



Increased prevalence of exercise-induced airway symptoms – A five-year follow-up from adolescence to young adulthood



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ABSTRACT

Background: Exercise-induced airway symptoms are common in adolescents. Little is known about the development of symptoms from adolescence to early adulthood. Therefore, we studied the prevalence, incidence, and remission of exercise-induced airway symptoms (including wheeze, cough, chest and throat tightness, hoarseness, and stridor) in adolescents, over a five-year period.

Methods: In 2011, all adolescents aged 12–13 years in Uppsala ($n = 3838$) were invited to answer a questionnaire on exercise-induced airway symptoms. All responding adolescents ($n = 2309$) were invited to answer the same questionnaire again after five years. In total, 1002 adolescents responded (43.4%).

Results: The prevalence of exercise-induced airway symptoms increased from 25% at baseline to 49% at follow-up ($p < 0.001$). More females than males reported symptoms at both time points. The incidence of airway symptoms was 42.2%, with no sex differences. More males than females reported symptom remission (20.2 vs. 10.7%, $p < 0.001$). Females reported a higher asthma prevalence at follow-up than at baseline (7.6 vs. 15.2%), while males did not (10.9 vs. 8.0%), leading to a sex difference in prevalence at follow-up ($p < 0.001$). Smoking and baseline respiratory symptoms were associated with an increased risk of reporting symptoms at follow-up.

Conclusions: A twofold increase in the prevalence of exercise-induced airway symptoms over a five-year period was found in this cohort. Females were more likely to report symptoms at both time points. Knowledge of these age-related changes in symptoms and their association to female gender is useful for future studies and healthcare providers.

1. Background

Self-reported exercise-induced airway symptoms are common in adolescents [1–3]. Compared with healthy controls, adolescents with airway symptoms in conjunction with exercise suffer from more daytime and nocturnal dyspnea, absence from school, and a lower health-related quality of life [1,4]. Previous studies on exercise-induced airway symptoms in adolescent populations have mainly studied single symptoms, such as exercise-induced wheeze or cough [2,5,6]. However, exercise-induced airway symptoms can manifest in other ways and can also be multifactorial.

The most widely studied cause of airway symptoms in adolescents is exercise-induced bronchoconstriction (EIB) [7], but the presence of exercise-related symptoms does not necessarily mean that an adolescent has EIB. Exercise-induced laryngeal obstruction or poor physical fitness, and more rare conditions such as cardiac disease and chronic lung

diseases other than asthma, may also cause airway symptoms [8–10]. The prevalence of exercise-induced airway symptoms has been found to be higher among adolescent females than among adolescent males [1,11]. The reason for this is unknown; the prevalence of EIB and exercise-induced laryngeal obstruction is similar in male and female adolescents [12].

Several retrospective and cross-sectional studies have investigated the causes of exercise-induced airway symptoms in adolescents using different methods and focusing on different diagnoses [10,12–14]. In most studies, a substantial proportion of the symptomatic subjects had not received a diagnosis. It is also not known if the prevalence of exercise-induced symptoms changes with age. To the best of our knowledge, no study has investigated the development of these symptoms from adolescence to early adulthood. Therefore, this study explores the prevalence, remission, and incidence of exercise-induced airway symptoms over a five-year period in an adolescent cohort from the

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general population, with special emphasis on sex differences and association to diagnosed asthma.

2. Methods

2.1. Study design and study population

The ANDAS study is a prospective cohort study among adolescents in a general Swedish population from Uppsala, Sweden. Two surveys have been completed: the baseline in 2011 (age 12–13 years old) and the follow-up five years later, in 2016 (age 17–18 years old).

In the baseline study, all adolescents aged 12–13 years in the city of Uppsala ($n = 3838$) were invited to complete an online self-administered questionnaire together with their parents. In total, 60% ($n = 2309$) of the adolescents answered the questionnaire. The recruitment procedure and the characteristics of participants and non-participants have been described in detail previously [1]. Five years later, adolescents who had answered the questionnaire in 2011 were invited to complete the same questionnaire once more. In March–April 2016, the subjects were contacted via post and asked to visit the study homepage to fill out the questionnaire again. A reminder was sent to subjects who did not respond within four weeks. If necessary, a second reminder was sent two weeks later.

