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Prevalence of airflow obstruction in smokers and never-smokers in Switzerland

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ABSTRACT: The aim of the present study was to measure age-specific prevalence of airflow obstruction in Switzerland in smokers and never-smokers using pulmonary function tests and respiratory symptoms from 6,126 subjects participating in the Swiss Cohort Study on Air Pollution and Lung Diseases in Adults.

The lower limit of normal of the forced expiratory volume in 1 s/forced vital capacity ratio was used to define airflow obstruction. Severity of airflow obstruction was graded according to the recommendations of the Global Initiative for Chronic Obstructive Lung Disease.

Prevalence of airflow obstruction ranged from 2.5% in subjects aged 30–39 yrs to 8.0% in those aged ⩾70 yrs. In multivariate analysis, age (OR 2.8, ⩾70 yrs *versus* 30–39 yrs), smoking (OR 1.8) and asthma (OR 6.7) were associated with airflow obstruction. Never-smokers constituted 29.3% of subjects with airflow obstruction. Never-smokers with airflow obstruction were younger, more likely to be male and reported asthma more frequently than obstructive smokers. Obstructive smokers and never-smokers had similar level of symptoms and quality of life impairment.

The prevalence of airflow obstruction in Switzerland is similar to other developed countries. Never-smokers account for a third of the prevalence, which is higher proportion than elsewhere. Airflow obstruction in never-smokers deserves attention because of its frequency and its similar health impact to that in smokers.

KEYWORDS: Asthma, bronchial hyperreactivity, chronic obstructive pulmonary disease, population study, sex differences, smoking

Chronic obstructive pulmonary disease (COPD) is a leading cause of death, morbidity and healthcare cost worldwide [1–3]. The Burden of Obstructive Lung Disease (BOLD) study reports between-countries variability in prevalence of stage 2–4 COPD according to the Global Initiative for Chronic Obstructive Lung Disease (GOLD) definition [4]. For example, in male subjects aged ⩾40 yrs, prevalence of GOLD stage ⩾2 varies from 8.5% in Iceland to 18.8% in the Philippines. Country-specific age distributions and smoking prevalence rates contribute most to these disparities. Nevertheless, never-smokers are also affected by COPD. CELLI *et al.* [5] found an obstruction rate of 9.1% in adult never-smokers in the third National Health and Nutrition Examination Survey (NHANES) and never-smokers accounted for 23% of the obstruction rate as defined by a forced expiratory volume in 1 s (FEV1)/forced vital capacity (FVC) ratio <0.7. Older age, male sex, low body mass index and allergy were the strongest risk factors for obstruction in never-smokers [5]. In Austria, LAMPRECHT *et al.* [6] found that the overall prevalence of GOLD stage 2–4 was 9.5% and that 27.7% of subjects with GOLD stage 2–4 obstruction were never-smokers.

So far, no population study has examined the prevalence of airflow obstruction in Switzerland, a developed country characterised by a low level of social inequalities and easy access to healthcare [7].

The main objectives of the present study were 1) to provide estimates of the prevalence of airflow obstruction in the Swiss adult population and 2) to examine the prevalence of airflow obstruction in never-smokers and the associated risk factors.

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METHODS

Study design and participants

For this study, we included 6,126 subjects from the SAPALDIA (Swiss Study on Air Pollution and Lung Diseases in Adults) cohort which has been described in detail elsewhere [8, 9]. Online supplementary figure A depicts the flow chart of SAPALDIA subjects for the present analyses. Characteristics predictive of participation in the follow-up survey SAPALDIA 2 are displayed in online supplementary table A.

Because airflow obstruction develops after long-lasting exposure to noxious agents, we based our estimates on data from SAPALDIA 2 (2002), in which participants had a median (range) age of 53 (30–73) yrs.

Definition of airflow obstruction

Pulmonary function tests (PFTs) were performed without bronchodilators by trained technicians according to the American Thoracic Society standards. We defined airflow obstruction according to the lower limit of normal (LLN) FEV_1/FVC derived from population-specific prediction equations [10]. In accordance with the recently published studies on the prevalence of COPD, we reported airflow obstruction in the presence of $FEV_1/FVC < LLN$ and $FEV_1 < 0.8$ predicted (modified stage 2–4 airflow obstruction) [4]. To facilitate international comparisons we also reported the prevalence of airflow obstruction as defined by the fixed GOLD criterion ($FEV_1/FVC < 0.7$).

Because respiratory symptoms are important predictors of FEV_1 decline and respiratory care use, we also reported the prevalence of symptomatic airflow obstruction [11, 12].

Chronic cough or phlegm, or chronic shortness of breath when walking were used to define respiratory symptoms. The underlying questions have been described in detail previously (online supplementary material) [12].

Methacholine bronchial challenge tests

Bronchial challenge tests were performed at SAPALDIA 1 with administration of methacholine chloride in subjects who had no contraindication [9]. The test was considered positive if FEV_1 decreased by 20% or more from the pre-test level.

Covariates

Subjects who answered yes to the questions ''have you ever had asthma?'' and, if yes, ''was this confirmed by a doctor?'' were classified as having ''physician-diagnosed asthma''.

Questionnaires were used to gather information on education level, nationality, comorbid conditions, smoking status, lifetime smoking (packs of cigarettes per day × smoking duration in yrs), environmental tobacco smoke (ETS) exposure and level of physical activity. Detailed methods regarding the definition of physical activity have been published before [13]. The Short Form-36 (SF-36) questionnaire was administered to assess health-related quality of life. Respiratory care utilisation was considered when inhaler use, emergency room visit, hospitalisation or an ambulatory visit (all for respiratory problems) was reported during the year preceding SAPALDIA 2.

