Airflow obstruction among young adults in Europe: a Chronic Airway Diseases Early Stratification (CADSET) collaboration with 48 612 individuals across eight population-based cohorts

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The Chronic Airway Diseases Early Stratification (CADSET) collaboration identified that up to 8% of young adults across Europe have airflow obstruction; its cause and its role in prior, concurrent and future airway disease merit further investigation https://bit.ly/47AMsEj

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Abstract

Background The extent to which airflow obstruction, a key feature of COPD, can be already present in early adulthood is unclear. We investigated the prevalence of airflow obstruction in young adults across European populations.

Methods We identified 48 612 individuals aged 20–40 years across eight population-based European cohorts in the Chronic Airway Diseases Early Stratification (CADSET) collaboration and applied two

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commonly used definitions of airflow obstruction: pre-bronchodilator forced expiratory volume in 1 s (FEV_1)/forced vital capacity (FVC) <0.70 and below the lower limit of normal (LLN). We explored how the prevalence of airflow obstruction according to both criteria was related to age, sex and smoking.

Results Airflow obstruction prevalence increased with increasing age from 2.3% in those aged 20–24.9 years to 6.3% in those aged 35–39.9 years according to FEV_1/FVC <0.70, and from 7.3% to 8.3% according to FEV_1/FVC <LLN. The corresponding increase in airflow obstruction prevalence was up to 8.8% in males *versus* 7.5% in females, and up to 9.0% in ever-smokers *versus* 6.9% in never-smokers. Difference in prevalence of airflow obstruction between FEV_1/FVC <0.70 and <LLN was highest for females and ever-smokers. Active smoking ranged from 19% to 28% and ever-smoking from 37% to 51%. The prevalence of airflow obstruction increased with pack-years, plateauing at ∼5 pack-years.

Conclusion Up to 8% of young adults across Europe have airflow obstruction; its cause and its role in prior, concurrent and future airway disease merit further investigation.

Introduction

Airflow obstruction is the core component of COPD diagnostic criteria. It is usually defined using a fixed ratio of forced expiratory volume in 1 s (FEV_1) and forced vital capacity (FVC), *i.e.* FEV_1/FVC <0.70. However, an alternative that accounts for age- and sex-dependent variation is the lower 5th percentile of the predicted value for FEV_1/FVC [1–3]. Investigating airflow obstruction in young adults in the general population according to their smoking behaviour may help identify strategies for earlier disease detection and be the basis of future intervention studies. Young adults with airflow obstruction according to FEV_1/FVC below the lower limit of normal (LLN) appear to be at greater risk of subsequently developing COPD than those with normal lung function [4]. Indeed, emerging evidence now suggests that COPD has its origin in early life, and develops across life [5–8]. Focusing on young adults with airflow obstruction therefore seems clinically relevant in order to prevent or halt progression towards COPD later in life [2, 9]. In the present study, we investigated the prevalence of airflow obstruction in young adults across European populations. For this purpose, we included 48 612 young adults from eight population-based cohorts in the Chronic Airway Diseases Early Stratification (CADSET) collaboration of the European Respiratory Society [10, 11].

Methods

Study design and populations

We obtained data from individuals aged ⩾20 years from European population-based cohorts enrolled with the intention of longitudinal follow-up and collated the data in the European Respiratory Society clinical research collaboration CADSET [10, 11]. In this project, we only included younger adults aged 20–40 years stratified in 5-year age bins (20–24.9 years, 25–29.9 years, 30–34.9 years and 35–39.9 years) with complete information on lung function. In total, eight European population-based cohorts were included in the present study: the Copenhagen City Heart Study (n=4083), European Community Respiratory Health Survey (ECRHS) (n=7758), Trøndelag Health Study (HUNT) (n=1273), Copenhagen General Population Study (n=7178), LifeLines (n=24 911), LEAD (Lung, Heart, Social, Body) (n=3001), West Sweden Asthma Study (n=269) and Obstructive Lung Disease in Northern Sweden (n=139). A short description of the cohorts can be found in the supplementary material.

