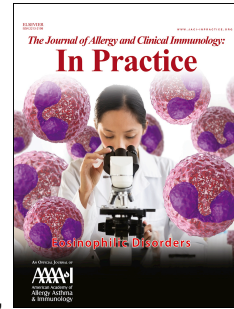


# Journal Pre-proof

Poor rhinitis and asthma control is associated with decreased health-related quality-of-life and utilities: A MASK-air study

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1 **Poor rhinitis and asthma control is associated with decreased**  
2 **health-related quality-of-life and utilities: A MASK-air study**

3

4 **Short title: EQ-5D-5L in allergic rhinitis and asthma in Europe**

5

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107 manuscript for publication.

108 **Abstract**

109

110 **Background:** Allergic rhinitis (AR) and asthma may impact health-related quality-of-life.  
111 However, national estimates on the quality-of-life of patients with AR or asthma are  
112 lacking.

113 **Objective:** To provide estimates for utility scores and EQ-5D Visual Analog Scale (VAS)  
114 for patients with AR or asthma.

115 **Methods:** We conducted a cross-sectional study using direct patient data from the MASK-  
116 air<sup>®</sup> app on European MASK-air<sup>®</sup> users with self-reported AR or asthma. We used a  
117 multiattribute instrument (EQ-5D) to measure quality-of-life (as utility scores and EQ-5D  
118 VAS values). Mean scores were calculated per country and disease control level using  
119 multilevel regression models with post-stratification, accounting for age and sex biases.

120 **Results:** We assessed data from up to 7905 MASK-air<sup>®</sup> users reporting a total of up to  
121 82,737 days. For AR, utilities ranged from 0.86-0.99 for good control *versus* 0.72-0.85 for  
122 poor control; EQ-5D VAS levels ranged from 78.9-87.9 for good control *versus* 55.3-64.2  
123 for poor control. For asthma, utilities ranged from 0.84-0.97 for good control *versus* 0.73-  
124 0.87 for poor control; EQ-5D VAS levels ranged from 68.4-81.5 for good control *versus*  
125 51.4-64.2 for poor control. Poor disease control was associated with a mean loss of 0.14  
126 utilities for both AR and asthma. For the same control levels, AR and asthma were  
127 associated with similar utilities and EQ-5D VAS levels. However, lower values were  
128 observed for asthma+AR when compared to AR alone.

129 **Conclusion:** Poor AR or asthma control are associated with reduced quality-of-life. The  
130 estimates obtained from mHealth data may provide valuable insights for health technology  
131 assessment studies.

132 **Highlights box:**

133

134 *What is already known about this topic?*

135 National estimates of patients' quality-of-life based on control of asthma/allergic rhinitis are  
136 lacking. Real-world data may provide insights into quality-of-life of patients with  
137 asthma/allergic rhinitis and improve the ability to provide care to these patients.

138

139 *What does this article add to our knowledge?*

140 This study provides country-specific estimates (per disease control level) for quality-of-life  
141 in patients with allergic rhinitis or asthma across multiple European countries, using EQ-5D  
142 utility index scores and EQ-5D visual analogue scale.

143

144 *How does this study impact current management guidelines?*

145 This study points to the importance of achieving a good rhinitis and asthma control.  
146 It also provides insights into patients' preferences regarding different control levels and  
147 comorbid status, which are essential for guideline development.

148

149 **Keywords:**

150 Allergic rhinitis; Asthma; EQ-5D-5L; Health-related quality of life; Mobile health; Quality  
151 of life; Real-world data; Utilities.

152

153 **Abbreviations:**

154 AR: Allergic rhinitis

155 CI: Confidence interval

- 156 CSMS: Combined Symptom-Medication Score
- 157 e-DASTHMA: Electronic Daily Control Score for Asthma
- 158 HRQoL: Health-related quality of life
- 159 MID: Minimal Important Difference
- 160 OECD: Organisation of Economic Cooperation and Development
- 161 QoL: Quality of life
- 162 SD: Standard deviation
- 163 SE: Standard error
- 164 VAS: Visual Analog Scale

**165 Introduction**

166 Allergic rhinitis (AR) and asthma can impact quality of life (QoL).<sup>1</sup> Quantifying the impact  
167 of AR and asthma on health-related QoL (HRQoL) is important for many purposes  
168 including health technology assessment studies, enabling cost-utility assessments of  
169 interventions for AR or asthma.<sup>2, 3</sup> However, national estimates on the HRQoL of patients  
170 with AR or asthma per level of disease control are not available.

171 HRQoL can be assessed using different methods. The EQ-5D questionnaire is the most  
172 widely used multi-attribute utility instrument.<sup>4</sup> It assesses five HRQoL domains and  
173 produces a 5-digit health state profile that can be converted into a single index value  
174 (utilities), quantifying the preferences of the population on the respective health states. The  
175 EQ-5D questionnaire also comprises a visual analog scale (VAS) for patients' self-  
176 assessment of their health status. Utilities and EQ-5D VAS may both be relevant to policy  
177 makers, as they provide different and complementary information.<sup>5</sup>

178 One source of information on QoL may come from real-world data obtained from mobile  
179 apps. For example, the EQ-5D-5L questionnaire is included in MASK-air<sup>®</sup>, a mobile app  
180 for asthma and rhinitis. In its review of MASK-air<sup>®</sup>, the Organisation of Economic  
181 Cooperation and Development (OECD) stressed the importance of providing data on  
182 HRQoL and utilities based on MASK-air<sup>®</sup> real-world data. A previous MASK-air<sup>®</sup> study  
183 found that worse AR control is associated with higher EQ-5D-5L levels, with a distinct  
184 impact in different EQ-5D-5L domains<sup>6</sup>. However, that independent study did not provide  
185 generalizable utilities and EQ-5D VAS estimates for these populations.

186 Therefore, in this study, we aimed to study how HRQoL varies with AR or asthma control  
187 and to provide populational estimates for the mean utility index score and EQ-5D VAS for  
188 these diseases.