Statistical analysis

Multivariate analysis involved mixed logistic regression models, systematically controlling for categories of age and smoking with the study area as a random effect variable. These variables were chosen *a priori* based on published literature. Covariates potentially associated with obstruction were tested one by one in models controlling for the aforementioned core variables.

Methods to evaluate bias related to nonparticipation are detailed on the online supplementary material.

Statistical analyses were carried out with Stata version 10 (StataCorp, College Station, TX, USA).

RESULTS

Prevalence of airflow obstruction

Table 1 compares the prevalence of airflow obstruction stage $\geqslant 2$ as defined by the LLN of FEV_1/FVC or the GOLD criterion. Compared to the LLN, the fixed FEV_1/FVC ratio led to higher airflow obstruction prevalence in older age categories (GOLD 15.2% (95% CI 11.1–20.3%) *versus* LLN 8.0% (95% CI 5.3–11.9%)). Overall, stage $\geqslant 2$ airflow obstruction was found in 5.1% (95% CI 4.3–5.9%) according to the LLN and 7.0% (95% CI 6.0–8.3%) according to the GOLD criterion.

TABLE 1 Airflow obstruction prevalence in the Swiss Study on Air Pollution and Lung Diseases in Adults (SAPALDIA 2) by age group and sex

Characteristics at SAPALDIA 2	Subjects n	$FEV_1/FVC < LLN$ stage 2–4		$FEV_1/FVC < 0.7$ stage 2–4	
		Males	Females	Males	Females
Overall	6126	6.1 (5.3–7.1)	4.0 (3.3–4.7)	9.4 (8.4–10.5)	4.8 (4.1–5.6)
Age 30–39 yrs	1109	3.2 (2.0–5.0)	1.9 (0.9–3.4)	3.4 (2.1–5.2)	0.9 (0.4–2.2)
Age 40–49 yrs	1525	3.2 (3.0–6.0)	4.0 (2.9–5.6)	5.8 (4.3–7.8)	4.0 (2.9–5.6)
Age 50–59 yrs	1811	6.1 (4.7–7.9)	4.7 (3.5–6.2)	9.2 (7.5–11.3)	5.4 (4.1–7.0)
Age 60–69 yrs	1378	8.9 (7.0–11.4)	5.0 (3.6–6.9)	15.2 (12.6–18.1)	7.4 (5.7–9.5)
Age $\geqslant$70 yrs	303	15.0 (9.9–22.1)	2.4 (0.8–6.1)	26.3 (19.5–34.4)	5.9 (3.2–10.6)
Chi-squared test p-value		<0.001	0.029	<0.001	<0.001

Data are presented as % (95% CI). FEV_1: forced expiratory volume in 1 s; FVC: forced vital capacity; LLN: lower limit of normal.

Overall, 10.0% (95% CI 8.5%–11.8%) of the adult population qualified for any stage LLN-defined ariflow obstruction. More than half of subjects with stage 1 airflow obstruction (166 out of 310 subjects, 53.6%) were free of respiratory symptoms.

Figure 1 shows the prevalence of any stage airflow obstruction and stage 2–4 airflow obstruction at SAPALDIA 2 with % reporting respiratory symptoms.

For subjects with FEV1/FVC <LLN (all stages) and those with stage 2–4 airflow obstruction, prevalence increased steadily with age and males were more frequently affected than females. Most subjects with stage 2–4 airflow obstruction reported one or more chronic respiratory symptoms (fig. 1c and d).

Physician-diagnosed asthma prevalence

Physician-diagnosed asthma prevalence by age is shown in figure 2. Asthma was less frequently reported in older age categories (5.7% (95% CI 3.5%–9.1%) for subjects aged ⩾70 yrs) compared to younger age categories (10% (95% CI 8.1–12.3%) for subjects aged 30–39 yrs). The concomitant presence of asthma and stage 2–4 airflow obstruction increased with age: up to 2.1% (95% CI 1.4–3.0%) for those aged 60–69 yrs. However, in the oldest age group (⩾70 yrs, n=303), both conditions were found in only four subjects (1.3%, 95% CI 0.5–3.5%).

Risk factors for airflow obstruction

Tables 2 and 3 compare the characteristics of normal subjects (normal spirometry and no report of respiratory symptoms) with 1) subjects with respiratory symptoms but no airflow obstruction, 2) stage 1 airflow obstruction or 3) stage 2–4 airflow obstruction.

Table 2 shows that airflow obstruction prevalence increases with smoking, ETS exposure, low education, non-Swiss citizenship and physical inactivity. Ever smokers (males 65.4%; females 49.8%) reported 26.2 pack-yrs (median 20.4; interquartile range 27.4) for males and 17.0 pack-yrs (median 11.5; interquartile range 21.0) for females. ETS during childhood, professional exposure to dust smoke or fumes or outdoor fine particulate matter exposure were not associated with airflow obstruction.

Subjects with stage 2–4 airflow obstruction also reported higher rate of comorbid conditions (table 3).

When examining risk factors for stage 2–4 airflow obstruction as defined using the fixed FEV1/FVC ratio instead of the LLN, we found that those risk factors were associated in a very similar manner with airflow obstruction.

