5D-5L levels for the domains of mobility (ORs range across the



* Data for patients with self-reported asthma only

FIGURE 1. Median visual analog scale (VAS) and combined symptom-medication score (CSMS) levels according to the EQ-5D-5L level for the different EQ-5D-5L domains. *EQ-5D-5L*, EuroQOL, 5 Domains, 5 Levels.

different performed models [which varied on the VAS/CSMS included as an independent variable]; 2.29-2.41) and anxiety/depression (OR range: 1.31-1.34) (Table IV; Tables E3-E7, available in this article’s Online Repository at www.jaci-inpractice.org).

DISCUSSION

This study is unique as it (1) assessed the EQ-5D-5L domains according to the control of asthma and rhinitis, and (2) compared rhinitis alone and rhinitis and asthma. Moreover, in the current study, we used a real-life approach with a validated mHealth app in a large population and in 25 countries. We evaluated MASK-air users who answered the EQ-5D-5L questionnaire, and we observed an association between worse control of rhinitis, conjunctivitis, or asthma (median VASs and the

CSMS) with an impairment of EQ-5D-5L levels. For anxiety/depression, this association was mostly observed for rhinitis-related tools (VAS nose, VAS global, and CSMS), although the presence of self-reported asthma was also associated with worse anxiety/depression. On the other hand, mobility was particularly associated with VAS asthma and with the presence of asthma.

Limitations and strengths

This study has some limitations. First, there was a selection bias within the MASK-air dataset, because the current study had higher VAS and CSMS levels than those observed in the entire database. This indicated that EQ-5D-5L was more often filled in on days when users were less well controlled (in MASK-air, answering to the EQ-5D-5L is not mandatory within the daily monitoring questionnaire, explaining the low average number of

TABLE III. Summary of the multivariable models with associations between VAS or CSMS and each EQ-5D-5L domain

Variable	Anxiety/depression, OR (95% CI) [P value]	Daily activities, OR (95% CI) [P value]	Mobility, OR (95% CI) [P value]	Pain/discomfort, OR (95% CI) [P value]	Self-care, OR (95% CI) [P value]
VAS global*	1.05 (1.01; 1.09) [.017]	1.79 (1.65; 1.93) [<.001]	1.01 (0.93; 1.10) [.792]	1.42 (1.37; 1.47) [<.001]	1.11 (0.95; 1.29) [.181]
VAS nose*	1.04 (1.00; 1.08) [.028]	1.58 (1.47; 1.70) [<.001]	0.97 (0.89; 1.05) [.444]	1.32 (1.28; 1.37) [<.001]	1.14 (0.98; 1.32) [.088]
VAS eye*	1.01 (0.97; 1.04) [.770]	1.45 (1.36; 1.55) [<.001]	0.92 (0.84; 1.01) [.074]	1.29 (1.24; 1.33) [<.001]	1.25 (1.08; 1.44) [.003]
VAS asthma*,†	0.98 (0.93; 1.03) [.453]	1.28 (1.19; 1.37) [<.001]	1.25 (1.13; 1.38) [<.001]	1.27 (1.21; 1.34) [<.001]	1.16 (0.98; 1.37) [.079]
CSMS*	1.03 (0.98; 1.09) [.288]	2.36 (2.10; 2.65) [<.001]	1.04 (0.91; 1.18) [.600]	1.73 (1.63; 1.83) [<.001]	1.46 (1.15; 1.85) [.002]

CI, Confidence interval; CSMS, combined symptom-medication score; EQ-5D-5L, EuroQOL, 5 Domains, 5 Levels; OR, odds ratio; VAS, visual analog scale.

*Results for the OR presented per 10 units of VAS or CSMS.

†Results for patients with self-reported asthma.

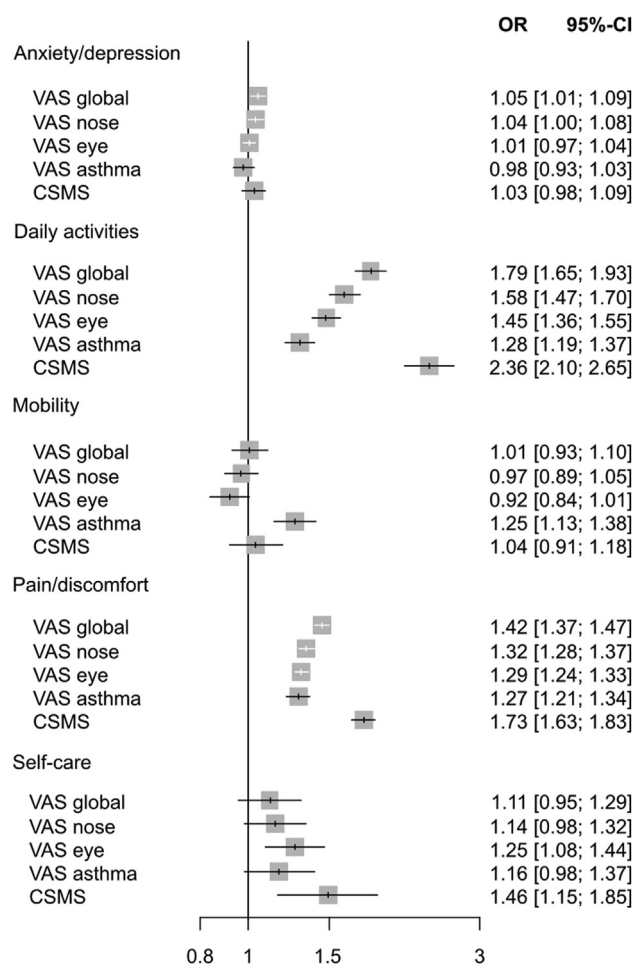


FIGURE 2. Summary of the multivariable models with associations between VAS or CSMS and each EQ-5D-5L domain. CI, Confidence interval; CSMS, combined symptom-medication score; EQ-5D-5L, EuroQOL, 5 Domains, 5 Levels; OR, odds ratio; VAS, visual analog scale.

observations per user). These differences may also extend to users' characteristics, as the country repartition of users differs from that of the entire database. Second, the characteristics of MASK-air users may differ from those of the general population. For example, the age range of users differs from the general population, with older patients being under-represented in the

current study. Third, and potentially related to the latter limitation, there may be an under-representation of users reporting more severe levels of EQ-5D-5L domains (even after pooling together data from the 2 more severe levels of each domain). On account of such low frequency, we (1) were not able to build certain multivariable models for the self-care domains, and (2) obtained some low-precision estimates in models considering the VASs and/or the CSMS as categorical variables.

