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1	Asthma prevalence in Olympic summer athletes and the general population: an

# 2 analysis of three European countries

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- 35
- 36 Key terms
- 37 Athletics, endurance, epidemiology, exercise, respiratory

# 39 Abbreviations

- 40 AQUA: Allergy Questionnaire for Athletes
- 41 ECRHS: European Community Respiratory Health Survey
- 42 GA<sup>2</sup>LEN: Global Allergy and Asthma European Network
- 43 WADA: World Anti-Doping Committee

#### 44 ABSTRACT

**Background:** Some studies have shown a higher prevalence of asthma in elite athletes as compared to the general population. It is inconclusive to what extent certain sport categories are especially affected. The present study offered a unique opportunity to assess these differences in asthma prevalence in the general population and elite summer athletes from a wide range of sport disciplines across various geographical areas.

51 **Methods:** Cross-sectional data for 1568 general population participants from the 52 European Community Respiratory Health Survey II and 546 elite athletes from the 53 Global Allergy and Asthma European Network Olympic study from three European 54 countries were analyzed. Using logistic regression, the asthma risks associated with 55 athlete sport practice, endurance level and aquatic sport practice, respectively, were 56 investigated.

Results: Athletes in the highest endurance category had increased risk of doctor-57 diagnosed asthma (OR 3.5; 95% CI 1.7-7.5), asthma symptoms (OR 3.0; CI 1.5-6.0) 58 and asthma symptoms or medication use (OR 3.5; CI 1.8-6.7) compared to the 59 general population. Aquatic athletes were at increased risk of doctor-diagnosed 60 61 asthma (OR 2.0; CI 1.1-3.9), asthma symptoms (OR 2.6; CI 1.3-5.0) and asthma symptoms or medication use (OR 2.3; CI 1.2-4.4) when compared to individuals not 62 involved in aquatic sports. Regarding the entire athlete population, no increase in 63 64 asthma was found when compared to the general population.

65 Conclusions: Practice of very high endurance and aquatic sports may be associated
66 with increased asthma risks. Athlete participation as such showed no association with
67 asthma risk.

#### 68 **INTRODUCTION**

69 Asthma is a chronic disorder affecting up to 300 million people worldwide [1]. Prevalence and incidence have been increasing over the past decades [2,3]. This is 70 71 a serious public health concern, especially as the risk factors for asthma are not fully understood. Some studies suggest that asthma may be more prevalent in elite 72 athletes than in the general population with up to 10% being affected, making it the 73 most common chronic disorder affecting this professional group [4,5], though the 74 evidence so far is limited. Asthma is not only a serious health risk for elite athletes, 75 but additionally its detrimental effects are magnified since asthma can drastically 76 77 interfere with athletic performance [6].

78

Within the group of elite athletes, the prevalence of asthma may differ by sport 79 80 discipline [6,7]. Athletes who participate in endurance sports seem to be at an increased risk for asthma than other athletes, possibly due to the vigorous activity 81 82 and regularly repeated higher ventilation rates over prolonged periods of time associated with their discipline [7,8]. Swimmers might also be at high risk, as 83 previous studies have suggested that pool athletes are predisposed to airway 84 85 dysfunctions, including asthma, due to their exposure to irritants such as chlorine and derived by-products in the pool environment [9,10]. This international cross-sectional 86 study offered a unique opportunity to assess differences in asthma prevalence 87 between the European general population and European summer athletes from a 88 89 wide range of sport disciplines across various geographical areas. Furthermore, differences in asthma risk among athletes participating in sports of various endurance 90 levels as well as aquatic sports were compared to the general population. 91

93 METHODS

### 94 Study Design

95 Two independent cross-sectional studies were conducted to assess the prevalence 96 of asthma and respiratory disorders; the first among the general population from 97 Norway, Germany and Spain and the second among the European summer Olympic 98 athletes representing these 3 countries.