Table 4 details the adjusted odds ratios of stage 2–4 and stage 1 airflow obstruction in SAPALDIA 2 for different exposures. Smoking was the strongest risk factor for all stages of airflow obstruction and age played a role for stage 2–4 airflow obstruction. However, the odds ratio of stage 2–4 airflow obstruction in association with smoking was higher than for stage 1 (stage 2–4 OR 1.25 (95% CI 1.19–1.30) *versus* stage 1 OR 1.12 (95% CI 1.05–1.30) for each 10-unit pack-yr increase). Obesity or physical

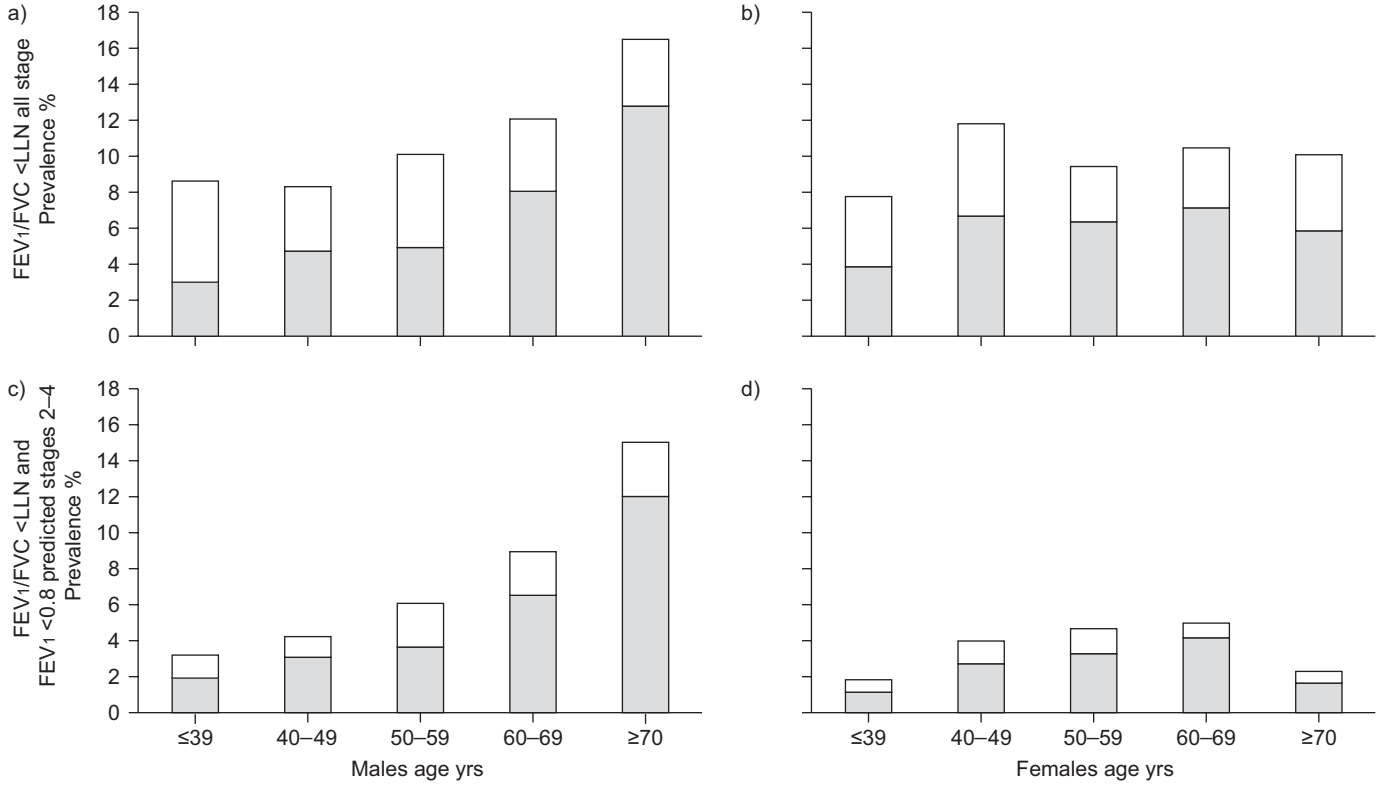

FIGURE 1. Prevalence of airflow obstruction in Swiss Study on Air Pollution and Lung Diseases in Adults (SAPALDIA 2). Pulmonary function tests were performed without bronchodilation. □: no respiratory symptoms; ■: respiratory symptoms (chronic cough or phlegm or shortness of breath by walking). FEV1: forced expiratory volume in 1 s; FVC: forced vital capacity; LLN: lower limit of normal.

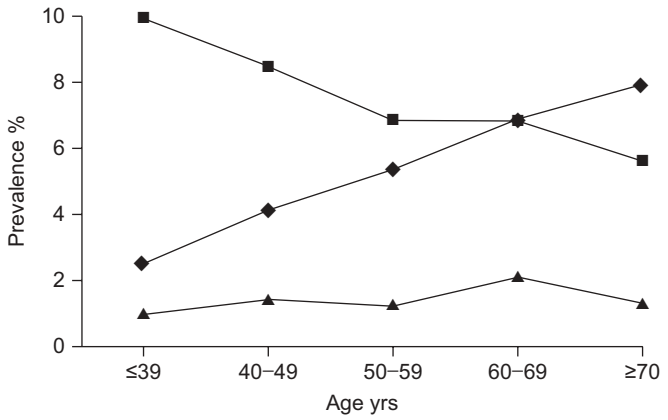

FIGURE 2. Prevalence of physician-diagnosed asthma by age group. ■: physician-diagnosed asthma; ◆: stage 2–4 airflow obstruction; ▲: concomitant asthma plus airflow obstruction.

inactivity were not associated with airflow obstruction. Physician-diagnosed asthma was associated with airflow obstruction for stage 1 and stage 2–4.

In a sensitivity analysis, when examining these exposures for stage 2–4 airflow obstruction as defined using the fixed ratio of FEV1/FVC instead of the LLN definition, we found a strong association between ageing and airflow obstruction for stages 1 and 2–4.

Quality of life and respiratory care utilisation for subjects with airflow obstruction

Table 5 details the quality of life scores of normal subjects and subjects with obstruction. Out of 6,126 subjects, 5,278 (86.2%) completed the SF-36. Airflow obstruction and symptomatic airflow obstruction were systematically associated with lower health-related quality of life and, more so, for those with stage 2–4 airflow obstruction and symptoms. Respiratory care utilisation increased with severity of airflow obstruction and symptoms.