Lung function

Lung function was measured using pre-bronchodilator FEV_1 and FVC. Predicted values were calculated according to the Global Lung Initiative (GLI) 2012 reference equations for individual participants at each cohort site using age and height separately for male and female [12]. For each individual, airflow obstruction was defined twice, either as FEV_1/FVC <0.70 or <LLN. LLN was defined as the bottom 5th percentile of the predicted value, calculated as the mean value minus 1.645 standard deviations again according to the GLI 2012 reference equations. Detailed description of lung function measurements is provided in supplementary table S1.

Statistical analyses

All cohorts provided anonymised summary data with means and standard errors stratified according to sex, smoking status, birth period (in 10 birth periods from 1920 until 2000), and age bins (in 5- and 10-year age bins from ⩾20 years), as described in detail elsewhere [11]. Analysis codes were prepared by the coordinating centre, sent to all centres, which was used by each centre to obtain the summary data. Each centre then sent the summary data to the coordinating centre. Only individuals with complete information on lung function at first examination were included. Since only summary data were provided by each cohort, pooled prevalence of airflow obstruction across all cohorts was determined using meta-analyses [13]. Fixed-effects models were used in main analyses, and random-effects models in sensitivity analyses. We used meta-regression to determine how airflow obstruction prevalence varied according to smoking amount (pack-years). Smoking amount in pack-years was calculated at the individual level in ever-smokers as the mean number of cigarettes smoked daily multiplied by the number of years smoked divided by 20, provided as summary data. Average smoking amount was hereafter summarised by including both never- and ever-smokers. Analyses were performed using Stata/SE 18.0 for Windows (StataCorp, College Station, Texas, USA).

Results

We included 48 612 young adults from across Europe, including Austria, Belgium, Denmark, Estonia, France, Germany, Iceland, Italy, the Netherlands, Norway, Spain, Sweden, Switzerland and the United Kingdom. Characteristics are provided in tables 1 and 2, and supplementary table S2.

Airflow obstruction

The prevalence of airflow obstruction according to FEV_1/FVC <0.70 increased with advancing age, from 2.3% in those aged 20–24.9 years to 6.3% in those aged 35–39.9 years (figure 1). In contrast, prevalence of airflow obstruction according to FEV_1/FVC <LLN was much higher at younger ages: 7.3% at ages 20–24.9 years and 8.2% at ages 35–39.9 years. Difference in prevalence of airflow obstruction between FEV_1/FVC <0.70 and <LLN was highest in the ages 20–24.9 years and became smaller with increasing age. Results were overall similar, albeit with wider confidence intervals, when using random-effects models (supplementary figure S1). A detailed meta-analysis revealed heterogeneity between the cohorts (supplementary figures S2–S5).

Smoking prevalence and amount

The prevalence of active smoking ranged from 19% to 28%; lowest for those aged 20–24.9 years and highest for those aged 35–39.9 years (figure 2a). In contrast, the prevalence of ever-smoking was much higher, ranging from 37% in those aged 20–24.9 years to 51% in those aged 35–39.9 years. Smoking amount increased from 3.6 pack-years in those aged 20–24.9 years to 9.7 pack-years in those aged 35–39.9 years (figure 2b).

Airflow obstruction according to sex and smoking

In male, with advancing age, the prevalence of airflow obstruction increased from 2.9% to 7.9% according to FEV_1/FVC <0.70 and from 7.1% to 8.8% according to FEV_1/FVC <LLN. In females, the corresponding increases were from 1.2% to 4.8% and from 6.7% to 7.5%, respectively (figure 3a). As expected, prevalence of airflow obstruction was higher for ever-smokers than never-smokers; up to 9.0% *versus* up to

TABLE 1 Characteristics of 48 612 young adults from eight population-based European cohorts in the Chronic Airway Diseases Early Stratification (CADSET) collaboration