99

## 100 Study participants

#### 101 General Population

Data for the general population (n=1568) were available through the European Community Respiratory Health Survey (ECRHS) II, conducted in the early 2000s (response 65.3% of those having participated in ECRHS I). The aim of ECRHS was to assess the prevalence, incidence, determinants and management of asthma in the adult population in various European countries. ECRHS was approved by local ethics committees and their methods have been published in detail elsewhere [11].

For the present analysis data were used of Norwegian (1 center), German (2 centers) and Spanish (5 centers) participants of less than 45 years of age, who formed part of the random sample of ECRHS II in 2002. From the ECRHS II questionnaire, we extracted data regarding asthma, exercise frequency and smoking habits.

112

## 113 Elite Athletes

Data for the elite athletes (n=546; response 65.2%) were available from a study on participants of the 2008 Beijing Olympics, conducted within the framework of the Global Allergy and Asthma European Network (GA<sup>2</sup>LEN) [12], which assessed allergic and respiratory illnesses among Olympic participants. The study used the Allergy Questionnaire for Athletes (AQUA) [13]. From the GA<sup>2</sup>LEN Olympic study we extracted data regarding asthma, exercise frequency, level of endurance, and type of sport.

121 In Norway, Germany and Spain, additional questions regarding asthma and smoking 122 habits were extracted from the ECRHS questionnaire. The common use of the 123 ECRHS questions in both study populations allowed for comparison between the two 124 groups. GA<sup>2</sup>LEN was approved by local ethics committees and their methods have 125 been published in detail elsewhere [12].

126

### 127 **Exposure definitions**

128 Three possible exercise-related exposures for asthma were defined:

129 1. Elite Athlete population

The first exposure was defined as whether or not the individual was a member of theelite athlete population, as compared to the general population.

132 2. Endurance Level

The second exposure was defined as sport endurance level. We categorized the sports based on the level of endurance as defined by Alaranta et al. [14]. For those sports included in the dataset, but not in the classifications by Alaranta et al. (badminton, modern pentathlon, tennis and weightlifting, n=18) we assigned a category based on a priori knowledge of the sport. The classifications are as follows:

- General population (reference level)
- Low / middle level of endurance: riding, gymnastics, taekwondo, table tennis,
   shooting, archery, sailing, badminton, modern pentathlon

High level of endurance: basketball, hockey, football, handball, volleyball,
fencing, judo, karate, wrestling, tennis, weightlifting

143	• Very high level of endurance: aquatic sports, track and field athletics,
144	canoeing, cycling, rowing, throwing
145	3. Aquatic Sports
146	The third exposure was defined as participation in aquatic sports:
147	• Non-aquatic: general population, all other sports, including those taking place
148	in natural water environments (reference level)
149	Aquatic sports: sports taking place in swimming pools typically treated with
150	chlorinated or other chemical disinfectants
151	
152	Outcome definitions
153	The following asthma outcome variables were defined as a positive response to the
154	following questionnaire items:
155	Doctor-diagnosed
156	<ul> <li>Have you ever had asthma, AND was this confirmed by a doctor?</li> </ul>
157	Asthma Symptoms
158	• Have you had wheezing or whistling in your chest at any time within the last 12
159	months, AND have you had this wheezing or whistling when you did not have
160	a cold?
161	Asthma symptoms or medication
162	• [Have you had wheezing or whistling in your chest at any time within the last
163	12 months, AND have you had this wheezing or whistling when you did not
164	have a cold?] OR [Are you currently taking medicines for asthma]
165	The second and the third outcomes were considered important as they take into
166	consideration the potential difference in doctors' diagnoses and medication use,
167	respectively, between the general population and elite athletes.
168	

#### 169 **Potential confounders**

Possible confounders that were considered include age, sex, smoking status (never, ever, current), country of origin (Norway, Germany, Spain), and frequency of exercise. Data on air pollution exposure, allergy and family history of asthma were not available.