Airflow obstruction in never-smokers

Of 307 subjects with stage 2–4 airflow obstruction at SAPALDIA 2, 90 (29.3%) were never-smokers. Prevalence of stage 2–4 airflow obstruction was 6.3% (95% CI 5.3–7.6%) for ever-smokers and 3.4% (95% CI 2.7–4.3%) for never-smokers. Table 6 reports the distribution of various risk factors and covariates for stage 2–4 airflow obstruction in subjects without or with smoking history. Never-smokers with stage 2–4 airflow obstruction were younger (p=0.003) and more likely to be female (52.2 *versus* 36.9%; p=0.013). A third of never-smokers with stage 2–4 airflow obstruction reported asthma at SAPALDIA 1 (34.8 *versus* 18.0% for smokers with similar airflow obstruction severity; p=0.001). Atopy was more frequent in never-smokers with airflow obstruction. Chronic cough and phlegm were similarly distributed and health-related quality of life impaired equally in smokers and never-smokers with airflow obstruction. Respiratory care utilisation tended to be more frequent in never-smokers with airflow

TABLE 2 Risk factor prevalence by severity of airflow obstruction in the Swiss Study on Air Pollution and Lung Diseases in Adults (SAPALDIA 2)[#]

Characteristics at SAPALDIA 2	FEV1/FVC ⩾LLN		FEV1/FVC <LLN, stage 1		FEV1/FVC <LLN, stage 2–4	
	No symptoms[¶]	With symptoms	All	With symptoms	All	With symptoms
Subjects n	3342	2161	310	144	307	216
Tobacco smoking exposure						
Ever smoker (2002)	1786 (53.5)	1265 (58.6)	191 (61.6)	99 (68.8)	217 (70.7)	161 (74.5)
p-value		<0.001	<0.001	<0.001	<0.001	<0.001
Ever-smoker[+] pack-yrs	10.0 (20.9)	16.0 (28.9)	16.2 (28.7)	20 (27.0)	31.2 (41.2)	35.0 (42.0)
p-value[§]		<0.001	<0.001	<0.001	<0.001	<0.001
ETS exposure						
Not exposed	2633 (78.8)	1536 (71.1)	229 (73.9)	98 (68.1)	212 (69.3)	147 (68.4)
⩽3 h·week^{-1}	443 (13.3)	373 (17.3)	55 (17.4)	29 (20.1)	54 (17.7)	40 (18.6)
>3 h·week^{-1}	265 (7.9)	250 (11.6)	26 (8.4)	17 (11.8)	40 (13.1)	28 (13.0)
p-value		<0.001	0.077	0.009	<0.001	0.001
Socio-educational level						
Low education[f]	129 (3.9)	190 (8.8)	22 (7.1)	15 (10.4)	26 (8.5)	21 (9.7)
p-value		<0.001	<0.001	<0.001	<0.001	<0.001
Non-Swiss nationals	390 (11.7)	341 (15.8)	30 (9.7)	16 (11.1)	50 (16.5)	35 (16.4)
p-value		<0.001	0.290	0.834	0.015	0.038
Physically active[##]	1053 (31.8)	518 (24.2)	105 (34.4)	47 (33.1)	75 (24.8)	45 (21.2)
p-value		<0.001	0.347	0.746	0.011	0.001

Data are presented as n (%), unless otherwise stated. p-values represent Chi-squared test, unless otherwise stated. FEV1: forced expiratory volume in 1 s; FVC: forced vital capacity; LLN: lower limit of normal; ETS: environmental tobacco smoke. [#]: n=6,126; [¶]: reference category; [+]: data are presented as median (interquartile range); [§]: Wilcoxon rank sum test; [f]: data missing for six subjects; [##]: data missing for 64 subjects.

TABLE 3 Prevalence of self-reported comorbid conditions by severity of airflow obstruction in the Swiss Study on Air Pollution and Lung Diseases in Adults (SAPALDIA 2)[#]

Characteristics at SAPALDIA 2	FEV1/FVC ⩾LLN		FEV1/FVC <LLN, stage 1		FEV1/FVC <LLN, stage 2–4	
	No symptoms[¶]	With symptoms	All	With symptoms	No symptoms[¶]	With symptoms
Diabetes[+]	71 (2.1)	84 (3.9)	4 (1.3)	2 (1.4)	16 (5.2)	10 (4.6)
p-value		0.001	0.406	0.360	0.001	0.017
Hypertension[§]	429 (12.8)	471 (21.8)	45 (14.5)	28 (19.4)	62 (20.2)	49 (22.7)
p-value		<0.001	0.402	0.022	<0.001	<0.001
Cardiac disease[f]	152 (4.6)	220 (10.2)	13 (4.2)	6 (4.2)	26 (8.5)	22 (10.2)
p-value		<0.001	<0.775	0.831	0.002	<0.001
BMI kg·m^{-2}						
<21	223 (6.7)	127 (5.9)	20 (6.5)	8 (5.6)	16 (5.2)	12 (5.6)
21–24.9	1520 (45.5)	740 (34.2)	146 (47.1)	66 (45.8)	96 (31.4)	61 (28.4)
25–29.9	1233 (36.9)	813 (37.6)	108 (34.8)	46 (31.9)	124 (40.5)	88 (40.9)
⩾30[##]	366 (11.0)	481 (22.3)	36 (11.6)	24 (16.7)	70 (22.9)	54 (25.1)
p-value		<0.001	<0.895	0.159	<0.001	<0.001
Atopy with rhinitis[¶¶,++]	487 (14.6)	288 (13.5)	37 (12.1)	14 (9.8)	50 (16.5)	33 (15.6)
p-value		0.226	0.202	0.103	0.394	0.726
Physician-diagnosed asthma[§§]	132 (4.0)	215 (10.0)	39 (12.6)	30 (20.8)	88 (28.7)	72 (33.3)
p-value		<0.001	<0.001	<0.001	<0.001	<0.001