2.2. Questionnaire variables

The questionnaire contained questions about height, weight, asthma, allergy, physical activity, and exercise-induced airway symptoms. Questions about asthma and allergy were based on the International Study of Asthma and Allergy in Childhood Questionnaire [15] and the European Community Respiratory Health Survey [16]. Questions about level of physical activity were based on the Health Behaviour of School-aged Children (HBSC), WHO Collaborative Cross-National Study [17,18]. Questions about exercise-induced airway symptoms were constructed for the ANDAS study. In the 2016 questionnaire, smoking habits were also investigated.

2.3. Definitions

Exercise-induced airway symptoms: “Have you had any or several of the following symptoms more than once during or after physical exercise throughout the last 12 months: wheeze, chest tightness, cough, throat tightness, hoarseness, or inspiratory stridor?”

Current asthma: Having ever been diagnosed with asthma by a physician and use of asthma medication and/or symptoms (wheeze, daytime or nocturnal dyspnea) during the last 12 months.

Wheeze: “Have you had wheezing or whistling in the chest during the last 12 months?” [16].

Daytime dyspnea: “Have you had an attack of shortness of breath that came on during the day when you were at rest at any time during the last 12 months?” [16].

Nocturnal dyspnea: “Have you been woken by an attack of shortness of breath at any time during the last 12 months?” [16].

Rhinitis: “Do you have hay fever or any other nasal allergy?” (16).

Physical activity: “During a typical or usual week, on how many days were you physically active for a total of at least 60 min per day? Physical activity is defined as any activity (school/work activities, transport to and from school/work and leisure activities) that raises your heart rate and makes you breathe hard.” [17,18].

Smoking: “Have you been smoking during the last month?”

2.4. Ethics

The study was approved by the Regional Ethics Committee, Uppsala, Sweden (Dnr. 2011:413 and Dnr. 2016:115).

2.5. Statistical analysis

The data were analyzed using STATA 14.2 (Stata Corp, College Station, Texas, USA).

The study population for incidence analysis consisted of all subjects who answered both questionnaires ($n = 1002$). Differences in percentage between groups were calculated using a two-sided chi-squared test or Fisher's exact test. Within-group comparisons were analyzed with the McNemar test. Paired t-tests were used to compare levels of physical activity between 2011 and 2016. A uni- and multivariate logistic regression model was used to analyze predictors for new-onset exercise-induced airway symptoms in 2016. The model included gender, current asthma, rhinitis, overweight and obesity, and exercise-induced airway symptoms at baseline in 2011 and smoking at follow-up in 2016 (as no smoking habits were recorded in 2011). Statistical significance was defined as an alpha level of 0.05.

3. Results

In 2016, 1002 (43.4%) participants responded to the follow-up questionnaire; they formed the study group. Among these participants, 563 (56.2%) were female and 439 (43.8%) were male.

3.1. Non-participants

Among non-responders in 2016 ($n = 1307$, of which 645 female), 18 had migrated, two were deceased, 19 letters were returned unopened due to incorrect addresses, 128 declared that they did not want to participate and the rest did not respond. Comparing data on non-participants and participants from the baseline in 2011 showed a lower proportion of females among non-participants (49.3 vs. 56.6%, $p < 0.001$). However, the analysis did not show differences in prevalence of exercise-induced airway symptoms (25.5 vs. 24.9%, $p = 0.70$), current asthma (9.1 vs. 8.4%, $p = 0.57$), wheeze (11.2 vs. 11.1%, $p = 0.94$), daytime dyspnea (3.4 vs. 2.3%, $p = 0.11$), nocturnal dyspnea (1.6 vs. 2.0%, $p = 0.48$), rhinitis (15.8 vs. 17.2%, $p = 0.40$), or proportion of participants being overweight or obese (18.5 vs. 21.5%, $p = 0.10$).