Another relevant limitation concerns the possibility of unmeasured confounders. In fact, the EQ-5D-5L is not an allergy-specific questionnaire and may be affected by the presence of several other comorbidities. In MASK-air, we do not have any information on the presence of such nonallergic comorbidities. We were therefore not able to adjust for them in our multivariable models. To partly compensate for this (and considering that a more advanced age is associated with a higher frequency of comorbidities, and that, in old-age adults, the results of EQ-5D-5L in allergic rhinitis should be considered with care),²² we included age as a covariate in those models and performed a sensitivity analysis in patients younger than 65 years. Moreover, the associations between most EQ-5D-5L domains and rhinitis or asthma control suggest that these effects are not very important.

Additional limitations concern the fact that we relied on self-reported asthma to identify patients with asthma, potentially resulting in information bias or reflecting across-country differences in the classification of patients as having asthma.

This study also has important strengths. The assessed VASs, the CSMS, and the EQ-5D-5L are tools that have been assessed on their validity, reliability, and responsiveness. We performed adjusted analyses for relevant demographical and allergy-related variables, and we obtained consistent results when performing analyses using different assumptions (eg, continuous vs categorical VASs or CSMS; all participants vs participants aged less than 65 years only). Finally, the assessed question is particularly innovative and relevant, having been assessed using real-world direct patient data. Studies using such data are becoming increasingly important as their population scopes are not as limited—and, thus, potentially far from that of the clinical practice—as those of randomized controlled trials.²³ Future studies may use MASK-air data on EQ-5D-5L to estimate utilities associated with different rhinitis and asthma control levels.

Interpretation of the data

Although some of the EQ-5D-5L domains are similar to other HR-QOL questionnaires (including the Rhinoconjunctivitis Quality-of-Life Questionnaire [RQLQ]), individual domains

TABLE IV. Summary of the multivariable models for the associations between self-reported asthma and EQ-5D-5L domain

Results for self-reported asthma	Anxiety/depression	Daily activities	Mobility	Pain/discomfort	Self-care
Range of OR	1.31-1.34	0.99-1.34	2.29-2.40	0.83-0.97	1.04-1.19
No. of models with significant results/No. of models	4/4	0/4	4/4	0/4	0/4

EQ-5D-5L, EuroQOL, 5 Domains, 5 Levels; OR, odds ratio.

have not been assessed in their association with rhinitis and/or asthma control. Moreover, regarding QOL, to the best of our knowledge, although few studies compared rhinitis and asthma using the same tool,^{24,25} or rhinitis and asthma in the same tool,²⁶ none compared rhinitis alone with rhinitis and asthma.

The personal burden of illness perceived by patients with allergic rhinitis extends beyond clinical symptoms, with an impact on social life and daily activities, as shown by numerous studies using QOL generic or specific instruments.²⁷

The current study showed that worse allergy control assessed by all VASs or CSMS was associated with higher impairment of pain/discomfort and daily activities. Results on daily activities are in line with numerous QOL studies. Pain and discomfort are part of the same domain in EQ-5D-5L, and the troublesome symptoms (eg, breathing difficulties) associated with rhinitis and/or asthma may create discomfort. Regarding anxiety/depression, we observed an association with VAS global and nose. This finding is in line with a previous cross-sectional study that identified an association between lack of allergic rhinitis control, according to the Control of Allergic Rhinitis and Asthma Test questionnaire, and symptoms of anxiety and depression.²⁸ Despite the underlying mechanisms remaining unclear, several explanations were proposed. Some studies suggest a structural and functional effect of allergic diseases in certain areas of the central nervous system involved in anxiety and depression pathways.^{29,30}

We were able to compare observations from patients with rhinitis alone with those from patients with rhinitis and asthma on EQ-5D-5L domains. The presence of asthma was associated with worse mobility. In addition, only VAS asthma was associated with the mobility dimension. This study is in accordance with Leynaert et al.³¹ using the 36-Item Short Form Survey (SF-36) questionnaire. In a population of young adults, patients with allergic rhinitis and asthma reported more mobility problems (worse SF-36 scores in the domains of physical functioning and role limitations due to physical problems) than patients with rhinitis alone. It should be noted that the mobility dimension was defined as “problems in walking about.” It may therefore not fully capture problems in physical activities such as doing sports (which also appear to be affected by rhinitis alone³²), but rather preferably reflect impairments patients feel in moving around due to problems in breathing.

An interesting finding is that in the multivariable models, we did not observe an association between worse VAS asthma and EQ-5D-5L levels for anxiety/depression, although the presence of self-reported asthma was consistently associated with worse EQ-5D-5L levels. This finding may be related to the worse control of rhinitis in patients with rhinitis and asthma than in those with rhinitis alone.¹²

Finally, we mostly observed negative results on the association between rhinitis or asthma symptoms and the self-care dimension of EQ-5D-5L. These results reinforce the adequacy of patient-centered therapeutic strategies, as the capacities of

patients do seem to be impaired by their respiratory allergy symptoms.

The EQ-5D-5L questionnaire is a useful tool in the assessment of patients with upper airway diseases. For example, a previous study reported that the average EQ-5D-5L index score and EQ-5D-5L VAS of adults with chronic rhinosinusitis were lower than those in the general population, indicating worse perceived health.³³ Furthermore, in MASK-air users, the EQ-5D-5L VAS was found to be moderately correlated with VAS global, VAS nose, and VAS work.³⁴ Finally, EQ-5D-5L has the strength of allowing the comparison of the 2 diseases (eg, rhinitis and asthma) and of allowing valuing health. For example, the EQ-5D-5L has allowed for the estimation of utilities, which were used to evaluate health gains associated with allergen immunotherapy,^{35,36} as well as its cost utility.⁸ On the other hand, EQ-5D-5L has some limitations. As a generic tool, it is usually less sensitive than the disease-specific tools for measuring asthma or rhinitis quality of life (eg, the Asthma Quality-of-Life Questionnaire or the RQLQ for rhinitis^{35,37,38}). In fact, EQ-5D-5L does not react very sensitively to small changes in asthma control⁶ and does not fully represent the deficits of HR-QOL in severe asthma.³⁹ In addition, self-reported EQ-5D-5L health status may differ between countries.^{17,40}

Generalizability

This study was carried out in 24 countries. We could not assess individual countries because of sample size constraints. However, in previous studies, we had found consistent results in sensitivity analyses for several outcomes in individual countries. Thus, the results presented herein are likely to be generalizable to many upper and upper-middle income countries.