Data are presented as n (%), unless otherwise stated. p-values represent Chi-squared test. FEV1: forced expiratory volume in 1 s; FVC: forced vital capacity; LLN: lower limit of normal; BMI: body mass index. [#]: n=6,126; [¶]: reference category; [+]: data missing for six subjects; [§]: data missing for nine subjects; [f]: data missing for five subjects; [##]: data missing for 19 subjects; [¶¶]: presence of atopy (positive phadiatop and rhinitis in SAPALDIA 2); [++]: data missing for 601 subjects; [§§]: data missing for four subjects.

obstruction (36.7 *versus* 27.2%; p=0.099) despite a higher rate of reported shortness of breath in smokers.

Table 7 shows the adjusted odds ratios of stage 2–4 airflow obstruction associated with various risk factors in never-smokers and smokers. Positive methacholine challenge was a risk factor for both categories.

However, for never-smokers, male sex and asthma at SAPALDIA 1 were stronger risk factors of airflow obstruction than for smokers. In contrast with never-smokers, smokers were older and had greater ETS exposure. Interestingly, in smokers, asthma was not associated with development of airflow obstruction at SAPALDIA 2 after adjustment for covariates.

We found a significant interaction between smoking status and asthma (p=0.044).

These analyses were repeated after exclusion of subjects with FEV1 <80% predicted at SAPALDIA 1 because they may already have airflow obstruction. We observed a similar relationship between risk factors and airflow obstruction in this restricted analysis in comparison to the ones in table 7. Interaction between asthma and smoking status remained significant.

In order to isolate potential risk factors associated with airflow obstruction in never smokers without asthma in 1991, we repeated these analyses after excluding subjects with asthma. Age and positive methacholine challenge test were still significantly associated with obstruction, while atopy was not (online supplementary table B).

Figure 3 shows the probability estimates of stage 2–4 airflow obstruction stratified on asthma and smoking status. Probabilities of stage 2–4 airflow obstruction were highest in males, aged ⩾60 yrs with asthma and positive methacholine challenge in 1991. In both sexes, for smokers and never-smokers, positive methacholine challenge and asthma predicted a high risk of airflow obstruction (p=0.044).

Sensitivity analysis

The effect of nonparticipation at SAPALDIA 2 on the prevalence of airflow obstruction is estimated in online supplementary table C. Using our logistic regression models, weighting each observation by the inverse of the propensity for participation, we found only slightly higher prevalence of airflow obstruction among older subjects (see online supplementary table A for variables entered into the model).

We also repeated our analyses using the European Respiratory Society reference values and the NHANES reference values. We found a slightly lower prevalence of stage 2–4 airflow obstruction using our population-specific reference values compared to the NHANES reference, mainly because some subjects moved from stage 2 disease to stage 1 airflow obstruction [14]. However, the proportion of subjects with airflow obstruction as defined by LLN, proportion of never-smokers in subjects with airflow obstruction and risk factors for airflow obstruction were not sensitive to changes in reference values.

DISCUSSION

The present study is the first to provide population-based estimates of the prevalence of airflow obstruction in

TABLE 4 Adjusted odds ratios of stage 2–4 airflow obstruction[#]

Characteristics at SAPALDIA 2[¶]	FEV1/FVC<LLN, stage 1	FEV1/FVC<LLN, stage 2–4
Subjects n/N	310/5819[f]	307/6126
Age yrs		
30–39	Reference	Reference
40–49	0.95 (0.68–1.32)	1.37 (0.87–2.17)
50–59	0.69 (0.48–0.98)	1.62 (1.05–2.51)
60–69	0.70 (0.48–1.02)	2.09 (1.34–3.25)
⩾70	0.82 (0.46–1.47)	2.76 (1.55–4.91)
Females *versus* males	1.67 (1.31–2.13)	0.82 (0.64–1.05)
Tobacco smoke exposure		
Ever- *versus* never-smoker	1.42 (1.11–1.80)	1.76 (1.36–2.28)
Pack-yrs per 10-unit increase[+]	1.12 (1.05–1.19)	1.25 (1.19–1.30)
ETS exposure		
Not exposed	Reference	Reference
⩽3 h·week^{-1}	1.08 (0.79–1.49)	1.09 (0.79–1.51)
>3 h·week^{-1}	0.79 (0.52–1.21)	1.25 (0.86–1.80)
ETS during childhood	1.44 (1.04–1.99)	0.82 (0.55–1.21)
Socioeconomic status		
Low *versus* high eductation	1.11 (0.66–1.85)	1.28 (0.78–2.11)
Non-Swiss *versus* Swiss nationals	0.80 (0.54–1.18)	1.25 (0.89–1.73)
Professional exposure to dust, smoke or fumes *versus* no exposure	1.01 (0.76–1.36)	0.91 (0.68–1.22)
Physical activity *versus* inactivity	1.29 (1.00–1.67)	0.88 (0.67–1.17)
Associated conditions		
Atopy with rhinitis[§] *versus* no atopy	0.90 (0.63–1.28)	1.67 (1.21–2.31)
Physician-diagnosed asthma *versus* no asthma	2.10 (1.47–3.00)	6.70 (5.04–8.91)
BMI kg·m^{-2}		
<21	Reference	Reference
21–24.9	1.26 (0.77–2.05)	0.80 (0.46–1.39)
25–29.9	1.12 (0.67–1.87)	0.91 (0.52–1.60)
⩾30	0.85 (0.48–1.52)	1.14 (0.64–2.05)

Data are presented as OR (95% CI), unless otherwise stated. SAPALDIA 2: Swiss Study on Air Pollution and Lung Diseases in Adults 2002; FEV1: forced expiratory volume in 1 s; FVC: forced vital capacity; LLN: lower limit of normal; ETS: environmental tobacco smoke; BMI: body mass index. [#]: adjusted for age, sex, smoking exposure and study area; [¶]: n=6,126; [+]: lifetime smoking for ever-smokers (per 10 pack-yr increase); [§]: at SAPALDIA 1; [f]: subjects with stage 2–4 were excluded.