As the two questionnaires assessed frequency of exercise differently, respective variables were re-coded into comparable categories (minimal, once per week, 2-3 times per week, 4-6 times per week, daily). The general population categories of "never", "less than one time per month" and "once per month" were combined into the category "minimal". Further, the athlete category "≤ 3 times per week" was re-coded into "2-3 times per week", based on the assumption elite athletes probably practice at least twice per week.

181

## 182 Statistical analysis

183 All analyses were performed using R (version 2.14.1). Three crude and three 184 adjusted logistic regression models were developed to assess the risk of having asthma, according to the above-described outcome definitions. Risk estimates for the 185 three defined asthma outcomes were modeled on the following exposure 186 comparisons: athlete versus non-athlete (Model 1), level of endurance (Model 2) and 187 aquatic versus non-aquatic sports (Model 3). For Models 1 and 2 the general 188 population was used as reference category, while for Model 3 the general population 189 190 and athletes not participating in an aquatic sport were included in the reference category. Adjustments were made for above-mentioned potential confounders. 191

## 193 Sensitivity analyses

To check the robustness of the models, age restriction to participants below the median age, restriction to never-smokers, and stratification by country were performed. As an additional sensitivity analysis we added random-effects terms to each model to investigate the between-country variance. Furthermore, to disentangle the effect on asthma due to endurance and aquatic sports, respectively, aquatic sports athletes were removed from the category 'very high endurance', to form a separate level in the categorical variable 'endurance level'.

201

# 202 **RESULTS**

#### 203 **Descriptives**

The demographic characteristics of study participants are summarized in Table 1.

# Table 1. Descriptive statistics of the general population

and the elite athlete population.

Variable	General Population	Athletes		
	(n = 1568)	(n = 546)		
Age (years)				
Mean (SD)	37.5 (4.4)	27.0 (5.5)		
Male n (%)	772 (49.2)	248 (45.7)		
Country n (%)				
Germany	309 (19.7)	291(53.5)		
Norway	337 (21.5)	77 (14.1)		
Spain	922 (58.8)	176 (32.4)		
Frequency of				
Exercise				
n (%)				
Minimal	761 (50.0)	-		
1x per week	255 (16.8)	-		
2-3x per week	336 (22.1)	7 (1.3)		
4-6x per week	87 (5.7)	113 (20.8)		
Daily	82 (5.4)	422 (77.9)		
Smoking n (%)				
Never	562 (35.9)	469 (84.5)		
Former	322 (20.6)	41 (7.7)		
Current	682 (43.5)	20 (3.8)		

Participants from the general population were on average older (mean age 37.5 vs. 27.0), were much more likely to be smokers (64% vs. 19% ever smoking), and were much less likely to exercise regularly (33.2% vs. 100% exercise frequency  $\geq$ 2 times per week) when compared to elite athletes.

213

# 214 Logistic regression models

After adjustment for potential confounders, elite athletes showed neither a statistically significant increased risk of doctor-diagnosed asthma, asthma symptoms nor of asthma symptoms and medication use, when compared to the general population (Table 2, Model 1).

 Table 2. Crude and adjusted risk estimates with corresponding odds ratios (OR) and 95% confidence intervals (95% CI) for three different logistic regression models, each modelling all three asthma outcomes.