	All individuals	Age years			
		20–24.9	25–29.9	30–34.9	35–39.9
Participants	48 612	7291	11 590	12 703	17 078
Age years	31.7±0.07	22.9±0.09	27.7±0.07	32.5±0.07	37.4±0.06
Female	28 004 (58)	4478 (61)	6622 (57)	7105 (56)	9799 (57)
BMI kg·m^{-2}	24.6±0.2	23.4±0.3	24.1±0.2	24.8±0.2	25.3±0.2
Lung function					
FEV_1 L	3.82±0.03	3.92±0.05	3.94±0.03	3.85±0.03	3.69±0.03
FEV_1 % predicted	96±0.7	96±0.9	96±0.7	96±0.7	96±0.6
FVC L	4.73±0.04	4.68±0.05	4.80±0.04	4.79±0.04	4.65±0.03
FVC % predicted	98±0.7	97±0.9	98±0.7	99±0.7	98±0.6
FEV_1/FVC	0.81±0.004	0.84±0.006	0.82±0.004	0.81±0.004	0.80±0.003
Smoking history					
Ever-smokers	23 037 (47)	2724 (37)	5266 (45)	6359 (50)	8688 (51)
Tobacco consumption pack-years[#]	4.0±0.2	1.4±0.1	2.7±0.1	4.2±0.2	5.8±0.2

Data are presented as n, mean±SE or n (%). Numbers may not add up to 100% due to rounding. Based on the Copenhagen City Heart Study (n=4083), European Community Respiratory Health Survey (n=7758), Trøndelag Health Study (HUNT) (n=1273), Copenhagen General Population Study (n=7178), LifeLines (n=24 911), LEAD (Lung, Heart, Social, Body) (n=3001), West Sweden Asthma Study (n=269) and Obstructive Lung Disease in Northern Sweden (n=139). BMI: body mass index; FEV_1: forced expiratory volume in 1 s; FVC: forced vital capacity. [#]: includes both never- and ever-smokers.

TABLE 2 Characteristics of 48 612 young adults according to age and sex from eight population-based European cohorts in the Chronic Airway Diseases Early Stratification (CADSET) collaboration[#]

	Age years							
	Male (n=20 608)				Female (n=28 004)			
	20–24.9	25–29.9	30–34.9	35–39.9	20–24.9	25–29.9	30–34.9	35–39.9
Participants	2813	4968	5598	7229	4478	6622	7105	9799
Age years	22.9±0.10	27.7±0.08	32.5±0.07	37.4±0.06	22.9±0.08	27.6±0.07	32.6±0.06	37.5±0.05
BMI kg·m^{-2}	23.5±0.3	24.5±0.2	25.3±0.2	25.8±0.2	23.2±0.3	23.9±0.2	24.4±0.2	24.9±0.2
Lung function								
FEV_1 L	4.70±0.06	4.61±0.04	4.49±0.04	4.33±0.03	3.43±0.03	3.41±0.03	3.39±0.03	3.22±0.02
FEV_1 % predicted	96±1.1	96±0.8	96±0.8	96±0.7	96±0.8	96±0.6	97±0.7	96±0.5
FVC L	5.68±0.08	5.71±0.05	5.65±0.06	5.49±0.04	4.05±0.04	4.12±0.03	4.11±0.03	4.03±0.02
FVC % predicted	98±1.1	98±0.7	98±0.7	98±0.7	97±0.8	98±0.6	99±0.6	99±0.5
FEV_1/FVC	0.83±0.007	0.81±0.004	0.80±0.004	0.79±0.004	0.85±0.005	0.83±0.003	0.82±0.003	0.80±0.003
Smoking history								
Ever-smokers	1117 (40)	2282 (46)	2837 (51)	3868 (54)	1607 (36)	2984 (45)	3522 (50)	4820 (49)
Tobacco consumption pack-years[#]	1.6±0.1	3.0±0.2	4.8±0.2	7.0±0.3	1.3±0.1	2.5±0.1	3.8±0.2	4.9±0.2

Data are presented as n, mean±SE or n (%). Numbers may not add up to 100% due to rounding. Based on the Copenhagen City Heart Study (n=4083), European Community Respiratory Health Survey (n=7758), Trøndelag Health Study (HUNT) (n=1273), Copenhagen General Population Study (n=7178), LifeLines (n=24 911), LEAD (Lung, Heart, Social, Body) (n=3001), West Sweden Asthma Study (n=269) and Obstructive Lung Disease in Northern Sweden (n=139). BMI: body mass index; FEV_1: forced expiratory volume in 1 s; FVC: forced vital capacity. #: includes both never- and ever-smokers.

6.9%, respectively (figure 3b). Results were overall similar when using random-effects models (supplementary figure S6). Difference in prevalence of airflow obstruction between FEV_1/FVC <0.70 and <LLN was highest for females and ever-smokers. The prevalence of airflow obstruction according to the two airflow obstruction criteria increased with smoking amount, but seemed to peak at a threshold of ~5 pack-years (figure 4 and supplementary figure S7).