3.2. Participants

The study group characteristics at baseline and follow-up are shown in Tables 1 and 2. There were no sex differences regarding proportion of participants being overweight or obese in either 2011 or 2016. The

Table 1
Characteristics of the participants ($n = 1002$).

	Baseline 2011	Follow-up 2016	p value
Age, years ($\pm$ SD)	12.7 ($\pm$ 0.7)	17.4 ($\pm$ 0.6)	
BMI, mean, ($\pm$ SD)	19.2 ($\pm$ 2.8)	22.4 ($\pm$ 3.7)	
Overweight and obesity ^a , n, (%)	209 (21.4)	161 (16.1)	0.006
Current asthma ^b , n (%)	91 (9.1)	121 (12.1)	0.004
Rhinitis, n %	172 (17.2)	289 (28.8)	< 0.001
Wheeze, n %	111 (11.1)	160 (16.0)	< 0.001
Daytime dyspnea, n %	23 (2.3)	61 (6.1)	< 0.001
Nocturnal dyspnea, n %	20 (2.0)	33 (3.3)	0.09
Physical activity ^c , days per week ($\pm$ SD)	4.1 ($\pm$ 1.8)	3.6 ($\pm$ 1.9)	< 0.001
Smoking last month, n (%)	–	91 (9.1)	
Attending high school, n (%)	–	909 (90.7)	

^a Overweight and obesity defined as BMI $\geq$ 85th percentile.

^b Ever physician-diagnosed and use of asthma medication and/or symptoms during last 12 months.

^c Physical activity, number of days per week with at least 60 min per day of physical activity.

Table 2

Prevalence (%) current asthma, rhinitis, current wheeze, daytime and nocturnal dyspnea among females (n = 563) and males (n = 439) answering the questionnaires at baseline and follow-up.

	Group	2011	2016	p value	2011 ^b	2016 ^b
Current asthma ^a %	Females	7.6	15.2	< 0.001	0.07	< 0.001
	Males	10.9	8.0	0.053		
Rhinitis, %	Females	15.3	28.4	< 0.001	0.07	0.72
	Males	19.6	29.4	< 0.001		
Wheeze, %	Females	11.9	19.0	< 0.001	0.35	0.002
	Males	10.2	11.9	0.37		
Daytime dyspnea, %	Females	2.3	8.1	< 0.001	0.97	0.002
	Males	2.3	3.4	0.42		
Nocturnal dyspnea, %	Females	1.8	4.6	0.009	0.57	0.009
	Males	2.3	1.6	0.63		

^a Ever physician-diagnosed and use of asthma medication and/or symptoms during last 12 months.

^b p value, difference by sex in study year 2011 and 2016, respectively.

prevalence of current asthma, wheeze and rhinitis as well as daytime dyspnea increased from baseline to follow-up (Table 1). This result was largely due to the female increase in prevalence for all of these variables; in males only the prevalence of rhinitis increased with age (Table 2). There was a significant decrease in level of physical activity from baseline to follow-up (Table 1). No sex differences were found regarding level of physical activity at baseline, while males reported higher levels of physical activity than females at follow-up (3.7 vs. 3.5 days/week, $p = 0.02$). No differences in level of physical activity were found between the groups with and without exercise-induced symptoms at baseline (4.2 vs. 4.1 days/week, $p = 0.86$) or at follow-up (3.5 vs. 3.6 days/week, $p = 0.49$). Smoking was reported by 9.1% of the participants at the follow-up, with no sex differences.

3.3. Exercise-induced airway symptoms

The prevalence of exercise-induced airway symptoms increased between baseline and follow-up for both sexes (Table 3). The most commonly reported specific exercise-induced symptoms were cough, throat tightness, chest tightness, and wheeze (Appendix Table A1). In the group of adolescents with asthma, the prevalence of exercise-induced symptoms was similar at baseline and follow-up. In contrast, there was a more than twofold increase in prevalence of symptoms from baseline to follow-up in adolescents without asthma (Fig. 1).

