

# **Impact of uncontrolled symptoms in health-related quality of life (EQ-5D-5L) of patients with allergic rhinitis: a MASK-air study**

## **Supplementary Methods**

### ***Study design***

We performed a cross-sectional study using real-life data from the MASK-air<sup>®</sup> mobile app. We assessed data reported by European MASK-air<sup>®</sup> users with self-reported AR aged between 16 (or 15 in countries with lower age of digital consent<sup>1</sup>) and 74 years old, who had filled-in the full EQ-5D-5L questionnaire (allowing for the computation of utilities) and/or the EQ-5D visual analog scale (VAS) alone, from May 2015 to December 2022.

### ***Data source***

MASK-air<sup>®</sup> comprises a daily monitoring questionnaire assessing (i) the daily impact of ocular, nasal, asthma and global allergy symptoms using VASs (0-100 scale, a higher score corresponds to a higher impact of symptoms) and (ii) the EQ-5D VAS (0-100 scale, the higher the value the better the patient is feeling on that day). In addition, users may opt to respond to the EQ-5D-5L questionnaire, a multi-attribute instrument for measuring preferences associated with an individual's health state. It covers five dimensions, allowing for the computation of health states which can be converted into utility index scores based on the available country-specific standard value sets for EQ-5D-5L<sup>2</sup>. Higher values of utilities indicate better health-related QoL, with utility values having a maximum value of 1.0 (corresponding to a perfect health state).

### ***Biases***

This study presents some limitations, mostly related to the use of mHealth apps. A bias is possible due to an overrepresentation of patients who are more concerned about their health and of those suffering from more severe disease. However, we performed the analyses stratified per level of symptom control, thus minimizing the risk of bias. Finally,

utilities were not elicited using the gold-standard method (namely, the standard gamble), but rather indirectly estimated based on health profiles obtained using the EQ-5D-5L questionnaire.

### ***Data analysis***

To study the association between different symptoms and QoL, we computed Spearman correlation coefficients between (i) the EQ-5D utility index score or the EQ-5D VAS, and (ii) VAS Eye/Nose/Asthma. We separately analyzed data on utilities and EQ-5D VAS, as they provide complementary information, with utilities being regarded as a societal valuation and the VAS as an individual valuation of the respondent's health state<sup>3</sup>.

Subsequently, we categorized each symptom VAS (Eye/Nose/Asthma) into “good”, “partial” and “poor” control, according to previously validated cut-off points<sup>4</sup>. We first studied the association between each symptom VAS and QoL by building multilevel mixed-effects linear regression models for each individual symptom<sup>5</sup>. In each symptom-based model, symptom control was based on the corresponding VAS (Nose, Eye, or Asthma) and was introduced as an independent categorical variable, whereas the EQ-5D (either the utility score or the VAS score) was the dependent variable. Additional covariates in the models included age and gender; observations were clustered by user, by country, and by month of the year (which were introduced as random effects). Importantly, worse nasal, ocular and asthma symptoms can frequently co-occur. Therefore, to more specifically assess the impact of each isolated uncontrolled symptom (i.e., to better measure which symptoms have the greatest impact in QoL, adjusting for confounding from the remaining symptoms), we performed additional multilevel mixed-effects linear regression analyses restricted to observations with “good” control of the two remaining symptom VASs simultaneously (e.g., to assess the impact of poor versus good control in VAS Eye, we considered only those observations in which there was simultaneously good control of VAS Nose and VAS Asthma, thereby allowing us to isolate the impact of ocular symptoms on quality of life). We performed such a stratified analysis as opposed to building classical mutually adjusted multivariable regression models due to (i) multicollinearity between allergy symptoms and (ii) the need to account for interactions in multivariable models, which would render regression coefficients difficult to interpret clinically. Separate analyses were performed considering

observations from (i) all patients with AR (regardless of whether or not they had asthma), (ii) patients with AR only, or (iii) patients with simultaneous AR and asthma<sup>6</sup>.