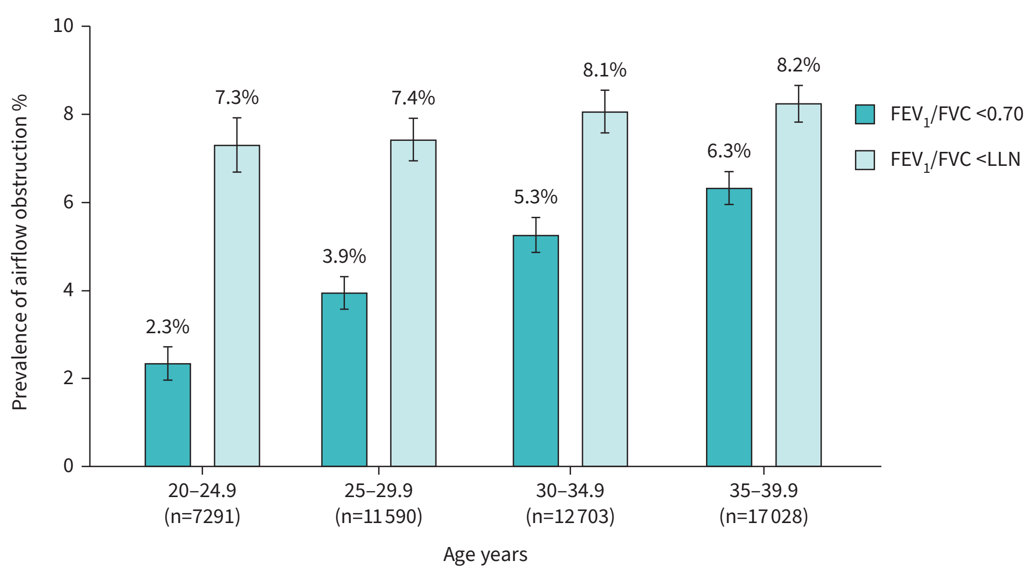

FIGURE 1 Prevalence of airflow obstruction in young adults in Europe. Based on the Copenhagen City Heart Study (n=4083), European Community Respiratory Health Survey (n=7758), Trøndelag Health Study (HUNT) (n=1273), Copenhagen General Population Study (n=7178), LifeLines (n=24 911), LEAD (Lung, Heart, Social, Body) (n=3001), West Sweden Asthma Study (n=269) and Obstructive Lung Disease in Northern Sweden (n=139). Data are presented with 95% CI. FEV_1: forced expiratory volume in 1 s; FVC: forced vital capacity; LLN: lower limit of normal.