3.4. Incidence and remission

Females had a higher prevalence of airway symptoms than males, both at baseline (27.9 vs. 21%, $p = 0.012$) and at follow-up (53.6 vs. 41.7%, $p = 0.001$). The incidence of airway symptoms was 42.2% with no sex differences (44.8 vs. 39.2%, $p = 0.12$). Remission of airway symptoms was found in 16.8% of the subjects. More males than females reported remission of symptoms (48.9 vs. 27.4%, $p < 0.001$) and more females than males reported persistent symptoms (20.2 vs. 10.7%, $p \leq 0.001$) (Fig. 2).

Table 3

Number, n (%), of participants reporting any exercise-induced airway symptom (n, %) at baseline and at follow-up presented for the total group (n = 1 002) and for females (n = 563) and males (n = 439).

	Group	Baseline 2011	Follow-up 2016	p value
Any exercise-induced airway symptoms	All	249 (24.9)	479 (48.7)	< 0.001
	Females	157 (27.9)	296 (53.6)	< 0.001
	Males	92 (21)	183 (41.7)	< 0.001

3.5. Determinants of reporting any exercise-induced airway symptoms at follow-up

Female gender and reporting exercise-induced airway symptoms at baseline in 2011 were independently associated with reporting any exercise-induced airway symptoms at follow-up in 2016, as was smoking last month at follow-up (Table 4).

4. Discussion

The prevalence of self-reported exercise-induced airway symptoms doubled from adolescence to early adulthood in the present cohort. Females had a higher prevalence of symptoms than males, at both baseline and follow-up. The incidence of exercise-induced symptoms did not differ between the sexes, but remission of symptoms was more common among males. Symptoms at baseline and smoking at follow-up were associated with an increased risk of reporting symptoms at follow-up, as was female gender.

The most striking result was the large proportion of adolescents reporting at least one symptom when exercising: one in four at baseline and almost one in two at follow-up (age 17–18 years). Comparisons with literature are difficult as previous studies have mainly described single symptoms, such as exercise-induced wheeze or cough, often as a symptom of underlying asthma. We found a 7% prevalence of exercise-induced wheeze in those aged 12–13 years and a 12% prevalence at follow-up (17–18 years). In general, other studies report higher prevalence of this specific symptom. In the ISAAC study [2], 11% of Swedish adolescents (13–14 years) reported exercise-induced wheeze and the global prevalence was 19%. A prevalence of exercise-induced wheeze almost twice as high as that in the present study has been reported from several international adolescent cohorts [5,6,19]. On the other hand, when screening 14-year-old high school athletes specifically for exercise-induced bronchoconstriction, Hallstrand et al. found a 9% prevalence of exercise-induced symptoms (i.e., chest tightness, wheeze or cough) [20]. Among subjects with current asthma, the prevalence of exercise-related symptoms was high and unchanged between baseline and at follow-up, around 80%. The values are similar to those reported by Ostrom et al., who found a 78% prevalence of exercise symptoms in a cross-sectional study in children with asthma (aged 4–17 years) [21].

Research on how exercise-induced symptoms develop over time is scarce. Jurca et al. have reported symptoms to increase with age; exercise-induced cough increased from 16% at age 7–9 years to 26% in age 14–17 years. The corresponding figures for exercise-induced wheeze were 9% at age 7–9 years and 13% at age 14–17 years [22,23].

Our study confirms the switch from male to female predominance in asthma diagnosis and symptoms during the second decade of life [24–26]. At baseline, there were no sex differences, but at follow-up five years later females had a higher prevalence of current asthma, wheeze, and daytime and nocturnal dyspnea.