CONCLUSIONS

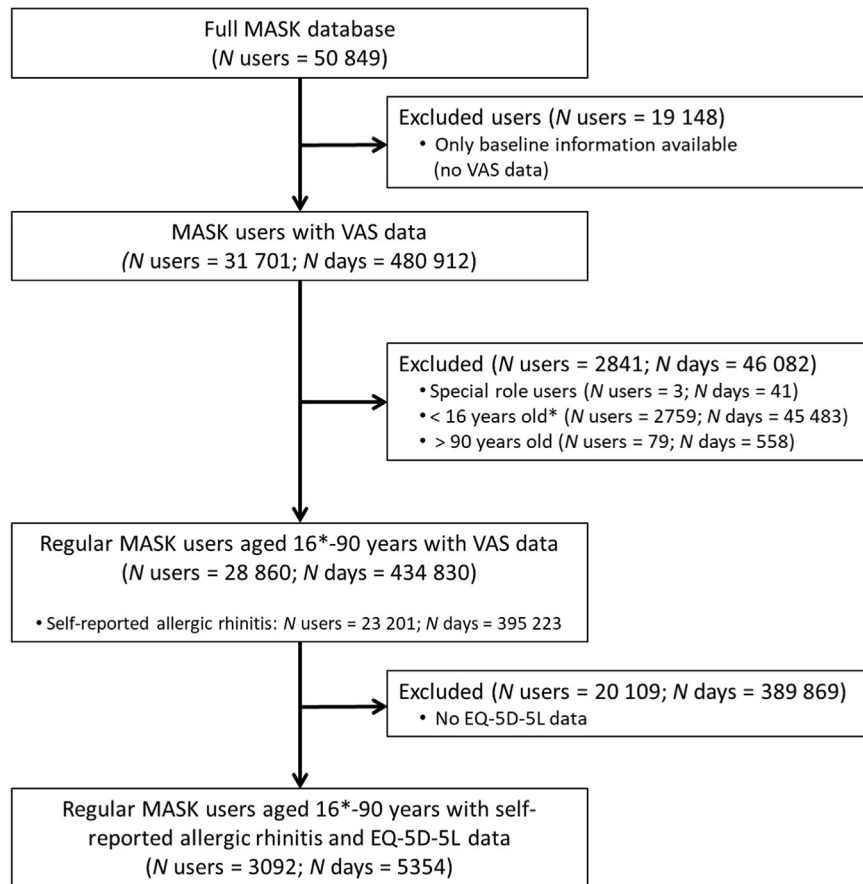
A poorer control of allergic rhinitis and asthma appears to be associated with a worse HR-QOL, particularly with more severe reported pain/discomfort and with more impairments in the performance of daily activities. We also observed that a poor rhinitis control tended to be associated with worse levels of anxiety/depression, whereas a poor asthma control had a negative impact on mobility (“walking around”). Although confirmatory studies applying classical epidemiological approaches should be conducted, this study suggests that rhinitis and asthma control may have a relevant but distinct impact on several key domains of HR-QOL.

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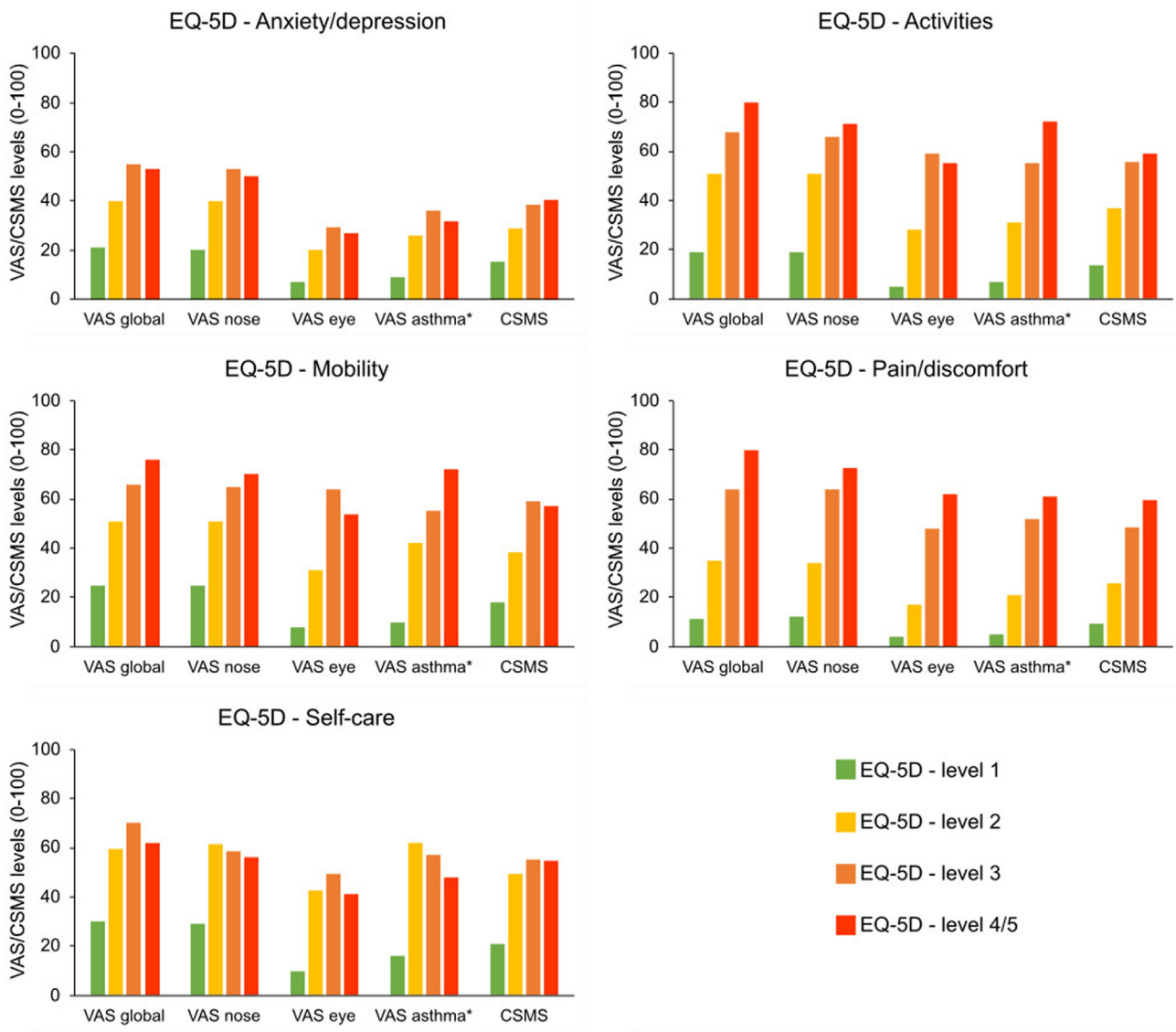
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*Or lower (not below 13 years old) for countries where the digital age of consent is lower