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## 189 **Methods**

### 190 *Study design*

191 We performed a cross-sectional study based on direct patient data from MASK-air<sup>®</sup>. We  
192 first used multinomial regression models to assess if the level of AR or asthma control was  
193 associated with differences in the utility index score and in the EQ-5D VAS. Then, we  
194 computed estimates computed for the mean utility index score and for the mean EQ-5D  
195 VAS in European patients with AR or asthma (by country and level of disease control).  
196 Furthermore, we applied multivariable models were with post-stratification to correct for  
197 biases in the age and sex distribution of MASK-air<sup>®</sup> users.

### 198 *Setting and participants*

199 MASK-air<sup>®</sup> is freely available on the Google Play and Apple App Stores of 29 countries  
200 ([www.mask-air.com](http://www.mask-air.com)).<sup>7</sup> It is a Good Practice of the Directorate-General for Health and Food  
201 Safety (European Commission) for digitally-enabled, patient-centered care in rhinitis and  
202 asthma multimorbidity<sup>7-9</sup>, and a Best Practice of OECD for Public Health on integrated care  
203 for chronic diseases<sup>10</sup>.

204 We assessed European MASK-air<sup>®</sup> users (i) aged between 15 or 16 years (depending on the  
205 age of digital consent in the country<sup>11</sup>) and 74 years, (ii) with self-reported AR or asthma,  
206 and (iii) who had filled-in the full EQ-5D-5L questionnaire (allowing for the computation  
207 of utilities) or the EQ-5D VAS alone. We analyzed utilities and EQ-5D VAS data, as they  
208 provide complementary information, with utilities being regarded as a societal valuation  
209 and the VAS as an individual valuation of the respondent's health state<sup>5</sup>.

210 We analyzed data (May 2016-December 2022) from European countries (i) with at least 20  
211 users reporting EQ-5D-5L, and (ii) for which a national value-set was available to compute  
212 utilities based on the EQ-5D-5L. We excluded countries in which data on the mean utilities  
213 for the general population were not available. For Denmark and Belgium, we were not able  
214 to analyze data on asthma due to limitations in sample size.

### 215 *Data sources and variables*

216 MASK-air<sup>®</sup> includes a daily monitoring questionnaire in which users report (i) the daily  
217 impact of asthma and AR symptoms through 0-100 VAS (with higher scores corresponding  
218 to higher impact of allergy symptoms), (ii) the EQ-5D VAS (0-100 scale - the higher the  
219 value, the better the patient is feeling on that day), and (iii) the daily use of asthma and  
220 rhinitis medication (using a scroll list of prescribed and over-the-counter medications  
221 customized for each country).<sup>7</sup> The data collected from daily symptoms and medication use  
222 allow for the computation of the ARIA-EAACI Combined Symptom-Medication Score  
223 (CSMS) and the electronic daily control score for asthma (e-DASTHMA)<sup>12, 13</sup> (Table E1).  
224 Additionally, MASK-air<sup>®</sup> users can optionally answer the EQ-5D-5L questionnaire, a  
225 multi-attribute instrument that assesses an individual's health status through a VAS and a  
226 descriptive system covering five dimensions (Supplementary Methods)<sup>4</sup>. Health states can  
227 be converted into utility index scores based on available country-specific standard value  
228 sets for the EQ-5D-5L.<sup>14-23</sup>

### 229 *Data analysis*

230 When responding to the MASK-air<sup>®</sup> daily monitoring questionnaire, it is not possible to  
231 skip any of the questions, and data are saved only after the final answer. This precludes any  
232 missing data within each questionnaire.

233 All analyses were performed using the software R. Categorical variables were described  
234 using absolute and relative frequencies, while continuous variables were described using  
235 mean and standard deviation (SD).

236 First, to study whether AR or asthma control are associated with differences in mean utility  
237 index scores and EQ-5D VAS levels, we built multilevel mixed-effects models considering  
238 the clustering of observations by user and by country (i.e., they were set as random effects).  
239 We selected the level of disease control (i.e., the CSMS categories for AR, or the e-  
240 DASTHMA score categories for asthma) as a fixed effect and included age and sex as  
241 covariates in the models (Supplementary Methods).

242 Subsequently, in our main analyses, we estimated mean utility index scores and mean EQ-  
243 5D VAS separately for patients with AR and for patients with asthma. Therefore, we  
244 assessed four different samples per country and per level of disease control: (i) utility index  
245 scores in patients with AR, (ii) utility index scores in patients with asthma, (iii) EQ-5D  
246 VAS in patients with AR, and (iv) EQ-5D VAS in patients with asthma. To correct for  
247 biases in the sex and age representativeness of MASK-air<sup>®</sup> users, we computed multilevel  
248 models with post-stratification. This methodology has previously been described<sup>24</sup>. It  
249 enabled the estimation of the expected nationwide mean utility index scores and EQ-5D  
250 VAS levels (by country and level of disease control), and considered the populational sex  
251 and age distribution of the patients with AR and asthma in the respective countries.

252 Uncertainty was assessed by performing 1000 simulations and computing the mean of the  
253 coefficients of the multilevel models with post-stratification of these 1000 random samples.

254 A graphical representation of our methodology is available in Figure 1, and a more detailed  
255 report is available in the Supplementary Methods (and tables E2-E4).

256 We performed sensitivity analyses on: (i) users with AR and no asthma, and (ii) users with  
257 AR and asthma. We were unable to perform additional analyses on patients with asthma  
258 only due to limitations in the sample size.

259 Differences between groups were assessed by comparison with the minimal important  
260 difference (MID; determined using  $0.5 \times$  standard-deviation), corresponding to 10 points for  
261 EQ-5D VAS<sup>11</sup> and 0.09 for utilities. As the MID may vary according to target population,  
262 this means that a difference of less than 10 points in the EQ-5D VAS or of less than 0.09 in  
263 the utility score would not be deemed clinically relevant.

#### 264 *Ethics*

265 MASK-air is *Conformité Européene*-registered and follows the European Union General  
266 Data Protection Regulation. An independent review board approval was not required for  
267 this specific study because (i) the use of MASK-air secondary data was approved by an  
268 independent review board (Köln-Bonn, Germany; reference number 17-069), (ii) all data  
269 were anonymized before the study using k-anonymity, and (iii) users agreed to the analysis  
270 of their data for research purposes in the terms of use (translated into all languages and  
271 customized according to the legislation of each country).