Outcome	Doctor-diagnosed <sup>a</sup>			Symptoms <sup>b</sup>			Symptoms or medication <sup>c</sup>		
		OR 95% CI			OR 95% CI			OR 95% CI	
	n (%)	Unadjusted	Adjusted <sup>d</sup>	n (%)	Unadjusted	Adjusted <sup>d</sup>	n (%)	Unadjusted	Adjusted <sup>d</sup>
Model 1 Elite athlete:									
General population Elite	118 (7.5)	1	1	207 (13.4)	1	1	223 (14.4)	1	1
Athlete	90 (17.2)	2.5 (1.9-3.4)	1.7 (0.9-3.3)	67 (12.9)	0.96 (0.71-1.29)	1.4 (0.7-2.6)	88 (16.9)	1.2 (0.9-1.6)	1.6 (0.9-2.8)
Model 2 Endurance level: General									
population Low-	118 (7.5)	1	1	207 (13.4)	1	1	223 (14.4)	1	1
middle	9 (9.7)	1.3 (0.6-2.7)	1.1 (0.4-2.6)	4 (4.3)	0.3 (0.1-0.8)	0.5 (0.2-1.5)	6 (6.5)	0.4 (0.2-1.0)	0.6 (0.2-1.7)
High	22 (11.2)	1.5 (1.0-2.5)	1.1 (0.5-2.4)	13 (6,7)	0.5 (0.3-0.8)	0.7 (0.3-1.7)	19 (9.7)	0.6 (0.4-1.1)	0.9 (0.4-1.9)
Very high	59 (25.5)	4.2 (3.0-6.0)	3.5 (1.7-7.5)	50 (21.6)	1.8 (1.3-2.5)	3.0 (1.5-6.0)	63 (27.4)	2.2 (1.6-3.1)	3.5 (1.8-6.7)
Model 3 Aquatic sports:									
No <sup>e</sup>	192 (9.5)	1	1	259 (12.9)	1	1	294 (14.7)	1	1
Yes	16 (26.2)	3.4 (1.9-6.1)	2.0 (1.1-3.9)	15 (24.2)	2.2 (1.2-3.9)	2.6 (1.3-5.0)	17 (27.9)	2.2 (1.3-4.0)	2.3 (1.2-4.4)

<sup>a</sup> Have you ever had asthma, AND was this confirmed by a doctor?

<sup>b</sup> Have you had wheezing or whistling in your chest at any time within the last 12 months, AND have you had this wheezing or

whistling when you did not have a cold?

<sup>c</sup> [Are you currently taking medicines for asthma] OR [Have you had wheezing or whistling in your chest at any time within the

last 12 months] AND have you had this wheezing or whistling when you did not have a cold?]

<sup>d</sup> Adjusted for age, sex, smoking, country of origin and frequency of exercise

<sup>e</sup> Includes the general population.

222 Among the athlete population, participating in a sport characterized by a very high 223 endurance level was associated with a statistically significant increased risk of doctor-diagnosed asthma (OR 3.5; 95%Cl 1.7-7.5), asthma symptoms (OR 3.0; 224 225 95%CI 1.5-6.0) and asthma symptoms or medication (OR 3.5; 95%CI 1.8-6.7) when compared to the general population (Table 2, Model 2). Participation in aquatic sports 226 was associated with a statistically significant increase in risk of doctor-diagnosed 227 228 asthma (OR 2.0; 95%CI 1.1-3.9), asthma symptoms (OR 2.6; 95%CI 1.3-5.0) and 229 asthma symptoms or medication (OR 2.3; 95%CI 1.2-4.4) when compared to nonaquatic sports and the general population (Table 2, Model 3). All models were robust 230 to performed sensitivity analyses; age restriction, restriction to non-smokers, the 231 disentanglement of aquatic sports athletes from the 'very high endurance' level, and 232 233 stratification by country. Specifically regarding the homogeneity of the results across 234 the different countries, for all models in Table 2, introducing random-effects terms never yielded an intraclass correlation coefficient above 0.2%, indicating a very low 235 236 between-country variance (data not shown).

237

#### 238 **DISCUSSION**

239 This study allowed for the assessment of differences in asthma prevalence in two diverse populations; summer athletes from a wide range of sport disciplines and an 240 established general population, both originating from countries that well represent 241 European climate and other geographical differences. Additionally, the asthma risk 242 according to level of endurance and aquatic sport participation were investigated. A 243 positive association between exposure to the highest level of endurance and an 244 increased risk of all three defined asthma outcomes was found. Athletes within this 245 group had, with regards to all three asthma outcomes, an approximately three times 246

higher risk when compared to the general population. Similarly, an approximate
twofold increase in risk of having asthma symptoms was found among athletes
performing aquatic sports compared to all other athletes and the general population.
However, with respect to all three asthma outcomes, our results suggest no
statistically significant risk increase of asthma among the entire athlete population
when compared to the general population.