FIGURE E1. Flow diagram of patient selection. *EQ-5D-5L*, EuroQOL, 5 Domains, 5 Levels; *VAS*, visual analog scale.



* Data for patients with self-reported asthma only

FIGURE E2. Median visual analog scale (VAS) and combined symptom-medication score (CSMS) levels according to the EQ-5D-5L level for the different EQ-5D-5L domains in users aged <65 years. *EQ-5D-5L*, EuroQOL, 5 Domains, 5 Levels.

TABLE E1. Visual analog scales (VASs) available in MASK-air and descriptions of the EQ-5D-5L questions

MASK-air VAS	Question
VAS global allergy symptoms	Overall, how much are your allergic symptoms bothering you today?
VAS nose	How much are your nose symptoms bothering you today?
VAS eyes	How much are your eye symptoms bothering you today?
VAS asthma	How much are your asthma symptoms bothering you today?
EQ-5D-5L domain and levels	Statement
Anxiety/depression	
Level 1	I am not anxious or depressed
Level 2	I am slightly anxious or depressed
Level 3	I am moderately anxious or depressed
Level 4	I am severely anxious or depressed
Level 5	I am extremely anxious or depressed
Activities	
Level 1	I have no problems doing my usual activities
Level 2	I have slight problems doing my usual activities
Level 3	I have moderate problems doing my usual activities
Level 4	I have severe problems doing my usual activities
Level 5	I am unable to do my usual activities
Mobility	
Level 1	I have no problems in walking about
Level 2	I have slight problems in walking about
Level 3	I have moderate problems in walking about
Level 4	I have severe problems in walking about
Level 5	I am unable to walk about
Pain/discomfort	
Level 1	I have no pain or discomfort
Level 2	I have slight pain or discomfort
Level 3	I have moderate pain or discomfort
Level 4	I have severe pain or discomfort
Level 5	I have extreme pain or discomfort
Self-care	
Level 1	I have no problems washing or dressing myself
Level 2	I have slight problems washing or dressing myself
Level 3	I have moderate problems washing or dressing myself
Level 4	I have severe problems washing or dressing myself
Level 5	I am unable to wash or dress myself

EQ-5D-5L, EuroQOL, 5 Domains, 5 Levels.

TABLE E2. Frequency of observations from each country

Country	Data assessed in this study	Full MASK-air dataset
	No. of days (%) [no. of users (%)]	No. of days (%) [no. of users (%)]
Argentina	67 (1.3) [54 (1.9)]	5223 (1.3) [372 (1.6)]
Australia	43 (0.8) [38 (1.3)]	2597 (0.7) [253 (1.1)]
Austria	49 (0.9) [40 (1.4)]	7639 (1.9) [705 (3.0)]
Belgium	45 (0.8) [38 (1.3)]	2055 (0.5) [229 (1.0)]
Brazil	406 (7.6) [318 (10.9)]	11,904 (3.0) [1964 (8.5)]
Canada	11 (0.2) [10 (0.3)]	479 (0.1) [79 (0.3)]
Czech Republic	1 (0.0) [1 (0.0)]	2211 (0.6) [80 (0.3)]
Denmark	35 (0.7) [24 (0.8)]	1343 (0.3) [119 (0.5)]
Finland	123 (2.3) [74 (2.5)]	5994 (1.5) [388 (1.7)]
France	571 (10.7) [376 (12.9)]	22,286 (5.6) [2222 (9.6)]
Germany	641 (12.0) [267 (9.2)]	33,328 (8.4) [1511 (6.5)]
Great Britain	200 (3.7) [135 (4.6)]	7655 (1.9) [640 (2.8)]
Greece	62 (1.2) [43 (1.5)]	9671 (2.4) [486 (2.1)]
Hungary	0 (0)	716 (0.2) [69 (0.3)]
Italy	613 (11.4) [347 (11.9)]	46,178 (11.7) [3346 (14.4)]
Japan	0 (0)	5037 (1.3) [408 (1.8)]
Lebanon	10 (0.2) [8 (0.3)]	651 (0.2) [55 (0.2)]
Lithuania	569 (10.6) [131 (4.5)]	51,744 (13.1) [985 (4.2)]
Mexico	467 (8.7) [230 (7.9)]	77,846 (19.7) [1972 (8.5)]
Netherlands	273 (5.1) [187 (6.4)]	9838 (2.5) [1102 (4.7)]
Poland	266 (5.0) [187 (6.4)]	23,619 (6.0) [1304 (5.6)]
Portugal	555 (10.4) [367 (12.6)]	19,612 (5.0) [1996 (8.6)]
Slovenia	0 (0)	1686 (0.4) [212 (0.9)]
Spain	255 (4.8) [164 (5.6)]	28,332 (7.2) [1073 (4.6)]
Sweden	58 (1.1) [29 (1.0)]	1958 (0.5) [207 (0.9)]
Switzerland	31 (0.6) [22 (0.8)]	5977 (1.5) [809 (3.5)]
Turkey	3 (0.1) [2 (0.1)]	9644 (2.4) [615 (2.7)]