## 272 **Results**

### 273 *Descriptive results*

274 The utility index score was estimated in 2424 users for AR (4008 observations [i.e., days],  
275 63.2% females, mean±SD age=36.3±13.1 years), and in 1032 users for asthma (1936  
276 observations, 66.6% females, mean age±SD=37.2±13.2 years) (Table 1 and Figure E1).

277 The EQ-5D VAS was estimated in 7905 users for AR (82,737 observations, 57.4% females,  
278 mean age±SD=36.4±13.1 years), and in 2821 users for asthma (36,046 observations, 61.1%  
279 females, mean age±SD=36.4±13.5 years) (Table 1 and Figure E1).

### 280 *Impact of disease control on HRQoL*

281 In multivariable mixed-effects regression models, when compared to good disease control,  
282 both partial and poor disease control were associated with decreased utilities for asthma and  
283 for AR (Table 2). Having a partial disease control was associated with a decrease of 0.03 to  
284 0.04 units in utilities, while for poor disease control, the decrease range was of 0.10 to 0.14  
285 units (Table 2). Regarding EQ-5D VAS, having a partial disease control was associated  
286 with a mean decrease of 9.2 to 9.7 units decrease in VAS for AR patients, and a 5.5 to 5.6  
287 decrease for asthma patients. However, poor disease control was associated with a mean  
288 decrease of 15.5-15.6 in asthma patients and 20.6 in AR (Table 2).

### 289 *Utility index score per country*

290 Mean utility scores per country and per level of disease control are available in Table 3 and  
291 Figure E2.

292 In all countries, we observed that worse AR or asthma control was associated with lower  
293 utilities. We found that good AR control was associated with a utility score ranging from  
294 0.86 (Belgium) to 0.99 (Poland), partial AR control from 0.83 (Belgium) to 0.96 (Poland),  
295 while poor AR control was associated with a utility score ranging from 0.72 (Belgium) to  
296 0.85 (Poland). On average, moving from good to partial control led to a loss of 0.03  
297 utilities, whereas moving from partial to poor control of disease led to a mean loss of 0.11  
298 utilities (higher than the MID). In other words, moving from good to poor disease control  
299 led to a mean loss of 0.14 utilities (higher than the MID).

300 For asthma, we found good control to be associated with a utility score ranging from 0.84  
301 (Netherlands) to 0.97 (Poland), partial control from 0.80 (Netherlands) to 0.94 (Poland),  
302 and poor control from 0.73 (Netherlands) to 0.87 (Poland). Moving from good to partial  
303 disease control led to an average loss of 0.03 utilities, while moving from partial to poor  
304 disease control led to an average loss of 0.08 utilities. In other words, moving from good to  
305 poor disease control led to a mean loss of 0.11 utilities (higher than the MID).

306 The between-country differences were smaller than the MID, except between Belgium  
307 *versus* Portugal or Poland, and between the Netherlands *versus* Poland, for both asthma and  
308 AR.

### 309 ***EQ-5D VAS per country***

310 Mean EQ-5D VAS levels per country and per level of disease control are available in Table  
311 4 and Figure E2.

312 In all countries, we observed that worse AR or asthma control was associated with lower  
313 EQ-5D VAS. Good AR control was associated with a mean EQ-5D VAS ranging from 78.9  
314 (Italy) to 87.9 (United Kingdom), partial control from 67.4 (Italy) to 76.3 (United  
315 Kingdom), and poor control from 55.3 (Italy) to 64.2 (United Kingdom). Moving from  
316 good to partial AR control was associated with an average decrease of 11.6 points in the  
317 EQ-5D VAS scale (higher than the MID), while moving from partial to poor AR control  
318 was associated with an average decrease of 11.7 points in the EQ-5D VAS scale (higher  
319 than the MID).

320 For asthma, we found good control to be associated with a mean EQ-5D VAS ranging from  
321 68.4 (Netherlands) to 81.5 (Portugal), partial control from 59.8 (Italy) to 72.8 (Portugal),  
322 and poor control from 51.4 (Netherlands) to 64.5 (Portugal). Compared to good disease  
323 control, on average, patients with partial disease control showed a decrease of 8.6 points in  
324 the EQ-5D VAS (lower than the MID), while patients with poor disease control showed a  
325 decrease of 16.4 points in the EQ-5D VAS (higher than the MID).

326 For both asthma and AR, all between-countries differences were lower than the MID.

### 327 ***Comparison between AR alone versus AR with asthma***

328 We performed an additional sensitivity analysis, estimating utilities for users with AR alone  
329 and for users with both asthma and AR (Figure 2; Tables E3-E4). Results were similar to  
330 those described above. We found mean utilities and mean EQ-5D VAS scores for patients  
331 with well-controlled or partially-controlled disease to be consistently higher in patients with  
332 AR alone than in those with both AR and asthma, although differences were not higher than

333 the MID. However, for patients with poorly-controlled disease, mean utilities were found to  
334 be similar in patients with AR alone and in patients with both asthma and AR.

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**335 Discussion**

336 This is the first study to produce utility and EQ-5D VAS estimates per country and per  
337 level of control in patients with AR or asthma for several European countries, and the first  
338 using real life mHealth data comparing HRQoL in AR and asthma. This study displays  
339 several relevant novel findings including: (i) similar utilities were observed in patients with  
340 AR versus those with asthma for poorly controlled disease; (ii) for patients with controlled  
341 or partly controlled AR, AR + asthma displayed overall lower mean utility estimates than  
342 AR alone; and (iii) a higher discrimination between different control levels was observed  
343 for the EQ-5D VAS than for the utility index score. Our results are especially relevant for  
344 health technology assessment studies in which national estimates of utilities for AR or  
345 asthma may be required.