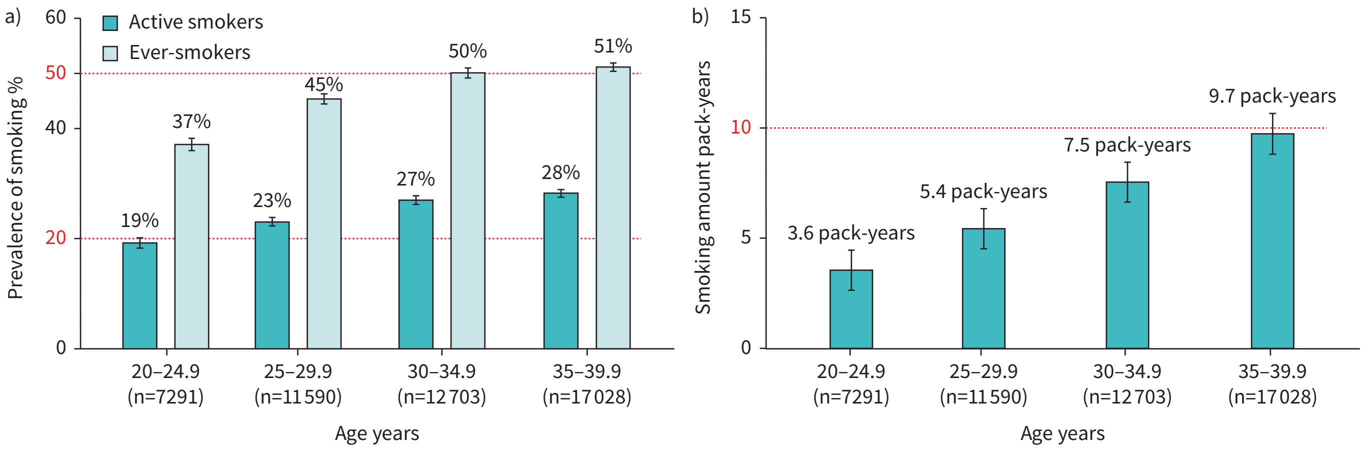

FIGURE 2 a) Prevalence of smoking and b) average smoking amount in young adults in Europe. Based on the Copenhagen City Heart Study (n=4083), European Community Respiratory Health Survey (n=7758), Trøndelag Health Study (HUNT) (n=1273), Copenhagen General Population Study (n=7178), LifeLines (n=24 911), LEAD (Lung, Heart, Social, Body) (n=3001), West Sweden Asthma Study (n=269) and Obstructive Lung Disease in Northern Sweden (n=139). A pack-year corresponds to smoking 20 cigarettes (or one pack) per day for 1 year. Data are presented with 95% CI. Smoking amount calculated including both never- and ever-smokers.

Discussion

Using data from ∼50 000 individuals across European population-based cohorts, we show here that up to 8% of adults aged 20–40 years have airflow obstruction, and that at these young ages, there is greater airflow obstruction in ever-smokers than never-smokers and in males compared to females.

It seems surprising that as many as 8% of young adults already have airflow obstruction. In a previous study utilising the ECRHS with a sample size of 5200 participants, prevalence of airflow obstruction among adults aged 20–44 years was estimated to be 2% according to FEV_1/FVC <0.70, and 6% according to FEV_1/FVC <LLN [14]. Furthermore, when these young adults with airflow obstruction were followed over 9 years, they displayed an accelerated lung function decline and an increased risk of hospitalisation due to COPD. Although COPD is a diagnosis more commonly established in older than younger adults, many patients with COPD already exhibit low lung function as young adults [5]. Our findings might reflect this lowered lung function trajectory in early adulthood, particularly given the strong relationship to smoking behaviour. However, genetic factors may also contribute, as recent evidence suggests that COPD-related genetic variants influence lung function as early as school age and beyond [15]. As reversible airflow obstruction can be a clinical feature of asthma, it could be suggested that airflow obstruction in the young group studied might partly reflect underlying asthma. This would also be an important finding, as reversible airflow obstruction has been shown to increase risk of subsequent persistent airflow obstruction, and may be another pathway towards COPD [16]. If left untreated, or without any intervention, progression of airflow obstruction can lead to more severe disease and early death [17]. Since 19–28% of young adults in the present study report active smoking, the first way of halting progression of airflow obstruction would be smoking cessation [18, 19], but early therapeutic intervention may also be potentially useful [6, 20, 21].

Since smoking is the single most important risk factor for COPD, it was expected that airflow obstruction would be more prevalent among ever-smokers rather than never-smokers. Furthermore, the sex differences observed in our study with a higher prevalence of airflow obstruction in males than in females, likely also reflects differences in smoking exposure, since males had a higher proportion of active smokers and greater tobacco consumption than females. We believe that a significant proportion of airflow obstruction in these groups probably represents young COPD or a stage immediately preceding this. This could be important for prevention efforts, as early diagnosis, before severe and irreversible airflow obstruction develops, could allow for intervention to halt development of COPD. One obvious intervention could be smoking cessation, which is the most effective strategy to prevent further lung function decline and reduce the risk of severe airflow obstruction. Additionally, raising awareness is essential for improving early detection, promoting smoking cessation, and ultimately reducing the burden of young COPD.