TABLE E3. Multivariable models assessing the association between rhinitis or asthma symptoms and EQ-5D-5L question on daily activities

Variable	VAS global, OR (95% CI) [P value]	VAS nose, OR (95% CI) [P value]	VAS eye, OR (95% CI) [P value]	VAS asthma, OR (95% CI) [P value]	CSMS, OR (95% CI) [P value]
VAS/CSMS*	1.79 (1.65; 1.93) [$<.001$]	1.58 (1.47; 1.70) [$<.001$]	1.45 (1.36; 1.55) [$<.001$]	1.28 (1.19; 1.37) [$<.001$]	2.36 (2.10; 2.65) [$<.001$]
Baseline symptoms	0.89 (0.75; 1.06) [.197]	0.86 (0.72; 1.02) [.085]	0.90 (0.76; 1.07) [.241]	1.05 (0.91; 1.21) [.493]	0.89 (0.75; 1.06) [.188]
Baseline impact	1.87 (1.53; 2.29) [$<.001$]	1.93 (1.57; 2.38) [$<.001$]	1.97 (1.61; 2.41) [$<.001$]	1.32 (1.11; 1.56) [.001]	1.89 (1.54; 2.32) [$<.001$]
Male gender	0.91 (0.55; 1.53) [.734]	0.79 (0.47; 1.34) [.385]	0.77 (0.48; 1.25) [.295]	0.78 (0.49; 1.23) [.283]	0.91 (0.54; 1.54) [.735]
Age	0.98 (0.96; 1.00) [.016]	0.98 (0.96; 1.00) [.046]	0.97 (0.96; 0.99) [.003]	0.98 (0.96; 0.99) [.002]	0.98 (0.96; 0.99) [.009]
Asthma	1.30 (0.77; 2.20) [.334]	1.34 (0.78; 2.30) [.293]	1.20 (0.72; 2.00) [.489]	—	0.99 (0.58; 1.69) [.972]
Conjunctivitis	1.24 (0.57; 2.72) [.584]	1.38 (0.62; 3.09) [.436]	0.70 (0.32; 1.51) [.363]	0.82 (0.42; 1.60) [.558]	1.02 (0.46; 2.25) [.954]
Daily use of rhinitis medication					
No medication	—†	—†	—†	—†	—†
Single medication	1.36 (0.93; 2.00) [.110]	1.37 (0.93; 2.01) [.114]	1.47 (1.01; 2.14) [.047]	1.18 (0.80; 1.73) [.410]	1.23 (0.84; 1.81) [.284]
Comedication	2.03 (1.30; 3.16) [.002]	2.63 (1.68; 4.12) [$<.001$]	2.37 (1.53; 3.67) [$<.001$]	2.35 (1.50; 3.67) [$<.001$]	1.62 (1.03; 2.54) [.036]
Daily use of asthma medication					
No medication	—†	—†	—†	—†	—†
Single medication	0.60 (0.35; 1.03) [.065]	0.66 (0.38; 1.12) [.123]	0.67 (0.40; 1.13) [.132]	0.72 (0.48; 1.06) [.099]	0.46 (0.27; 0.79) [.005]
Comedication	1.48 (0.71; 3.08) [.299]	1.52 (0.72; 3.22) [.276]	1.61 (0.77; 3.34) [.203]	0.95 (0.57; 1.58) [.839]	1.04 (0.50; 2.19) [.912]
Immunotherapy	0.54 (0.28; 1.04) [.067]	0.47 (0.24; 0.92) [.029]	0.43 (0.23; 0.83) [.011]	0.55 (0.32; 0.97) [.038]	0.51 (0.26; 1.00) [.049]
EQ-5D-5L mobility	8.83 (6.39; 12.2) [$<.001$]	9.73 (7.00; 13.5) [$<.001$]	9.66 (7.02; 13.3) [$<.001$]	4.06 (3.01; 5.48) [$<.001$]	8.88 (6.40; 12.3) [$<.001$]
EQ-5D-5L anxiety/depression	1.63 (1.35; 1.96) [$<.001$]	1.71 (1.41; 2.07) [$<.001$]	1.73 (1.43; 2.09) [$<.001$]	1.29 (1.09; 1.53) [.004]	1.68 (1.39; 2.03) [$<.001$]
EQ-5D-5L self-care	4.43 (2.92; 6.73) [$<.001$]	4.32 (2.84; 6.56) [$<.001$]	4.06 (2.69; 6.13) [$<.001$]	2.50 (1.74; 3.60) [$<.001$]	4.05 (2.66; 6.17) [$<.001$]
EQ-5D-5L pain/discomfort	7.39 (5.77; 9.47) [$<.001$]	9.38 (7.31; 12.1) [$<.001$]	10.1 (7.96; 12.7) [$<.001$]	4.38 (3.38; 5.67) [$<.001$]	7.50 (5.86; 9.61) [$<.001$]

CI, Confidence interval; CSMS, combined symptom-medication score; EQ-5D-5L, EuroQOL, 5 Domains, 5 Levels; OR, odds ratio; VAS, visual analog scale.

*Results for the OR presented per 10 units of VAS. For VAS asthma, results only concern users with self-reported asthma.

†Referenced category.

TABLE E4. Multivariable models assessing the association between rhinitis or asthma symptoms and EQ-5D-5L question on pain/discomfort