253

254 These results both confirm and refute results of earlier studies. The null finding of this analysis, with respect to the difference in asthma risk between the general and 255 athlete populations, is similar to an Australian study [15] but contrasting to the 256 German GA<sup>2</sup>LEN study [16]. The latter difference might potentially be explained by 257 higher medical surveillance among our general population or lower medical 258 259 surveillance among our athlete population. Thereto, the German study applied different adjustments and used a different general population compared with present 260 261 analysis. Our null finding might also result from a healthy worker effect in the athlete 262 population, if those athletes most affected by asthma are no longer participating in their sport. Although the ECRHS II should contain a representative number of 263 symptomatic subjects [17,18], defining ECRHS II participants as the general 264 population might have introduced selection bias. It is possible that a retention bias 265 led to a disproportionate number of individuals with asthma from ECRHS I agreeing 266 to continue into ECRHS II. This potential bias would lead to an underestimation of the 267 268 asthma risk based on the comparison between the athlete population and the 269 ECRHS II population.

Based on the German results of the GA<sup>2</sup>LEN study, which used a different reference 271 population, an approximate two-fold increased risk of doctor-diagnosed asthma and 272 asthma symptoms or asthma medication was detected for athletes performing at the 273 274 highest level of endurance [16]. Our study demonstrated risk estimates in the same direction, although of even higher magnitude (OR=3.5; 95% CI 1.7-7.5 and OR=3.5; 275 95% CI 1.8-6.7). Similarly, Parsons et al. found that athletes in high endurance sports 276 277 were 23% more symptomatic than athletes in lower endurance sports [19]. This increased prevalence in elite endurance athletes has been attributed to the repeated 278 physical strain causing epithelial damage, increasing inflammation in the respiratory 279 280 mucosa, as well as to prolonged hyperventilation and increased exposure to inhalant allergens and irritants during endurance training and competition [8,9,17,20] (add 281 Jerning et al. 2013)]. Regarding two of our asthma outcomes - asthma symptoms 282 283 and asthma symptoms or asthma medication - a U-shaped relationship was found with increasing levels of endurance. A similar relationship, albeit strictly negative, 284 285 was found in another study based on the ECHRS II survey [21], which examined the 286 influence of frequency and duration of physical activity on bronchial hyperresponsiveness, an asthmatic precursor [22,23]. Thus, evidence suggests that 287 288 physical activity, and to a certain degree also moderate endurance exercise, might 289 induce a protective effect against asthma and its precursors [24].

290

The approximate twofold increased risk for asthmatic symptoms in aquatic athletes found in our study has been similarly shown in previous studies, including a metaanalysis of six studies showing that swimmers have increased odds for asthma compared to other competitive athletes (OR=2.57; 95% CI 1.87-3.54)<sup>10</sup>[1]. Additionally, Stadelmann et al. found that over 80% of a sample of elite swimmers self-reported respiratory problems [25]. Furthermore, emerging evidence suggests
that in addition to inhalation, skin exposure to allergens and irritants such as chlorine
may be linked to the pathogenesis of asthma, which is important to consider in the
context of swimmers [26].

300

301 Strengths of this study include the relatively large sample sizes and geographical variation of the study populations. Moreover, this study takes into account the 302 303 assumed regional differences in asthma prevalence [27-29] by using data of ECRHS II from Norway, Germany and Spain, and thus covers diverse geographic regions of 304 305 Europe. However, our mixed-effects models showed a between-country variance 306 close to zero and stratification by country did not change reported results significantly, suggesting any regional differences in our study population to be 307 308 negligible. Finally, the geographical representativeness and the large study population increase the power and generalizability of our study findings. 309