Switzerland as defined by LLN, FEV1/FVC ratio and FEV1 <0.8 predicted. We found that airflow obstruction prevalence steadily increases from 3.2 % of the Swiss male adult population aged 30–39 yrs to 8.9% for those aged 60–69 yrs and 15.0% in those aged ⩾70 yrs. Females were less affected, with prevalence growing from 1.9% for those aged 30–39 yrs to 5.0% for those aged 60–69 yrs. One-third of subjects with stage 2–4 airflow obstruction had never smoked. Prevalence of stage 2–4 airflow obstruction was 6.3% in smokers and 3.4% in never-smokers.

International comparisons

Compared to the multinational BOLD or the Epidemiological Study of COPD in Spain (EPI-SCAN) studies, which used post-bronchodilation GOLD criteria to define and grade COPD, prevalence of airflow obstruction in Switzerland appears in the lower range both for males and for females, despite the fact that no post-bronchodilator PFTs were performed in SAPALDIA [4, 15]. In particular, prevalence of stage 2–4 airflow obstruction in Switzerland is lower for subjects aged ⩾60 yrs compared with the age-specific strata of the BOLD study. This finding remained valid when the fixed FEV1/FVC ratio was used instead of the LLN. For example, in Salzburg (Austria), post-bronchodilator stage 2–4 airflow obstruction prevalences are 22.3% and 25.0% for males and females aged ⩾70 yrs; in SAPALDIA these rates were 15.0% for males and 2.4% for females of similar age groups. Lower prevalence of smoking and lower smoking exposure for smokers in SAPALDIA than in the BOLD study may explain part of these differences. Other factors could contribute to the lower prevalence of COPD in Switzerland: high household income, easy access to healthcare and low exposure to fumes from wood stoves or organic dust [7].

In accordance with previously published literature on COPD, ageing, smoking, male sex and low education were all associated with airflow obstruction [4, 16, 17].

Airflow obstruction in never-smokers

One-third of subjects with airflow obstruction are never-smokers. From a different perspective, 3.4% of never-smokers have clinically significant (FEV1 <0.8 predicted) obstruction. The proportion of never-smokers in subjects with airflow

TABLE 5 Quality of life scores and respiratory healthcare utilisation in normal subjects, subjects with airflow obstruction and/or respiratory symptoms in the Swiss Study on Air Pollution and Lung Diseases in Adults (SAPALDIA 2)#

SF-36 scores at SAPALDIA 2	$FEV_1/FVC \geqslant LLN$		$FEV_1/FVC < LLN$, stage 1		$FEV_1/FVC < LLN$, stage 2–4	
	No symptoms	With symptoms	All	With symptoms	No symptoms	With symptoms
Physical functioning	93.7±12.9	84.2±19.4***	89.2±15.7***	84.5±16.6***	80.6±20.2***	78.3±19.2***
Role physical	92.3±21.8	82.6±31.4***	88.4±27.5***	83.2±33.1***	81.1±33.1***	80.3±32.5***
Bodily pain	85.4±21.1	73.9±24.3***	80.0±23.6***	74.5±25.1***	76.8±25.2***	75.0±25.1***
General health	65.0±11.4	61.1±13.1***	63.5±12.9+	61.7±13.0***	59.8±13.5***	58.2±13.5***
Vitality	67.5±15.0	59.0±17.1***	63.9±17.3***	59.6±18.8***	59.5±18.4***	58.2±18.1***
Social functionning	90.3±16.1	82.5±20.4***	85.8±20.9***	79.5±24.4***	83.8±19.7***	82.8±19.2***
Role emotional	92.1±21.7	82.6±31.2***	86.8±29.7***	78.3±36.4***	82.9±32.2***	81.6±32.7***
Mental health	77.6±13.7	70.9±16.6***	74.6±16.6***	70.6±18.8***	72.8±15.4***	71.9±15.7***
Physical component summary	53.3±6.5	50.1±9.4***	52.0±8.0***	50.6±8.8***	48.6±9.6***	48.0±9.1***
Mental component summary	51.7±7.5	48.5±9.3***	50.1±9.5***	47.5±11.4***	49.8±8.8***	49.4±9.1***
Respiratory care utilisation¶	206/3344 (6.2)	405/2161 (18.7)***	50/310 (16.1)***	36/144 (25.0)***	92/307 (30.0)***	81/216 (37.5)***

Data are presented as mean±SD or n/N (%). All statistical comparisons (Chi-squared test or unpaired and unequal t-test for unequal variances) made with reference group ''$FEV_1/FVC \geqslant LLN$ and no respiratory symptoms''. SF-36: Short Form-36; FEV_1: forced expiratory volume in 1 s; FVC: forced vital capacity; LLN: lower limit of normal. #: n=6,126; ¶: report of emergency room visit, hospitalisation, ambulatory visit (all for respiratory problems) or report of inhaler use during the year preceding SAPALDIA 2; +: p=0.06; ***: p<0.001.

obstruction is higher than described in other population-based studies. In epidemiological studies from developed countries, this percentage ranges 12.2–27.7% [5, 6, 18–21]. It is likely that the proportion of never-smokers among subjects with COPD will increase in the future, since the proportion of COPD attributable to smoking will slowly decrease in parallel with tobacco consumption, at least in developed countries [22].