Variable	VAS global, OR (95% CI) [P value]	VAS nose, OR (95% CI) [P value]	VAS eye, OR (95% CI) [P value]	VAS asthma, OR (95% CI) [P value]	CSMS, OR (95% CI) [P value]
VAS/CSMS*	1.42 (1.37; 1.47) [$<.001$]	1.32 (1.28; 1.37) [$<.001$]	1.29 (1.24; 1.33) [$<.001$]	1.27 (1.21; 1.34) [$<.001$]	1.73 (1.63; 1.83) [$<.001$]
Baseline symptoms	0.96 (0.89; 1.02) [.184]	0.93 (0.87; 1.00) [.047]	0.95 (0.89; 1.02) [.143]	1.01 (0.91; 1.12) [.862]	0.95 (0.88; 1.01) [.111]
Baseline impact	1.10 (1.02; 1.18) [.015]	1.11 (1.03; 1.19) [.008]	1.14 (1.06; 1.23) [$<.001$]	1.15 (1.03; 1.30) [.016]	1.11 (1.03; 1.20) [.008]
Male gender	0.84 (0.68; 1.02) [.083]	0.78 (0.64; 0.95) [.015]	0.76 (0.63; 0.93) [.008]	0.86 (0.61; 1.19) [.357]	0.84 (0.68; 1.03) [.088]
Age	1.00 (1.00; 1.01) [.440]	1.00 (1.00; 1.01) [.191]	1.00 (0.99; 1.01) [.743]	0.99 (0.98; 1.01) [.353]	1.00 (0.99; 1.01) [.696]
Asthma	0.97 (0.79; 1.21) [.811]	0.97 (0.79; 1.20) [.807]	0.93 (0.75; 1.15) [.505]	—	0.83 (0.67; 1.03) [.087]
Conjunctivitis	1.18 (0.87; 1.61) [.277]	1.27 (0.94; 1.72) [.116]	0.83 (0.62; 1.13) [.240]	1.21 (0.75; 1.96) [.438]	1.06 (0.78; 1.45) [.691]
Daily use of rhinitis medication					
No medication	—†	—†	—†	—†	—†
Single medication	1.12 (0.93; 1.35) [.226]	1.13 (0.94; 1.36) [.188]	1.22 (1.02; 1.47) [.031]	0.87 (0.65; 1.16) [.339]	1.07 (0.88; 1.28) [.508]
Comedication	1.01 (0.81; 1.25) [.951]	1.10 (0.89; 1.36) [.386]	1.06 (0.86; 1.32) [.574]	0.79 (0.57; 1.11) [.175]	0.84 (0.67; 1.05) [.130]
Daily use of asthma medication					
No medication	—†	—†	—†	—†	—†
Single medication	1.57 (1.19; 2.06) [.001]	1.65 (1.26; 2.16) [$<.001$]	1.68 (1.28; 2.20) [$<.001$]	1.30 (0.96; 1.75) [.092]	1.31 (1.00; 1.73) [.051]
Comedication	1.36 (0.97; 1.90) [.074]	1.39 (1.00; 1.93) [.053]	1.40 (1.00; 1.95) [.048]	1.08 (0.73; 1.59) [.705]	1.09 (0.77; 1.52) [.635]
Immunotherapy	1.00 (0.78; 1.29) [.970]	0.94 (0.74; 1.20) [.623]	0.89 (0.70; 1.13) [.336]	0.66 (0.45; 0.98) [.041]	0.99 (0.77; 1.27) [.936]
EQ-5D-5L mobility	1.81 (1.57; 2.09) [$<.001$]	1.84 (1.60; 2.12) [$<.001$]	1.84 (1.59; 2.12) [$<.001$]	1.71 (1.40; 2.09) [$<.001$]	1.76 (1.52; 2.03) [$<.001$]
EQ-5D-5L activities	3.27 (2.85; 3.76) [$<.001$]	3.73 (3.26; 4.27) [$<.001$]	4.00 (3.49; 4.58) [$<.001$]	3.89 (3.18; 4.77) [$<.001$]	3.26 (2.84; 3.75) [$<.001$]
EQ-5D-5L self-care	1.33 (1.07; 1.65) [.011]	1.31 (1.05; 1.62) [.016]	1.20 (0.96; 1.49) [.104]	1.08 (0.81; 1.43) [.591]	1.25 (1.00; 1.55) [.050]
EQ-5D-5L anxiety/depression	1.69 (1.54; 1.86) [$<.001$]	1.70 (1.55; 1.87) [$<.001$]	1.74 (1.58; 1.91) [$<.001$]	1.85 (1.62; 2.11) [$<.001$]	1.71 (1.56; 1.89) [$<.001$]

CI, Confidence interval; CSMS, combined symptom-medication score; EQ-5D-5L, EuroQOL, 5 Domains, 5 Levels; OR, odds ratio; VAS, visual analog scale.

*Results for the OR presented per 10 units of VAS. For VAS asthma, results only concern users with self-reported asthma.

†Referenced category.

TABLE E5. Multivariable models assessing the association between rhinitis or asthma symptoms and EQ-5D-5L question on anxiety/depression