346 We found that poorer disease control was associated with decreased HRQoL. This is  
347 consistent with previous studies that showed poorer asthma control or increased asthma or  
348 AR severity to be associated with decreased QoL.<sup>25-30</sup> In AR, however, many studies using  
349 EQ-5D-5L were performed during immunotherapy trials<sup>31</sup> or did not differentiate between  
350 controlled and uncontrolled rhinitis.<sup>32</sup> As for asthma, in a meta-analysis published in  
351 2022,<sup>33</sup> seven studies assessed utilities based on ED-5D-5L with observed utilities ranging  
352 from 0.83 to 0.88 (results similar to ours). In the two studies assessing uncontrolled asthma,  
353 mean EQ-5D-5L utilities were 0.69.<sup>34, 35</sup> Studies based on ED-5D-3L also showed that  
354 severe asthma impairs utilities.<sup>33</sup>

355 We computed mean utilities and EQ-5D VAS scores for 10 European countries and three  
356 validated control levels.<sup>36</sup> Therefore, for the first time, we found HRQoL for the same level

357 of control - whether measured through the utility index score or through the EQ-5D VAS -  
358 to be similar in patients with AR and in patients with asthma, especially those with poor  
359 disease control. This is in line with a previous epidemiologic study in young adults, which  
360 suggested a similar impairment in HRQoL for patients with AR and for patients with  
361 asthma, although disease control was not assessed in this study.<sup>37</sup> Importantly, we also  
362 found the differences in HRQoL between good and partial disease control to be smaller  
363 than those between partial and poor disease control, both for AR and for asthma. Another  
364 relevant finding in our study is that, compared with utilities, the EQ-5D VAS could better  
365 differentiate AR patients with well-, partly-, or poorly-controlled disease.

366 In our study, most patients with asthma also had AR. This, however, may reflect real life,  
367 as there have been estimates indicating that over 80% of patients with asthma have AR.<sup>38</sup>  
368 Importantly, we found mean utility estimates to be consistently lower for comorbid AR +  
369 asthma compared to AR alone. This assessment is of particular importance, given that AR  
370 alone and AR + asthma display relevant genetic, immunologic, epidemiologic, and clinical  
371 findings.<sup>39</sup>

372 Our study showed that rhinitis and asthma may have an important impact on HRQoL,  
373 which may be underappreciated. For example, the mean utility value for patients with type  
374 2 diabetes mellitus is 0.79<sup>40</sup>, a value which is not too dissimilar from the utility values of  
375 poorly-controlled AR or asthma. The latter are also similar to the utilities estimated for  
376 New York Heart Association Classes I and II of heart failure (0.79–0.86 for class I and  
377 0.75–0.81 for class II)<sup>41</sup> or for low disease activity rheumatoid arthritis (0.73)<sup>42</sup>. This  
378 highlights the need for physicians to systematically assess their patients on their rhinitis and

379 asthma symptoms and to promote a good control of allergic diseases (something which is  
380 of utmost relevance considering that AR is frequently undervalued in the clinical practice).  
381 Finally, the present study used an app and showed that EQ-5D and VAS can be monitored  
382 using mHealth as previously reported.<sup>43</sup>

383 This study has some limitations. First, we rely on self-reported data regarding the diagnosis  
384 of AR and asthma. We were unable to calculate national utility and EQ-5D VAS estimates  
385 for asthma and AR considering all control levels together, as information on the  
386 distribution of AR and asthma severity levels per country were not widely available. For  
387 AR, only regional (as opposed to national) estimates of the prevalence of AR were  
388 available for Denmark and Poland. For the Netherlands, specific data on the prevalence of  
389 AR were not available and we had to use data on the prevalence of respiratory allergic  
390 disorders. Likewise, for Spain, we considered data on the prevalence of general allergies  
391 (excluding asthma), as specific data for the prevalence of AR per sex and age group were  
392 not available. For some of the included countries, estimates of the prevalence of AR or  
393 asthma were not available in sufficient detail for all age groups. In these cases, we assumed  
394 the prevalence of the disease to be constant throughout each age interval provided in the  
395 respective studies. Additionally, we were not able to assess non-allergic comorbidities (as  
396 these are not collected in the MASK-air app). However, we believe that their frequency and  
397 severity are not highly impacted by the control of allergic diseases. MASK-air also does not  
398 collect user information such as income, education level and occupation. Collecting such  
399 data could present a privacy threat and limit the feasibility of mHealth studies. Importantly,  
400 we provide stratified analyses by control level, which limits biases related to disease control  
401 (which may be influenced by social determinants). We included Belgium and Denmark in

402 the analysis for AR but not for asthma, as a limited sample was available. However, our  
403 methodology relies on data from all countries to allow for the computation of country-  
404 specific utilities and has been shown to provide reliable estimates with smaller sample sizes  
405 than the ones included in this study<sup>24</sup>.

406 This study also has important strengths. We assessed real-world data from a large set of  
407 participants from 10 European countries, with the structure of MASK-air<sup>®</sup> precluding the  
408 existence of missing data within each daily questionnaire. The CSMS and the e-  
409 DASTHMA have been previously assessed on their validity, reproducibility and MID (with  
410 several observed differences being larger than the MID).<sup>12, 13</sup> The methodology we  
411 employed (multilevel models with post-stratification), while innovative in this field, has  
412 been previously validated<sup>24</sup>. We found consistent results in different models in sensitivity  
413 analyses, pointing to the robustness of the results. In addition, we found that, using both  
414 multilevel mixed-effects models and multilevel models with post-stratification, AR and  
415 asthma control were associated with worse disease control. By providing our estimates per  
416 level of disease control, we limit the risk of bias which may arise from mHealth app users  
417 displaying higher disease severity. We report utility index scores and EQ-5D VAS for  
418 several European countries. This is especially important as the EQ-5D VAS and the utility  
419 index scores calculated from EQ-5D-5L profiles are complementary and may both be  
420 relevant for decision makers<sup>44</sup>. Finally, we quantify the impact on HRQoL for several  
421 European countries both for AR and for comorbid AR and asthma.

422 To the best of our knowledge, this is the first study (i) to estimate HRQoL measures for  
423 patients with AR or asthma in several European countries, and (ii) to assess AR alone and  
424 AR+asthma. These national estimates may be used in cost-utility studies, in decision

425 analysis models, or in other health technology assessment studies in which national  
426 estimates of utilities for AR or asthma may be required. This allows for an assessment of  
427 AR or asthma interventions, considering not only their effectiveness in symptom control  
428 but also their expected impact on the HRQoL.

429 Our study has produced estimates of the mean utility score and EQ-5D VAS for patients  
430 with AR or asthma in up to 10 European countries. Importantly, we found differences in  
431 utility index scores which may be explained not only by different national standard value  
432 sets used to compute utilities, but also by differences in HRQoL across countries, as shown  
433 by the across-country differences in EQ-5D VAS (which is independent of any country  
434 specific conversion). As such, these results - although generalizable for each of the  
435 countries studied - may not be generalizable for other countries. Additionally, our  
436 methodology, in particular the usage of multilevel regression models with post-  
437 stratification, may be employed in other contexts to correct for sampling biases.