310

311 Our results are based on cross-sectional self-reported data, which rules out any causal inference from the study findings. Moreover, data for the athletes and the 312 general population originated from two different source studies (ECRHS II and 313 314 GA<sup>2</sup>LEN) that were performed nearly a decade apart in time. Defining ECRHS II participants as the general population might have introduced selection bias, as 315 ECRHS II participants are unlikely representative of the entire adult population of 316 317 Norway, Germany and Spain. Furthermore, taking into account the mentioned increase in the prevalence of asthma during the latest years [3,4,8,27], the temporal 318 319 gap between the two studies might to some extent have weakened the comparability of the two study populations. Additionally, the mean age of the two study populations 320

321 differed by approximately ten years. Sensitivity analyses, however, did not change 322 our main results; age-restriction of the general population, only using those below the median age, yielded estimates in the same direction (data not shown). Further 323 324 sensitivity analysis showed that inclusion of smokers into the model did not lead to biased results, as estimate direction and magnitudes remained relatively consistent 325 326 after the exclusion of former and current smokers. The cross-sectional questionnaire 327 data also did not include information on some potential confounders and effect modifiers, including air pollution, allergy prevalence, and family history of asthma and 328 allergies, all of which could have influenced the prevalence of asthma in the two 329 330 populations. Additionally, no marker for socioeconomic status was included in the analysis. A similar study comparing German Beijing Olympic athletes with a German 331 332 general population showed that the level of education was generally higher in the 333 athlete population as compared to the general population [16]. If higher level of education in our population in turn was associated with, for example, a lower 334 335 exposure to passive smoke or ambient air pollution earlier in life, the comparison 336 between the two populations in our study could be confounded.

337

338 As earlier studies have demonstrated that athletes have a very high degree of 339 medical surveillance [16,30], risk estimates of doctor-diagnosed asthma modeled on the comparison of athletes and non-athletes might have been biased due to a 340 differential misclassification of outcome. Further, based on the assumption that the 341 342 athlete population has higher health awareness than the general population, a lower degree of recall bias in the assessment of asthma symptoms and medication use 343 should be expected in the athlete population. Thus, also risk estimates modeled on 344 the comparison of the two populations might have been biased due to differential 345

misclassification Finally, inadequate 346 of outcome. diagnosis and potential 347 incongruence of asthma treatment with asthma diagnosis in athletes might be an issue since the World Anti-Doping Committee (WADA) and the International Olympic 348 349 Committee removed the need to document asthma by lung function tests before the use of inhaled  $\beta$ 2-agonists in 2009 [4]. However, the larger body of evidence 350 suggests that B2-agonists within the controlled concentrations have no ergogenic 351 352 effects and do not improve exercise performance [4,31,32].

Although mostly based on cross-sectional studies, there is an increasing body of evidence suggesting that participation in very high-level endurance sports or aquatic sports is associated with an increased risk of asthma and asthma symptoms. To further test this association and to gain information on causality, we suggest for future research the use of a cohort study design.

358

Regarding implications for practice, we hope that our findings eventually will increase awareness among physicians about asthma risk associated with high endurance and aquatic sports. This in turn might lead to higher medical surveillance of elite athletes performing high endurance and aquatic sports. Additionally, preventive asthma tests in early life may help guide adolescents in their choice of sport.

364

#### 365 **CONCLUSIONS**

Our study supports earlier evidence that practice of very high endurance sports and aquatic sports may be associated with increased risks of asthma among athletes. The excess risk is possibly attributed to high frequency of repeated physical strain and excessive ventilation and exposure to allergens and irritants in swimming pools, respectively. With respect to all three asthma outcomes, no increased risk was found

- among athletes when compared to the European general population, suggesting an
- approximately similar medical surveillance and treatment of the two.

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376

# 377 Author contributions

Jacob Burns, Catherine Mason, Natalie Mueller and Johan Ohlander shared equally in the conception and completion of the statistical analysis, and drafting the manuscript; thus, if possible, these authors should all be stated as first authors. Katja Radon contributed to and coordinated the drafting of the manuscript. Jan-Paul Zock made valuable contributions to the analysis and manuscript. All authors read, contributed to, and approved the final manuscript.

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