Variable	VAS global, OR (95% CI) [P value]	VAS nose, OR (95% CI) [P value]	VAS eye, OR (95% CI) [P value]	VAS asthma, OR (95% CI) [P value]	CSMS, OR (95% CI) [P value]
VAS/CSMS*	1.05 (1.01; 1.09) [.017]	1.04 (1.00; 1.08) [.028]	1.01 (0.97; 1.04) [.770]	0.98 (0.93; 1.03) [.453]	1.03 (0.98; 1.09) [.288]
Baseline symptoms	0.95 (0.87; 1.03) [.237]	0.95 (0.87; 1.03) [.203]	0.95 (0.87; 1.03) [.244]	0.99 (0.88; 1.13) [.920]	0.95 (0.87; 1.03) [.207]
Baseline impact	1.10 (1.00; 1.21) [.049]	1.10 (1.00; 1.21) [.046]	1.10 (1.00; 1.21) [.041]	1.01 (0.88; 1.17) [.856]	1.10 (1.00; 1.21) [.054]
Male gender	0.69 (0.53; 0.88) [.004]	0.68 (0.53; 0.87) [.003]	0.67 (0.52; 0.86) [.002]	0.86 (0.58; 1.29) [.473]	0.68 (0.53; 0.88) [.003]
Age	0.97 (0.96; 0.98) [<.001]	0.97 (0.96; 0.98) [<.001]	0.97 (0.96; 0.98) [<.001]	0.99 (0.97; 1.00) [.035]	0.97 (0.96; 0.98) [<.001]
Asthma	1.34 (1.03; 1.74) [.030]	1.34 (1.03; 1.74) [.029]	1.32 (1.02; 1.72) [.035]	–	1.31 (1.04; 1.66) [.023]
Conjunctivitis	1.07 (0.73; 1.57) [.714]	1.08 (0.74; 1.58) [.694]	1.05 (0.72; 1.54) [.803]	0.90 (0.50; 1.62) [.731]	1.07 (0.73; 1.56) [.731]
Daily use of rhinitis medication					
No medication	–†	–†	–†	–†	–‡
Single medication	0.74 (0.59; 0.92) [.007]	0.74 (0.59; 0.92) [.007]	0.76 (0.61; 0.94) [.012]	0.50 (0.36; 0.70) [<.001]	–‡
Comedication	0.81 (0.62; 1.05) [.112]	0.81 (0.63; 1.06) [.125]	0.84 (0.64; 1.09) [.182]	0.80 (0.54; 1.17) [.242]	–‡
Daily use of asthma medication					
No medication	–†	–†	–†	–†	–‡
Single medication	1.08 (0.79; 1.47) [.641]	1.09 (0.80; 1.49) [.586]	1.08 (0.79; 1.48) [.625]	1.21 (0.86; 1.70) [.280]	–‡
Comedication	0.97 (0.64; 1.45) [.873]	0.99 (0.66; 1.48) [.950]	0.98 (0.65; 1.46) [.908]	1.10 (0.70; 1.74) [.673]	–‡
Immunotherapy	0.87 (0.63; 1.18) [.367]	0.86 (0.63; 1.17) [.334]	0.84 (0.62; 1.15) [.274]	0.99 (0.61; 1.59) [.960]	0.86 (0.63; 1.17) [.338]
EQ-5D-5L mobility	1.35 (1.14; 1.59) [<.001]	1.34 (1.14; 1.58) [<.001]	1.34 (1.14; 1.58) [<.001]	1.34 (1.08; 1.67) [.008]	1.33 (1.13; 1.56) [.001]
EQ-5D-5L activities	1.57 (1.35; 1.83) [<.001]	1.60 (1.37; 1.86) [<.001]	1.64 (1.41; 1.91) [<.001]	1.46 (1.18; 1.81) [.001]	1.60 (1.37; 1.86) [<.001]
EQ-5D-5L self-care	1.94 (1.52; 2.46) [<.001]	1.93 (1.52; 2.45) [<.001]	1.91 (1.51; 2.43) [<.001]	1.99 (1.47; 2.70) [<.001]	1.93 (1.52; 2.45) [<.001]
EQ-5D-5L pain/discomfort	2.07 (1.81; 2.36) [<.001]	2.09 (1.84; 2.38) [<.001]	2.16 (1.89; 2.46) [<.001]	2.25 (1.88; 2.68) [<.001]	2.11 (1.85; 2.41) [<.001]

CI, Confidence interval; CSMS, combined symptom-medication score; EQ-5D-5L, EuroQOL, 5 Domains, 5 Levels; OR, odds ratio; VAS, visual analog scale.

*Results for the OR presented per 10 units of VAS. For VAS asthma, results only concern users with self-reported asthma.

†Referenced category.

‡Not present in the model to ensure convergence.

TABLE E6. Multivariable models assessing the association between rhinitis or asthma symptoms and EQ-5D-5L question on mobility

Variable	VAS global, OR (95% CI) [P value]	VAS nose, OR (95% CI) [P value]	VAS eye, OR (95% CI) [P value]	VAS asthma, OR (95% CI) [P value]	CSMS, OR (95% CI) [P value]
VAS/CSMS*	1.01 (0.93; 1.10) [.792]	0.97 (0.89; 1.05) [.444]	0.92 (0.84; 1.01) [.074]	1.25 (1.13; 1.38) [<.001]	1.04 (0.91; 1.18) [.600]
Baseline symptoms	0.93 (0.72; 1.19) [.563]	0.94 (0.73; 1.21) [.624]	0.94 (0.73; 1.21) [.633]	1.02 (0.82; 1.27) [.825]	0.93 (0.72; 1.19) [.555]
Baseline impact	0.98 (0.74; 1.29) [.870]	0.98 (0.74; 1.29) [.878]	0.97 (0.73; 1.28) [.824]	1.00 (0.73; 1.36) [.977]	0.98 (0.74; 1.29) [.871]
Male gender	0.51 (0.23; 1.13) [.098]	0.51 (0.23; 1.13) [.095]	0.49 (0.22; 1.10) [.083]	0.36 (0.14; 0.92) [.033]	0.51 (0.23; 1.14) [.100]
Age	1.06 (1.03; 1.09) [<.001]	1.06 (1.03; 1.09) [<.001]	1.06 (1.03; 1.09) [<.001]	1.06 (1.03; 1.09) [<.001]	1.06 (1.03; 1.09) [<.001]
Asthma	2.40 (1.10; 5.23) [.028]	2.34 (1.07; 5.08) [.032]	2.29 (1.05; 5.00) [.037]	—‡	2.38 (1.10; 5.18) [.029]
Conjunctivitis	1.17 (0.36; 3.81) [.795]	1.14 (0.35; 3.69) [.831]	1.27 (0.39; 4.13) [.695]	—	1.17 (0.36; 3.79) [.799]
Daily use of rhinitis medication					
No medication	—†	—†	—†	—†	—†
Single medication	1.52 (0.86; 2.67) [.148]	1.56 (0.89; 2.75) [.124]	1.59 (0.90; 2.81) [.109]	2.08 (1.08; 3.99) [.027]	1.50 (0.85; 2.65) [.162]
Comedication	1.31 (0.68; 2.52) [.416]	1.39 (.72; 2.65) [.326]	1.47 (0.77; 2.84) [.245]	1.51 (0.72; 3.17) [.278]	1.28 (0.66; 2.48) [.470]
Daily use of asthma medication					
No medication	—†	—†	—†	—†	—†
Single medication	1.00 (0.47; 2.13) [.993]	0.99 (0.46; 2.11) [.978]	0.98 (0.46; 2.10) [.958]	0.78 (0.39; 1.57) [.485]	0.99 (0.46; 2.11) [.973]
Comedication	0.96 (0.36; 2.57) [.928]	0.93 (0.35; 2.50) [.885]	0.91 (0.33; 2.45) [.845]	0.71 (0.29; 1.78) [.467]	0.94 (0.35; 2.54) [.909]
Immunotherapy	1.36 (0.51; 3.61) [.541]	1.33 (0.50; 3.53) [.567]	1.31 (0.49; 3.49) [.590]	—‡	1.36 (0.51; 3.63) [.533]
EQ-5D-5L anxiety/depression	1.67 (1.31; 2.14) [<.001]	1.67 (1.31; 2.14) [<.001]	1.69 (1.32; 2.16) [<.001]	1.50 (1.14; 1.98) [.004]	1.67 (1.31; 2.14) [<.001]
EQ-5D-5L activities	8.96 (6.48; 12.4) [<.001]	9.22 (6.68; 12.7) [<.001]	9.46 (6.85; 13.1) [<.001]	7.88 (5.46; 11.4) [<.001]	8.88 (6.42; 12.3) [<.001]
EQ-5D-5L self-care	19.5 (11.7; 32.5) [<.001]	19.8 (11.9; 33.1) [<.001]	20.4 (12.2; 34.2) [<.001]	7.41 (4.30; 12.7) [<.001]	19.3 (11.6; 32.2) [<.001]
EQ-5D-5L pain/discomfort	2.71 (2.05; 3.57) [<.001]	2.79 (2.12; 3.67) [<.001]	2.87 (2.18; 3.78) [<.001]	2.23 (1.65; 3.03) [<.001]	2.68 (2.03; 3.54) [<.001]