#### 438 **Conclusion**

439 Using mHealth data from the MASK-air<sup>®</sup> app, we estimated mean utilities and EQ-5D  
440 VAS for AR and asthma, per level of disease control. We obtained national estimates for 10  
441 different European countries corrected for biases in the age and sex distribution of MASK-  
442 air<sup>®</sup> users. We observed consistent results across countries showing that (i) poor AR or  
443 asthma control is associated with low HRQoL, and (ii) for the same control levels, the  
444 HRQoL in AR is similar to that in asthma. This study has not only provided estimates that  
445 can be used in future health technology assessment studies (namely cost-utility analyses)  
446 but has also highlighted the importance of achieving a good AR and asthma control.

447 Importantly, the results of this real-life study can be used to show the impact of AR alone  
448 or with asthma to policy-makers, as recommended by OECD.<sup>45</sup>

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601 **Tables**

602

603 **Table 1. Characteristics of the MASK-air sample used to estimate nationwide utility index**604 **score and EQ-5D Visual Analog Scale (VAS) for allergic rhinitis (AR) and asthma.**

	Utility index score <sup>a</sup>		EQ-5D VAS <sup>b</sup>	
	AR	Asthma	AR	Asthma
<i>N</i> users ( <i>N</i> observations)	2424 (4008)	1032 (1936)	7905 (82737)	2821 (36046)
<b>Belgium</b>	39 (45)	NA	72 (339)	NA
<b>Denmark</b>	24 (35)	NA	37 (67)	NA
<b>France</b>	510 (744)	177 (263)	2146 (25963)	613 (7653)
<b>Germany</b>	324 (808)	141 (498)	833 (19847)	308 (10650)
<b>Italy</b>	417 (709)	177 (254)	2667 (9042)	836 (3007)
<b>Netherlands</b>	190 (280)	72 (105)	278 (1504)	109 (301)
<b>Poland</b>	211 (294)	90 (191)	402 (6683)	155 (2952)
<b>Portugal</b>	388 (614)	224 (378)	765 (11311)	469 (8485)
<b>Spain</b>	181 (274)	91 (154)	450 (6567)	227 (2464)
<b>United Kingdom</b>	140 (205)	60 (93)	255 (1414)	104 (534)
<b>Females — <i>N</i> (%)</b>	1534 (63.2)	687 (66.6)	4540 (57.4)	1725 (61.1)
<b>Age — Mean (SD)</b>	36.3 (13.1)	37.2 (13.2)	36.4 (13.1)	36.4 (13.5)
<b>AR + Asthma — <i>N</i> (%)</b>	1454 (60.0)	944 (91.5)	5388 (68.2)	2473 (91.2)
<b>Disease control — <i>N</i> (%)<sup>b</sup></b>				
<b>Days of good control</b>	1465 (36.6)	875 (45.2)	47562 (57.5)	22561 (62.6)
<b>Days of partial control</b>	1019 (25.4)	326 (16.8)	21685 (26.2)	6598 (18.3)
<b>Days of poor control</b>	1523 (38.0)	735 (40.0)	13489 (16.3)	6887 (19.1)
<b>VAS</b>				
<b>VAS global — Median (IQR)</b>	34 (54)	35 (52)	14 (31)	15 (29)
<b>VAS eye — Median (IQR)</b>	16 (49)	17 (59)	6 (21)	8 (21)
<b>VAS nose — Median (IQR)</b>	33 (56)	31 (54)	15 (33)	15 (30)
<b>VAS asthma — Median (IQR)</b>	5 (30)	23 (47)	3 (14)	11 (26)

605

NA = Not available. SD = Standard deviation; VAS = Visual Analog Scale.

606

<sup>a</sup> — Characteristics of the MASK-air sample used to estimate nationwide EQ-5D Visual Analog Scale (VAS) scores. The EQ-5D VAS is a 0-100 scale in

607

which higher scores reflect better overall health on that day. <sup>b</sup> — Characteristics of the MASK-air sample used to estimate nationwide utility index scores.

608 Utilities quantify the preferences of the population on the respective health states, with 1 representing full health and 0 representing being dead. <sup>c</sup> — AR  
609 control was assessed based on the combined symptom-medication score (CSMS) and asthma control based on the electronic daily control score for asthma  
610 (e-DASTHMA).  
611

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612 **Table 2. Multilevel mixed-effects models assessing the association between disease**  
 613 **control and utility index score/EQ-5D Visual Analog Scale (VAS).**

	Utility index score <sup>a</sup> (Coefficient (95% CI) [ <i>p</i> -value])	EQ-5D VAS <sup>b</sup> (Coefficient (95% CI) [ <i>p</i> -value])
<b>Allergic rhinitis (All patients)</b>		
Partial vs. good control	-0.03 (-0.04; -0.02) [ $<0.001$ ]	-9.2 (-9.4; -9.0) [ $<0.001$ ]
Poor vs. good control	-0.13 (-0.14; -0.11) [ $<0.001$ ]	-20.6 (-20.9; -20.3) [ $<0.001$ ]
Poor vs. partial control	-0.10 (-0.11; -0.08) [ $<0.001$ ]	-11.4 (-11.7; -11.1) [ $<0.001$ ]
<b>Allergic rhinitis only</b>		
Partial vs. good control	-0.03 (-0.04; -0.02) [ $<0.001$ ]	-9.7 (-10.0; -9.4) [ $<0.001$ ]
Poor vs. good control	-0.12 (-0.14; -0.10) [ $<0.001$ ]	-20.6 (-20.9; -20.2) [ $<0.001$ ]
Poor vs. partial control	-0.09 (-0.11; -0.07) [ $<0.001$ ]	-10.9 (-11.2; -10.5) [ $<0.001$ ]
<b>Asthma (All patients)</b>		
Partial vs. good control	-0.03 (-0.05; -0.01) [0.003]	-5.6 (-6.0; -5.3) [ $<0.001$ ]
Poor vs. good control	-0.13 (-0.14; -0.11) [ $<0.001$ ]	-15.6 (-16.1; -15.2) [ $<0.001$ ]
Poor vs. partial control	-0.07 (-0.09; -0.04) [ $<0.001$ ]	-10.0 (-10.5; -9.5) [ $<0.001$ ]
<b>Asthma + Allergic rhinitis</b>		
Partial vs. good control	-0.04 (-0.06; -0.01) [0.002]	-5.5 (-5.9; -5.1) [ $<0.001$ ]
Poor vs. good control	-0.10 (-0.12; -0.08) [ $<0.001$ ]	-15.5 (-16.0; -15.0) [ $<0.001$ ]
Poor vs. partial control	-0.06 (-0.09; -0.04) [ $<0.001$ ]	-10.0 (-10.5; -9.5) [ $<0.001$ ]