**Table S1. Characteristics of the MASK-air sample used.**

	Utility index score	EQ-5D VAS
<i>N</i> observations ( <i>N</i> users)	4008 (2424)	82 737 (7905)
AR only — <i>N</i> observations ( <i>N</i> users)	2232 (1454)	50 928 (5388)
AR + Asthma — <i>N</i> observations ( <i>N</i> users)	1776 (970)	31 809 (2517)
Females — <i>N</i> (%)	2453 (61.2)	42 864 (51.8)
Age — Mean (SD)	39.9 (13.1)	41.0 (14.9)
Immunotherapy — <i>N</i> (%)	716 (19.1)	7910 (10.8)
SCIT — <i>N</i> (%)	262 (6.9)	4471 (6.1)
SLIT — <i>N</i> (%)	454 (12.1)	3439 (4.7)
VAS eye — Median (IQR)	16 (49)	6 (21)
Days of good control — <i>N</i> (%)	2198 (54.8)	61 260 (74.0)
Days of partial control — <i>N</i> (%)	462 (11.5)	8817 (10.7)
Days of poor control — <i>N</i> (%)	1348 (33.6)	12 660 (15.3)
VAS nose — Median (IQR)	33 (56)	15 (33)
Days of good control — <i>N</i> (%)	1542 (38.5)	48 241 (58.3)
Days of partial control — <i>N</i> (%)	537 (13.4)	12 546 (15.2)
Days of poor control — <i>N</i> (%)	1929 (48.1)	21 950 (26.5)
VAS asthma — Median (IQR) <sup>a</sup>	24 (48)	12 (26)
Days of good control — <i>N</i> (%) <sup>a</sup>	848 (47.7)	20588 (66.0)
Days of partial control — <i>N</i> (%) <sup>a</sup>	211 (11.9)	4918 (14.7)
Days of poor control — <i>N</i> (%) <sup>a</sup>	717 (40.4)	6303 (19.3)

<sup>a</sup> – only for patients with asthma

**Table S2. Spearman correlation coefficients between Visual Analogue Scales (VAS) referring to allergy symptoms and utilities or EQ-5D VAS (both considering all patients and restricting to patients who had filled in the full EQ-5D questionnaire).**

	VAS Eye	VAS Nose	VAS asthma <sup>a</sup>
	(Correlation coefficient (95% CI))	(Correlation coefficient (95% CI))	(Correlation coefficient (95% CI))
Utility index score	-0.38 (-0.41; -0.36)	-0.41 (-0.43; -0.38)	-0.40 (-0.44; -0.36)
EQ-5D VAS			
All patients	-0.38 (-0.39; -0.37)	-0.51 (-0.52; -0.50)	-0.40 (-0.44; -0.36)
Patients reporting the full EQ-5D questionnaire	-0.40 (-0.43; -0.36)	-0.46 (-0.49; -0.42)	-0.45 (-0.49; -0.42)

CI = Confidence interval; <sup>a</sup> — computed for patients with allergic rhinitis and asthma only.

**Table S3. Differences in utilities and EQ-5D VAS levels associated with not well controlled nose, eye, and asthma symptoms, considering all participants.**