Risk factors of obstruction differ in smokers and never-smokers [23]. Air pollution has been associated with respiratory symptoms, adult onset asthma and lung function decline [24–26]. ETS may lower quality of life and trigger respiratory symptoms in never-smokers [27]. However, in this study, neither air pollution nor ETS were associated with stage 2–4 airflow obstruction in never-smokers. BEHRENDT [28] or CELLI *et al.* [5], both using the NHANES population, were also not able to identify ETS as a risk factor for COPD. This contrasts with two recent Chinese studies, which found an association between ETS and obstruction in never-smokers [29, 30]. Such an association might be missed if subjects with obstruction succeed in avoiding exposure to ETS. Interestingly, we found that ETS was an independent predictor of obstruction in smokers after controlling for smoking history. This suggests that ETS indeed exerts a negative effect on lung function when it cannot be avoided.

We found that positive methacholine challenge test was associated with airflow obstruction in smokers and never-smokers with airflow obstruction. Asthma and bronchial hyperreactivity play a specific and important role in increasing the risk of airflow obstruction in never-smokers. A previous SAPALDIA publication described this association extensively [31] and asthma has previously been found to be associated with COPD in never-smokers [28, 32]. The finding that bronchial hyperreactivity is a marker and a risk factor for COPD has been described as the ''Dutch hypothesis'' [33]. This hypothesis is supported by recent genetic association studies. Genetic single-nucleotide polymorphism variants appear to reduce the risk of both asthma and COPD in subjects exposed to smoking [34, 35]. However, to date, no similar genetic variants have been described to explain the risk of airflow obstruction in never-smokers. Interestingly, when analysing the risk factors for airflow obstruction after excluding subjects reporting asthma at SAPALDIA 1, we found a similar role of bronchial hyperreactivity. Under-reporting of asthma could explain this association, as suggested by other studies [36].

Erroneous classification of COPD as asthma in SAPALDIA 1 could have biased our estimates of airflow obstruction caused by asthma in SAPALDIA 2. To rule out this possibility, we excluded subjects with low FEV_1 (more likely to have airflow obstruction) at SAPALDIA 1 and found that asthma still predicted airflow obstruction at SAPALDIA 2. This provides strong evidence that asthma is a risk factor for future airflow obstruction, as suggested by other longitudinal studies [32, 37–39].

Airflow obstruction in never-smokers is important for several reasons. First, symptoms are equally present, quality of life similarly altered and respiratory care utilisation tends to be higher in never-smokers compared with smokers with airflow obstruction. DOMINGO-SALVANY *et al.* [40] showed that symptoms and quality of life are strong predictors of mortality in COPD. Secondly, the common diseases associated with COPD in smokers are also reported in never-smokers with COPD. For example, TURNER *et al.* [41] found an increased risk of lung cancer (hazard ratio 1.66) for never-smokers with COPD compared to those without COPD. Other studies reported an association between low FEV_1 and incident cardiovascular disease, independently of smoking [42].

TABLE 6 Characteristics of never-smokers and smokers with stage 2–4 airflow obstruction in the Swiss Study on Air Pollution and Lung Diseases in Adults (SAPALDIA 2)[#]

Characteristics at SAPALDIA 2	FEV1/FVC<LLN, stage 2–4		p-value
	Never-smokers	Ever-smokers	
Subjects	90	217	
Age yrs	52.4±12.3	56.8±9.7	0.003[++]
30–39	15 (16.7)	13 (6.0)	<0.001
40–49	26 (28.9)	37 (17.1)	
50–59	18 (20.0)	79 (36.4)	
60–69	26 (28.9)	69 (31.8)	
⩾70	5 (5.6)	19 (8.8)	
Males	43 (47.8)	137 (63.1)	0.013
Females	47 (52.2)	80 (36.9)	
ETS			
Not exposed	74 (83.2)	137 (63.1)	0.003
⩽3 h·week^{-1}	10 (11.2)	44 (20.3)	
>3 h·week^{-1}	5 (5.6)	35 (16.1)	
Asthma and atopy at SAPALDIA 1			
Physician-diagnosed asthma	31/89 (34.8)	39/217 (18.0)	0.001
Physician-diagnosed asthma at SAPALDIA 2	33/90 (36.7)	55/217 (25.4)	0.046
Atopy with rhinitis	24/88 (27.3)	26/215 (12.1)	0.001
Atopy[¶]	50/85 (58.8)	74/195 (38.0)	0.001
Positive phadiatop	43/85 (50.6)	64/195 (32.8)	0.005
Seasonal rhinoconjunctivitis	28/89 (31.5)	35/215 (16.3)	0.003
Total IgE	47 (34–66)[§]	53 (44–65)[##]	0.643[§§]
Positive methacholine challenge	25/43 (58.1)	67/110 (60.9)	0.753
Respiratory symptoms at SAPALDIA 2			
Any respiratory symptoms	55 (61.1)	161 (74.2)	0.022
Chronic cough	12 (13.3)	39 (18.0)	0.320
Chronic phlegm	17 (18.9)	50 (23.0)	0.423
Chronic shortness of breath	33 (36.7)	116 (53.5)	0.007
SF-36 scores at SAPALDIA 2			
Physical component summary	49.6±9.4[f]	48.2±9.7[¶¶]	0.305[++]
Mental component summary	49.5±8.4[f]	49.8±9.0[¶¶]	0.806[++]
Respiratory care utilisation[+]	33 (36.7) [f]	59 (27.2) [¶¶]	0.099

Data are presented as n, mean±SD, n (%) or geometric mean (95% CI), unless otherwise stated. FEV1: forced expiratory volume in 1 s; FVC: forced vital capacity; LLN: lower limit of normal; ETS: environmental tobacco smoke; Ig: immunoglobulin; SF-36: Short Form-36. [#]: n=307; [¶]: defined as positive phadiatop and skin prick test; [+]: report of emergency room visit, hospitalisation, ambulatory visit (all for respiratory problems) or report of inhaler use during the year preceding SAPALDIA 2; [§]: n=81; [f]: n=73; [##]: n=187; [¶¶]: n=185; [++]: unequal variances t-test; [§§]: Wilcoxon rank sum test.