Females had a higher prevalence of exercise-induced airway symptoms than males, at both baseline and follow-up. More females reported persistent symptoms, while a higher remission rate was found in males. This could imply that there is still underdiagnosing of asthma among females, but other explanations are possible. First, airway symptoms, such as throat tightness, hoarseness, or stridor, are often associated with disorders in the larynx or upper airways [8]. Exercise-induced laryngeal obstruction has been reported to be more common among females in some [8], but not all studies [12]. Second, the sex difference in exercise-related dyspnea is associated with lower absolute lung volumes, weaker respiratory muscles, and a decreased surface area for pulmonary gas exchange in females [27] and even when matched for height and/or lung size, women have airways of smaller diameter than men (i.e., dysanapsis) [28]. This sex-based difference can impact upon the respiratory response to exercise, making women more likely to experience mechanical ventilatory constraints. At a given ventilation,

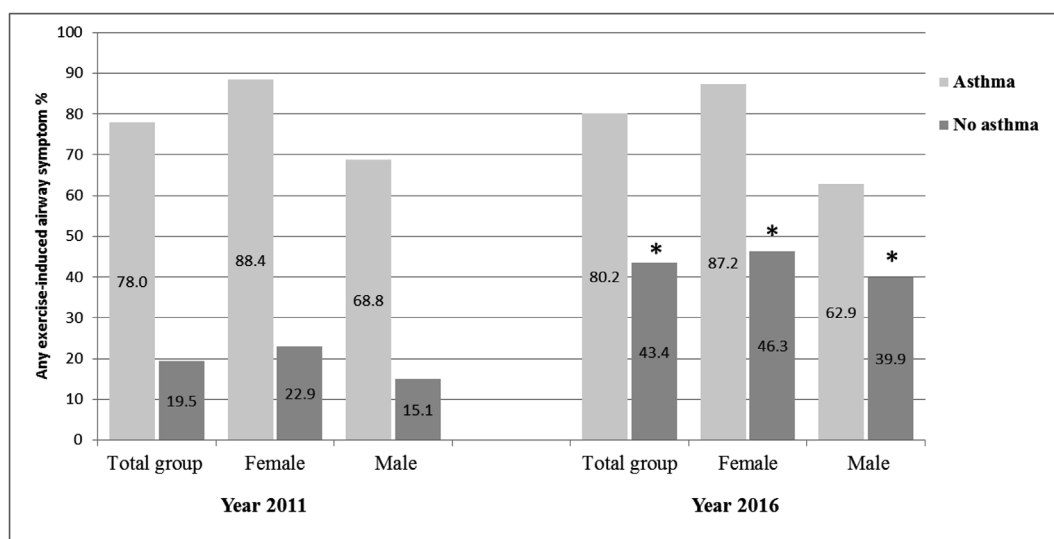


Fig. 1. Percentage of participants with and without current asthma reporting any exercise-induced airway symptom at baseline in 2011 and at follow-up in 2016. * Denotes change in prevalence of symptoms from baseline to follow-up ($p < 0.001$).

women have a higher work and oxygen cost of breathing, which might contribute to females experiencing and reporting more respiratory symptoms. A third possibility might be that the result is related to women consistently showing higher symptom reports than men in health surveys. This is especially true when healthy subjects are asked to recall symptoms. The reason for this is not fully understood [29].

We found an increased risk of reporting exercise-induced symptoms among smokers, which confirms the results of others [30]. No difference was found in level of physical activity between adolescents with

and without exercise-induced airway symptoms at baseline or at follow-up. This challenges the findings of Nystad et al., who found that active non-asthmatic children and adolescents reported more wheezing and whistling in the chest compared with inactive participants [31]. However, as participants were not asked specifically about exercise-induced symptoms, the results are hard to compare with ours.

This study adds information to the few data currently available on the incidence of exercise-induced respiratory symptoms from adolescence to young adulthood. Strengths include that it is based on an