	Ocular symptoms <sup>a</sup> — Mean difference (95% CI) [ <i>p</i> value]	Nasal symptoms <sup>b</sup> — Mean difference (95% CI) [ <i>p</i> value]	Asthma symptoms <sup>c</sup> — Mean difference (95% CI) [ <i>p</i> value]
<b>Difference in Utilities</b>			
AR (All)			
Poor vs. good control	-0.10 (-0.11; -0.08) [ $<0.001$ ]	-0.08 (-0.09; -0.07) [ $<0.001$ ]	NA
Partial vs. good control	-0.05 (-0.06; -0.03) [ $<0.001$ ]	-0.02 (-0.03; -0.01) [0.005]	NA
Poor vs. partial control	-0.05 (-0.06; -0.03) [ $<0.001$ ]	-0.06 (-0.07; -0.04) [ $<0.001$ ]	NA
AR only			
Poor vs. good control	-0.09 (-0.10; -0.08) [ $<0.001$ ]	-0.07 (-0.08; -0.05) [ $<0.001$ ]	NA
Partial vs. good control	-0.04 (-0.06; -0.03) [ $<0.001$ ]	-0.01 (-0.03; 0.00) [0.298]	NA
Poor vs. partial control	-0.05 (-0.07; -0.03) [ $<0.001$ ]	-0.06 (-0.08; -0.04) [ $<0.001$ ]	NA
AR + asthma			
Poor vs. good control	-0.10 (-0.12; -0.08) [ $<0.001$ ]	-0.09 (-0.11; -0.07) [ $<0.001$ ]	-0.11 (-0.12; -0.09) [ $<0.001$ ]
Partial vs. good control	-0.05 (-0.07; -0.02) [ $<0.001$ ]	-0.03 (-0.08; -0.01) [ $<0.001$ ]	-0.03 (-0.06; -0.01) [0.006]
Poor vs. partial control	-0.05 (-0.07; -0.02) [ $<0.001$ ]	-0.06 (-0.08; -0.04) [ $<0.001$ ]	-0.07 (-0.10; -0.05) [ $<0.001$ ]
<b>Difference in EQ-5D VAS</b>			
AR (All)			
Poor vs. good control	-12.9 (-13.2; -12.6) [ $<0.001$ ]	-14.0 (-14.2; -13.7) [ $<0.001$ ]	NA
Partial vs. good control	-5.8 (-6.1; -5.5) [ $<0.001$ ]	-5.6 (-5.8; -5.3) [ $<0.001$ ]	NA
Poor vs. partial control	-7.1 (-7.4; -6.7) [ $<0.001$ ]	-8.4 (-8.7; -8.1) [ $<0.001$ ]	NA
AR only			
Poor vs. good control	-13.4 (-13.8; -13.1) [ $<0.001$ ]	-14.1 (-14.4; -13.8) [ $<0.001$ ]	NA
Partial vs. good control	-6.3 (-6.7; -6.0) [ $<0.001$ ]	-5.6 (-5.9; -5.3) [ $<0.001$ ]	NA
Poor vs. partial control	-7.1 (-7.5; -6.7) [ $<0.001$ ]	-8.5 (-8.8; -8.1) [ $<0.001$ ]	NA
AR + asthma			
Poor vs. good control	-12.2 (-12.7; -11.7) [ $<0.001$ ]	-13.8 (-14.2; -13.4) [ $<0.001$ ]	-14.8 (-15.2; -14.4) [ $<0.001$ ]
Partial vs. good control	-5.2 (-5.6; -4.7) [ $<0.001$ ]	-5.5 (-5.9; -5.1) [ $<0.001$ ]	-6.0 (-6.4; -5.6) [ $<0.001$ ]
Poor vs. partial control	-7.0 (-7.5; -6.4) [ $<0.001$ ]	-8.4 (-8.8; -7.9) [ $<0.001$ ]	-8.8 (-9.3; -8.3) [ $<0.001$ ]

AR = Allergic rhinitis; CI = Confidence interval; VAS = Visual Analogue Scale; <sup>a</sup> — This column displays differences in EQ-5D utilities and EQ-5D VAS when comparing days with poor vs. good, partial vs. good, and poor vs. partial control of ocular symptoms (VAS eye); <sup>b</sup> — This column displays differences in EQ-5D utilities and EQ-5D VAS when comparing days with poor vs. good, partial vs. good, and poor vs. partial control of nasal symptoms (VAS nose); <sup>c</sup> — This column displays differences in EQ-5D utilities and EQ-5D VAS when comparing days with poor vs. good, partial vs. good, and poor vs. partial control of asthma symptoms (VAS asthma).

## References

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