CI, Confidence interval; CSMS, combined symptom-medication score; EQ-5D-5L, EuroQOL, 5 Domains, 5 Levels; OR, odds ratio; VAS, visual analog scale.

*Results for the OR presented per 10 units of VAS. For VAS asthma, results only concern users with self-reported asthma.

†Referenced category.

‡Not present in the model to ensure convergence.

TABLE E7. Multivariable models assessing the association between rhinitis or asthma symptoms and EQ-5D-5L question on self-care

Variable	VAS global, OR (95% CI) [P value]	VAS nose, OR (95% CI) [P value]	VAS eye, OR (95% CI) [P value]	VAS asthma, OR (95% CI) [P value]	CSMS, OR (95% CI) [P value]
VAS/CSMS*	1.11 (0.95; 1.29) [.181]	1.14 (0.98; 1.32) [.088]	1.25 (1.08; 1.44) [.003]	1.16 (0.98; 1.37) [.079]	1.46 (1.15; 1.85) [.002]
Baseline symptoms	1.08 (0.67; 1.74) [.746]	1.08 (0.67; 1.73) [.767]	1.08 (0.66; 1.78) [.752]	0.83 (0.51; 1.34) [.439]	1.09 (0.66; 1.80) [.724]
Baseline impact	0.63 (0.39; 1.04) [.070]	0.63 (0.39; 1.03) [.068]	0.66 (0.39; 1.10) [.112]	0.83 (0.47; 1.45) [.512]	0.61 (0.37; 1.02) [.061]
Male gender	1.29 (0.30; 5.63) [.730]	1.27 (0.29; 5.59) [.748]	1.33 (0.29; 6.09) [.711]	2.09 (0.41; 10.6) [.372]	1.44 (0.31; 6.65) [.643]
Age	1.00 (0.95; 1.05) [.869]	1.00 (0.95; 1.05) [.940]	0.99 (0.94; 1.04) [.794]	1.01 (0.96; 1.07) [.587]	1.00 (0.95; 1.05) [.912]
Asthma	1.10 (0.27; 4.42) [.895]	1.10 (0.27; 4.45) [.895]	1.19 (0.28; 4.97) [.814]	—	1.04 (0.25; 4.32) [.958]
Conjunctivitis	0.69 (0.07; 7.08) [.758]	0.72 (0.07; 7.55) [.787]	0.45 (0.04; 5.33) [.530]	1.02 (0.10; 10.5) [.990]	0.63 (0.05; 7.19) [.707]
Daily use of rhinitis medication					
No medication	—†	—†	—†	—†	—†
Single medication	0.71 (0.27; 1.85) [.482]	0.69 (0.26; 1.80) [.450]	0.63 (0.24; 1.65) [.344]	1.08 (0.35; 3.33) [.890]	0.62 (0.23; 1.63) [.330]
Comedication	0.69 (0.22; 2.17) [.524]	0.71 (0.22; 2.23) [.553]	0.53 (0.16; 1.74) [.296]	1.40 (0.38; 5.15) [.609]	0.49 (0.15; 1.62) [.240]
Daily use of asthma medication					
No medication	—†	—†	—†	—†	—†
Single medication	2.60 (0.80; 8.50) [.113]	2.71 (0.82; 8.94) [.101]	2.66 (0.79; 8.99) [.115]	1.12 (0.36; 3.41) [.848]	2.10 (0.62; 7.11) [.233]
Comedication	2.96 (0.65; 13.4) [.159]	3.05 (0.66; 14.0) [.152]	3.36 (0.72; 15.7) [.123]	1.32 (0.30; 5.91) [.715]	2.37 (0.51; 11.1) [.272]
Immunotherapy	4.07 (0.74; 22.4) [.106]	3.97 (0.71; 22.1) [.115]	4.18 (0.72; 24.1) [.110]	3.46 (0.56; 21.3) [.181]	4.62 (0.80; 26.6) [.086]
EQ-5D-5L mobility	8.67 (5.29; 14.2) [<.001]	8.80 (5.35; 14.5) [<.001]	9.50 (5.68; 15.9) [<.001]	6.33 (3.62; 11.1) [<.001]	9.24 (5.54; 15.4) [<.001]
EQ-5D-5L activities	3.47 (2.15; 5.59) [<.001]	3.46 (2.14; 5.58) [<.001]	3.43 (2.12; 5.55) [<.001]	3.15 (1.82; 5.46) [<.001]	3.23 (1.99; 5.26) [<.001]
EQ-5D-5L anxiety/depression	1.84 (1.28; 2.64) [.001]	1.85 (1.29; 2.66) [.001]	1.78 (1.23; 2.57) [.002]	2.23 (1.46; 3.41) [<.001]	1.88 (1.30; 2.71) [.001]
EQ-5D-5L pain/discomfort	2.73 (1.71; 4.35) [<.001]	2.80 (1.76; 4.44) [<.001]	2.65 (1.66; 4.23) [<.001]	2.24 (1.34; 3.75) [.002]	2.49 (1.55; 4.00) [<.001]

CI, Confidence interval; CSMS, combined symptom-medication score; EQ-5D-5L, EuroQOL, 5 Domains, 5 Levels; OR, odds ratio; VAS, visual analog scale.

*Results for the OR presented per 10 units of VAS. For VAS asthma, results only concern users with self-reported asthma.

†Referenced category.