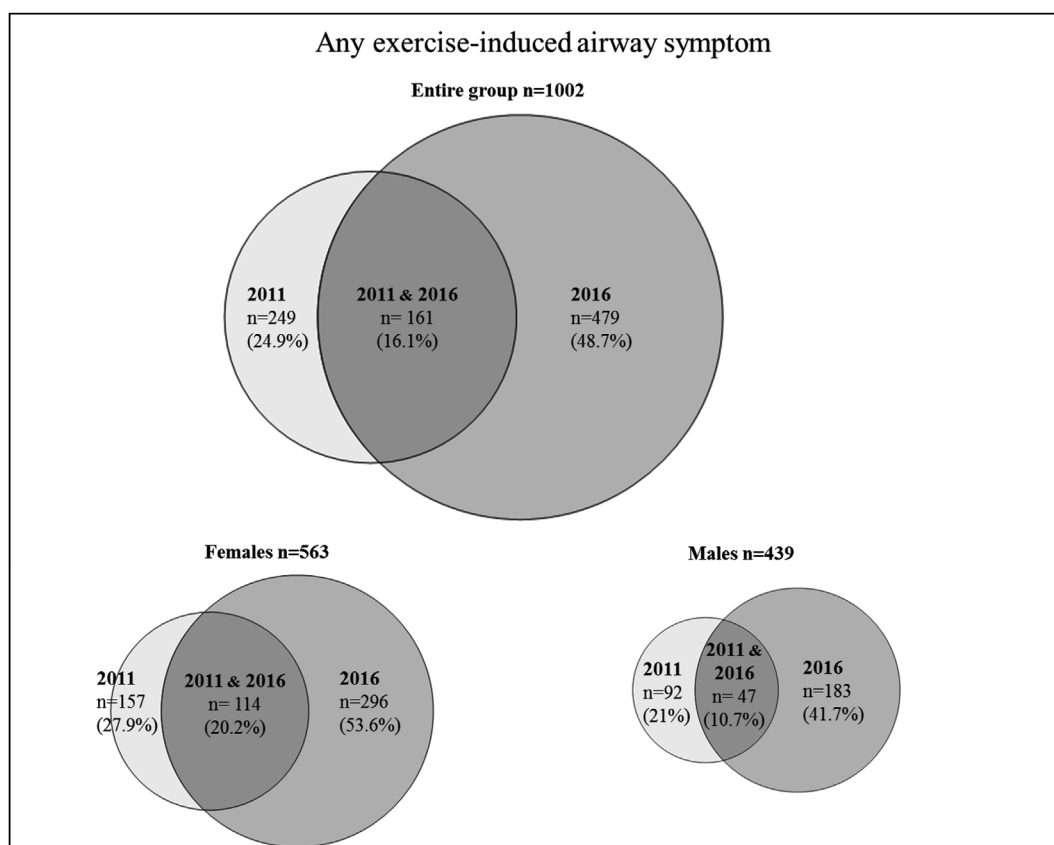


Fig. 2. Number, n (%), of participants with any exercise-induced airway symptoms at baseline in 2011, at follow-up in 2016, and at both time points.

Table 4

Predictors of reporting any exercise-induced airway symptoms at follow-up in 2016. Odds ratio (OR) and 95% confidence interval (CI) in univariate and multivariate logistic regression models.

	Univariate model			Multivariate model		
	OR	95% CI	p value	OR	95% CI	p value
Female gender	1.55	1.2–2.0	0.001	1.51	1.2–2.0	0.002
Current asthma, at baseline	2.16	1.4–3.4	0.001	1.41	0.8–2.4	0.19
Rhinitis, at baseline	1.28	0.9–1.8	0.14	1.05	0.73–1.5	0.78
Overweight and obesity, at baseline	1.00	0.7–1.4	0.98	0.90	0.65–1.2	0.52
Physical activity > 4 days/week, at baseline	1.22	0.9–1.6	0.13	1.29	0.98–1.7	0.062
Smoking last month, at follow-up	2.53	1.6–4.01	< 0.001	2.34	1.4–3.8	0.001
Any exercise-induced airway symptoms, at baseline	2.50	1.8–3.4	< 0.001	2.2	1.5–3.1	< 0.001

unselected sample of adolescents from the general population and that it encompasses a wide range of questions regarding exercise-induced symptoms. Furthermore, even though the response rate dropped from 60% to 43% from baseline to follow-up the non-responders did not differ significantly from participants according to baseline data. There are also a number of limitations to consider regarding this study. The data were collected from participants answering two questionnaires at two different time points. Such self-reported data may have been affected by the veracity of the participants, as the terminology defining respiratory symptoms in conjunction with exercise has not been validated. For the baseline questionnaire, but not the follow-up questionnaire, the participants were asked to respond together with a parent. This might have had an impact on the answers. On the other hand, good agreement has been reported between parental and self-completed questionnaires on asthma and airway symptoms in teenagers [32]. Lastly, we did not assess the severity of the exercise-induced symptoms, or if the adolescents had consulted healthcare regarding their symptoms.