Strengths and limitations

Our estimates of airflow obstruction among adults living in Switzerland are likely to be accurate, because the SAPALDIA study is a large, representative sample of the population [8]. For instance, the prevalence of smoking in the SAPALDIA cohort is very close to that determined in a larger population-based survey in Switzerland [43].

There are several limitations of our study. First, our PFTs were performed without bronchodilators. Lack of bronchodilation may overestimate the prevalence of airflow obstruction [44, 45]. Misclassification due to the lack of bronchodilation has been shown to be greater among younger subjects and those with normal FEV1. The median age of our cohort was 53 yrs and we focused our analyses on subjects with FEV1 <0.8 predicted. In addition, we integrated respiratory symptoms into our report to further reduce overdiagnosis. Differential loss for follow-up might, in turn, lead to an underestimation of the prevalence of obstruction at SAPALDIA 2. Nonetheless, our weighted analysis, taking into account the factors linked to nonparticipation at follow-up, provided estimates close to the actual results.

Conclusions

In summary, prevalence of symptomatic stage 2–4 airflow obstruction in Switzerland steadily increases from 3.2% and 1.9% in young males and females, respectively, to 15.0% and 5.0% in older age categories. These prevalences appear to be at the lower range compared to other parts of the world with similar age distribution. One-third of subjects with obstruction are never-smokers who frequently report a history of asthma

TABLE 7 Adjusted ORs of stage 2–4 airflow obstruction in never-smokers and smokers

	FEV_1/FVC <LLN, stage 2–4 in never-smokers	FEV_1/FVC <LLN, stage 2–4 in ever-smokers
Subjects n/N	42/2065	110/2718
Age per 1-yr increase	1.01 (0.98–1.03)	1.03 (1.01–1.05)
Age yrs		
30–39	Reference	Reference
40–49	1.38 (0.58–3.30)	1.86 (0.68–5.12)
50–59	0.72 (0.27–1.96)	2.34 (0.87–6.29)
60–69	1.34 (0.52–3.45)	3.74 (1.37–10.20)
⩾70	1.59 (0.40–6.27)	3.57 (0.96–13.22)
Males	Reference	Reference
Females	0.45 (0.23–0.87)	0.92 (0.59–1.43)
ETS		
Not exposed at SAPALDIA 2	Reference	Reference
⩽3 h·week^{-1}	0.91 (0.30–2.71)	1.10 (0.64–1.91)
>3 h·week^{-1}	1.54 (0.44–5.32)	1.87 (1.05–3.31)
Characteristics at SAPALDIA 1		
Positive methacholine challenge	8.20 (4.16–16.17)	9.64 (6.20–15.02)
Physician-diagnosed asthma	3.25 (1.45–7.31)	1.32 (0.67–2.56)

Data are presented as OR (95% CI), unless otherwise stated. Adjusted for age (categorical), sex, methacholine challenge test, environmental tobacco smoke (ETS; categorical), smoking, physician-diagnosed asthma at Swiss Study on Air Pollution and Lung Diseases in Adults (SAPALDIA) 1 and study area (random effect). FEV_1: forced expiratory volume in 1 s; FVC: forced vital capacity; LLN: lower limit of normal. p-value of goodness of fit test for never-smokers p=0.92 and ever-smokers p=0.22.

and have positive methacholine challenge test. Awareness of airflow obstruction in never-smokers deserves attention, because it appears to be frequent and has a similar health impact in smokers.

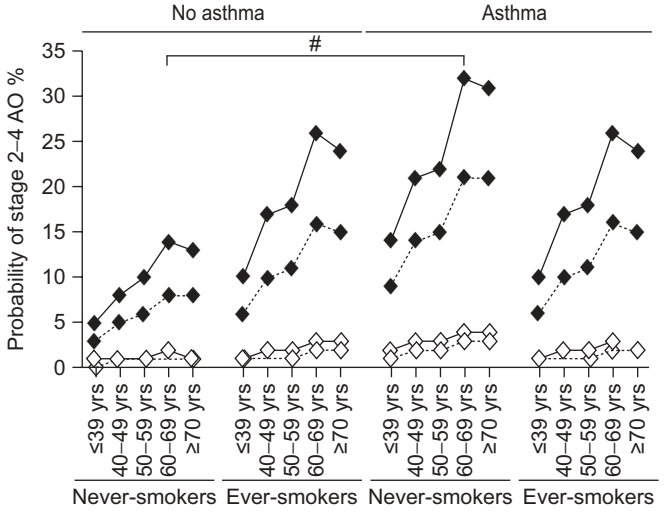

FIGURE 3. Probabilities of stage 2–4 airflow obstruction (AO) in the Swiss Study on Air Pollution and Lung Diseases in Adults (SAPALDIA 2) (2002) by categories of asthma and smoking status, controlled for age, sex, methacholine challenge test, environmental tobacco smoke and study area. Asthma is defined as physician-diagnosed asthma at SAPALDIA 1 (1991). —: males; ---: females; ◇: no methacholine bronchial hyperresponsiveness (BHR); ◆: methacholine BHR. #: p=0.044 for interaction between smoking status and asthma.

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STATEMENT OF INTEREST

None declared.

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