614 <sup>a</sup> — The EQ-5D VAS is a 0-100 scale in which higher scores reflect better overall health on that day. <sup>b</sup> — Utilities quantify the preferences of the population  
 615 on the respective health states, with 1 representing full health and 0 representing being dead.

616 CI = Confidence interval.

617

618 **Table 3. Mean utility index score<sup>a</sup> (standard error) per country and per level of disease**  
 619 **control.**

	Allergic rhinitis control			Asthma control		
	Good	Partial	Poor	Good	Partial	Poor
<b>Belgium</b>	0.86 (0.05)	0.83 (0.05)	0.72 (0.05)	NA	NA	NA
<b>Denmark</b>	0.94 (0.05)	0.90 (0.05)	0.80 (0.05)	NA	NA	NA
<b>France</b>	0.96 (0.05)	0.92 (0.05)	0.82 (0.05)	0.91 (0.03)	0.88 (0.03)	0.81 (0.03)
<b>Germany</b>	0.91 (0.05)	0.88 (0.05)	0.77 (0.05)	0.89 (0.03)	0.86 (0.03)	0.79 (0.03)
<b>Italy</b>	0.94 (0.04)	0.91 (0.04)	0.80 (0.04)	0.90 (0.03)	0.87 (0.03)	0.80 (0.03)
<b>Netherlands</b>	0.88 (0.05)	0.85 (0.05)	0.74 (0.05)	0.84 (0.04)	0.80 (0.04)	0.73 (0.04)
<b>Poland</b>	0.99 (0.04)	0.96 (0.04)	0.85 (0.04)	0.97 (0.04)	0.94 (0.04)	0.87 (0.04)
<b>Portugal</b>	0.97 (0.04)	0.94 (0.04)	0.83 (0.04)	0.94 (0.03)	0.91 (0.03)	0.84 (0.03)
<b>Spain</b>	0.92 (0.05)	0.88 (0.05)	0.78 (0.05)	0.87 (0.04)	0.83 (0.04)	0.76 (0.04)
<b>United Kingdom</b>	0.93 (0.05)	0.90 (0.05)	0.79 (0.05)	0.87 (0.04)	0.84 (0.04)	0.77 (0.04)

620 <sup>a</sup> — Utilities quantify the preferences of the population on the respective health states, with 1 representing full health and 0 representing being dead.

621 NA — Not available.

622

623 **Table 4. Mean EQ-5D Visual Analog Scale<sup>a</sup> (standard error) per country and per level of**  
 624 **disease control.**

	Allergic rhinitis control			Asthma control		
	Good	Partial	Poor	Good	Partial	Poor
<b>Belgium</b>	84.6 (7.3)	73.0 (7.3)	60.9 (7.3)	NA	NA	NA
<b>Denmark</b>	82.6 (7.6)	71.0 (7.6)	61.7 (7.6)	NA	NA	NA
<b>France</b>	82.4 (7.2)	70.8 (7.2)	59.0 (7.2)	74.4 (5.2)	65.8 (5.2)	57.4 (5.2)
<b>Germany</b>	85.3 (7.7)	73.7 (7.7)	61.7 (7.7)	77.5 (5.2)	68.9 (5.2)	60.5 (5.2)
<b>Italy</b>	78.9 (7.1)	67.4 (7.1)	55.3 (7.1)	68.4 (5.2)	59.8 (5.2)	51.4 (5.2)
<b>Netherlands</b>	83.5 (7.1)	71.9 (7.1)	59.9 (7.1)	75.1 (5.4)	66.5 (5.4)	58.1 (5.4)
<b>Poland</b>	86.3 (7.1)	74.7 (7.1)	62.7 (7.1)	80.5 (5.5)	71.8 (5.5)	63.5 (5.5)
<b>Portugal</b>	87.1 (7.1)	75.5 (7.1)	63.5 (7.1)	81.5 (5.2)	72.8 (5.2)	64.5 (5.2)
<b>Spain</b>	85.6 (7.1)	74.0 (7.1)	62.0 (7.1)	77.5 (5.3)	68.8 (5.3)	60.5 (5.3)
<b>United Kingdom</b>	87.9 (7.1)	76.3 (7.1)	64.2 (7.1)	78.8 (5.4)	70.1 (5.4)	61.8 (5.4)

625 <sup>a</sup> — The EQ-5D VAS is a 0-100 scale in which higher scores reflect better overall health on that day.

626 NA — Not available.

627 **Figure 1. Graphical summary of the data analysis methodology. Individual data were obtained**  
628 **from the MASK-air mobile app (e.g., sex, age, disease control, and utilities/EQ-5D Visual**  
629 **Analog Scale (VAS)) and combined with contextual information on the quality of life of the**  
630 **general population as well as on the prevalence of allergic rhinitis (AR) and asthma to compute**  
631 **the mean utilities/EQ-5D VAS for AR and asthma, per level of disease control and country.**  
632 **Uncertainty in the estimates was assessed by means of 1000 simulations.**  
633