In conclusion, prevalence of self-reported exercise-induced airway symptoms doubled from adolescence to early adulthood and the prevalence of exercise-induced symptoms was higher in females than males, at both baseline and follow-up. This research raises however also questions and warrants further studies. We need a better understanding

of both the underlying causes for experiencing exercise-induced airway symptoms in general and why symptoms are more common and more persistent among females than males. Since physical exercise is associated with numerous health benefits, it is also important to resolve whether these symptoms actually hamper exercise and sport activities in adolescents and to what extent they have a negative impact on health-related quality of life.

Contributors

HJ, KN, and AM contributed to the study concept and design and analyzed data. HJ wrote the draft manuscript and AM and KN revised the manuscript.

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Conflicts of interest

All authors declare that they have no conflict of interest in relation to this article.

Appendix

Table A1

Number, n (%) of participants with exercise-induced airway symptoms (n, %) in 2011 and 2016 presented for the total group (n = 1 002) and for females (n = 563) and males (n = 439), respectively.

	Group	Prevalence baseline 2011	Prevalence follow-up 2016	p value	Incidence of symptoms	Remission of symptoms
Wheeze, n (%)	All	72 (7.2)	122 (12.2)	< 0.001	84 (9.0)	31 (43.1)
	Female	49 (8.7)*	96 (17.1)*	< 0.001	63 (12.3) †	15 (30.6)
	Male	23 (5.2)	26 (5.9)	0.40	21 (5.0)	16 (69.6) ‡
Cough, n (%)	All	149 (14.9)	273 (27.2)	0.03	216 (26.0)	91 (61.2)
	Female	88 (15.6)	165 (29.3)	< 0.001	128 (26.9)	50 (56.8)
	Male	61 (13.9)	108 (24.6)	< 0.001	88 (23.8)	41 (67.2)
Chest tightness, n (%)	All	90 (9.0)	177 (17.7)	< 0.001	145 (15.9)	54 (60.0)
	Female	65 (11.5)*	126 (22.4)*	< 0.001	98 (19.7) †	33 (50.8)
	Male	25 (5.4)	51 (11.0)	< 0.001	47 (11.4)	21 (84.0) ‡
Throat tightness, n (%)	All	83 (8.3)	186 (18.6)	< 0.001	143 (15.7)	38 (45.8)
	Female	58 (10.3)*	142 (25.2)*	< 0.001	105 (20.8) †	21 (36.2)
	Male	25 (5.7)	44 (10.0)	< 0.001	38 (9.2)	17 (68.0) ‡
Hoarseness, n (%)	All	89 (8.9)	118 (11.8)	< 0.001	92 (10.1)	62 (69.7)
	Female	57 (10.1)	81 (14.4)*	< 0.001	58 (11.5)	33 (57.9)
	Male	32 (7.3)	37 (8.4)	0.30	34 (8.4)	29 (90.6) ‡
Inspiratory stridor, n (%)	All	53 (5.3)	119 (11.9)	< 0.001	97 (10.2)	30 (56.6)
	Female	41 (7.3)*	88 (15.6)*	< 0.001	67 (12.8) †	20 (48.8)
	Male	12 (2.7)	31 (7.1)	< 0.001	30 (7.0)	10 (83.3) ‡

*Denotes significant differences (p < 0.05) in prevalence between females and males in 2011 and 2016, respectively.

†Denotes significant differences (p < 0.05) in incidence of symptoms between females and males.

‡Denotes significant differences (p < 0.05) in remission of symptoms between females and males.

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