Journal Pre-proof

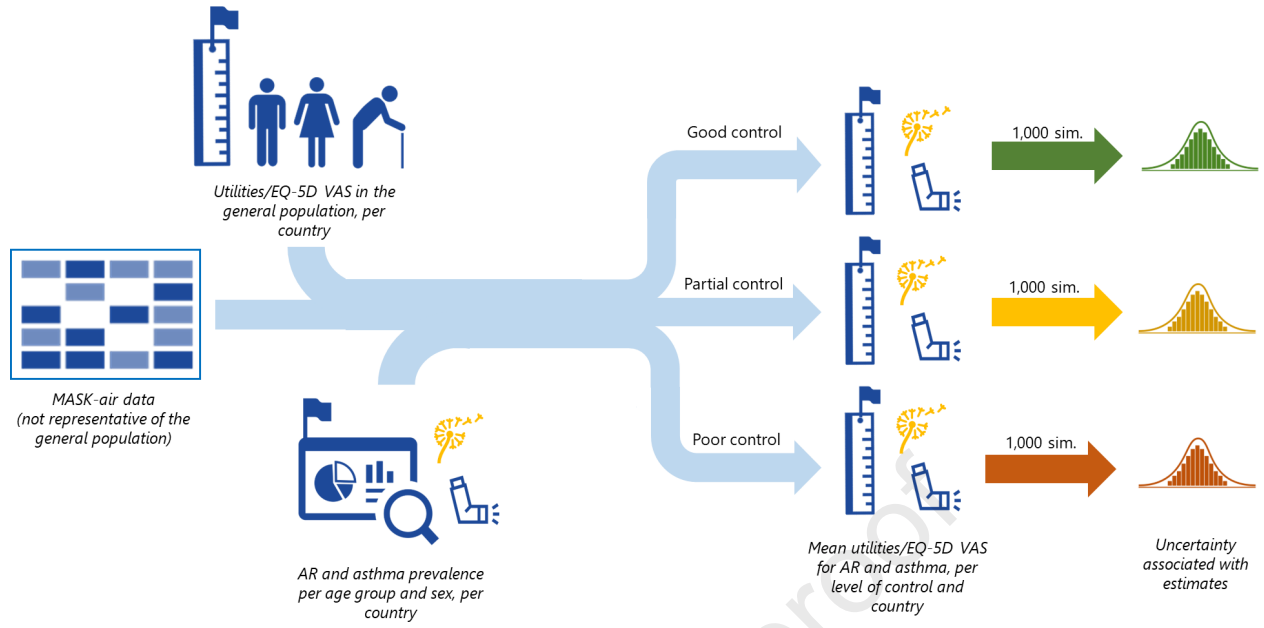
634 **Figure 2. Utility index score (A) and EQ-5D Visual Analog Scale (VAS) (B) of patients with**  
635 **Allergic Rhinitis only and patients with both Asthma and Allergic Rhinitis per country and per**  
636 **level of control (as per the CSMS for Allergic Rhinitis and the e-DASTHMA for Asthma +**  
637 **Allergic Rhinitis).**

638

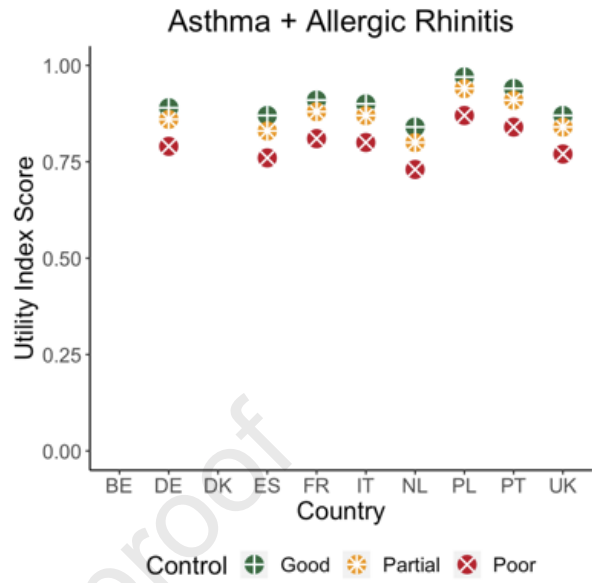
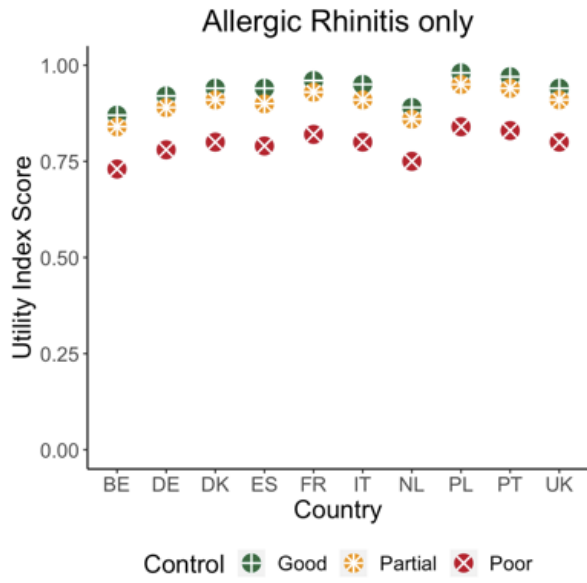
639 BE = Belgium; DE = Germany; DK = Denmark; ES = Spain; FR = France; IT = Italy; NL = Netherlands; PL = Poland; PT = Portugal;

640 UK = United Kingdom

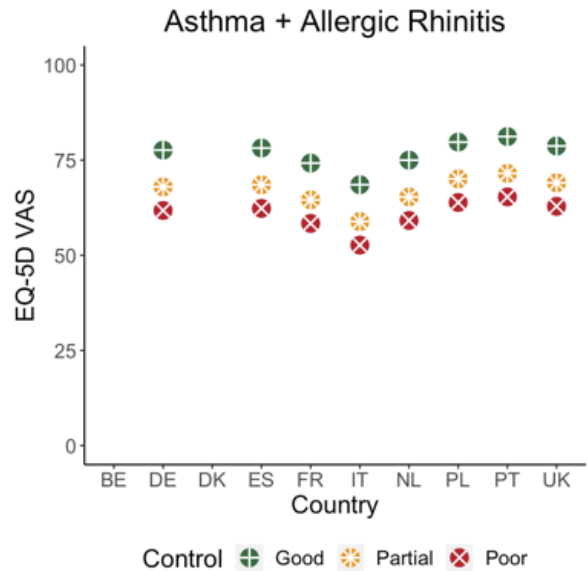
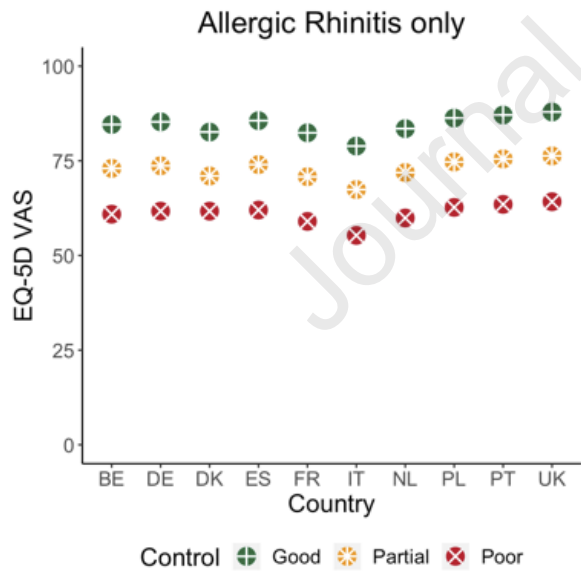
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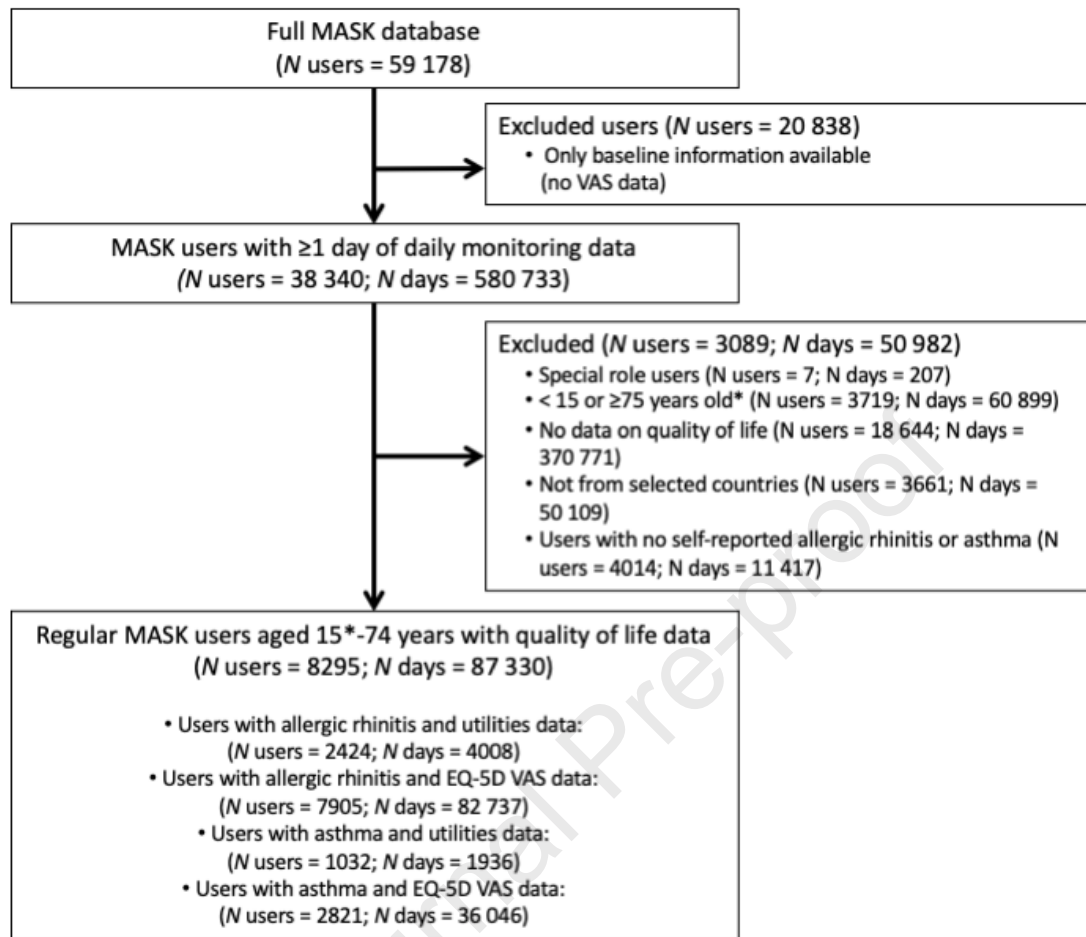


**A**



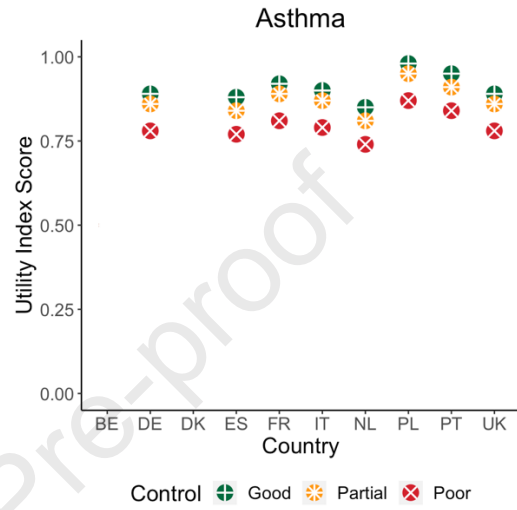
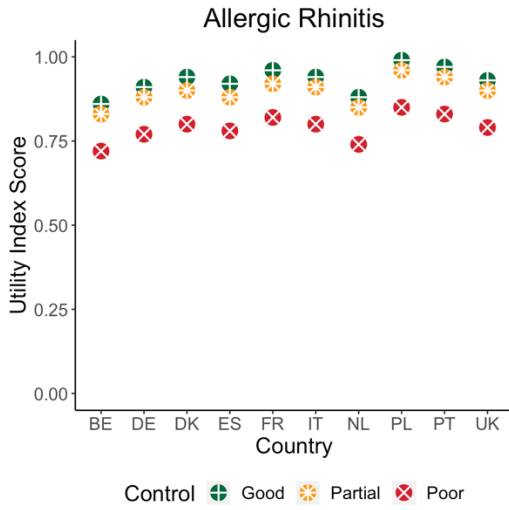
**B**





\*Or older than 16 years for countries where the digital age of consent is higher

**A**



**B**