Prevalence of airflow obstruction according to FEV_1/FVC <LLN was higher than when using FEV_1/FVC <0.70 in this young age group, especially in females. Arguably, this discordant group, *i.e.* those with

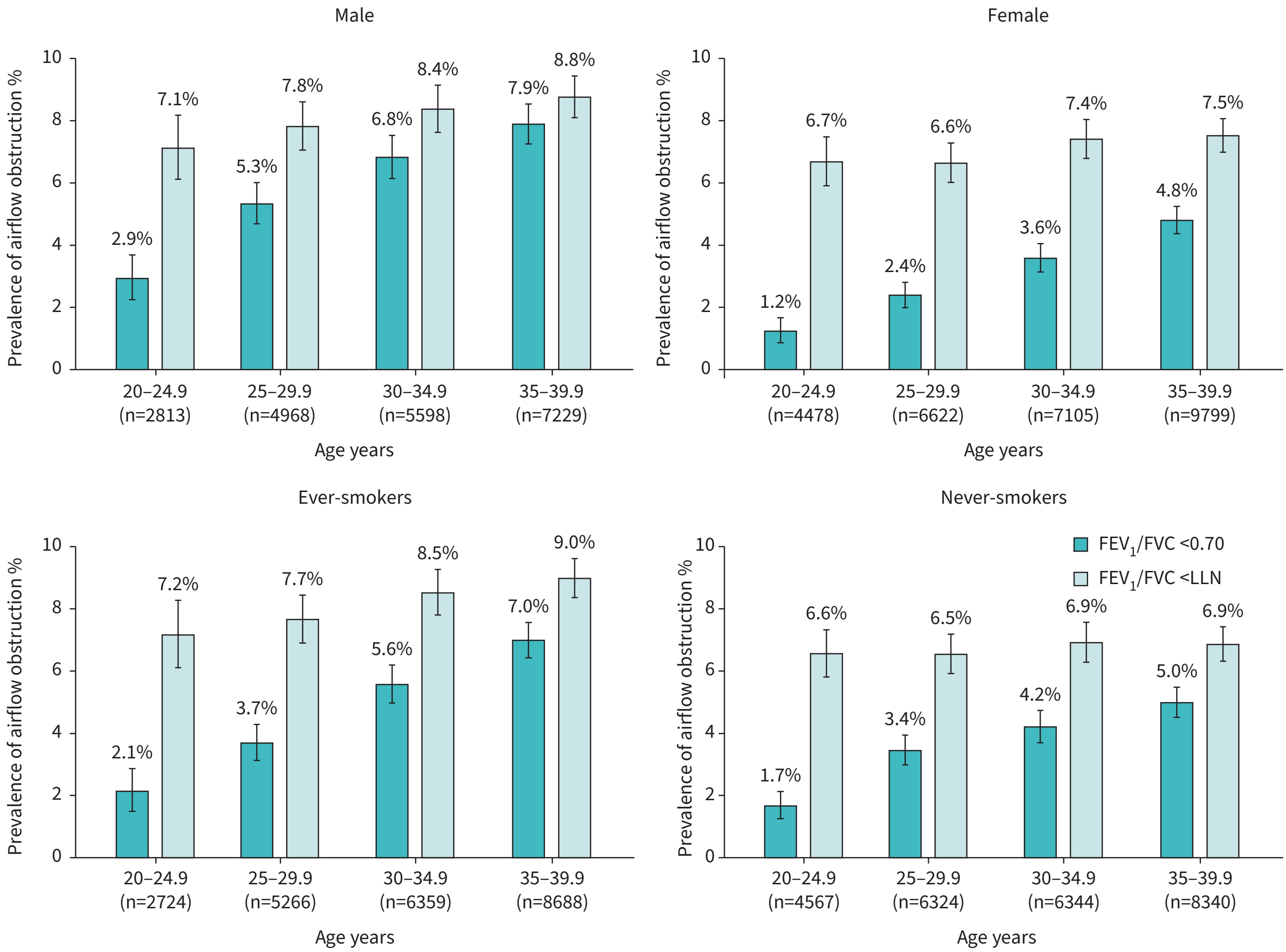

FIGURE 3 Prevalence of airflow obstruction according to sex and smoking in young adults in Europe. Based on the Copenhagen City Heart Study (n=4083), European Community Respiratory Health Survey (n=7758), Trøndelag Health Study (HUNT) (n=1273), Copenhagen General Population Study (n=7178), LifeLines (n=24 911), LEAD (Lung, Heart, Social, Body) (n=3001), West Sweden Asthma Study (n=269) and Obstructive Lung Disease in Northern Sweden (n=139). Data are presented with 95% CI. FEV_1: forced expiratory volume in 1 s; FVC: forced vital capacity; LLN: lower limit of normal.

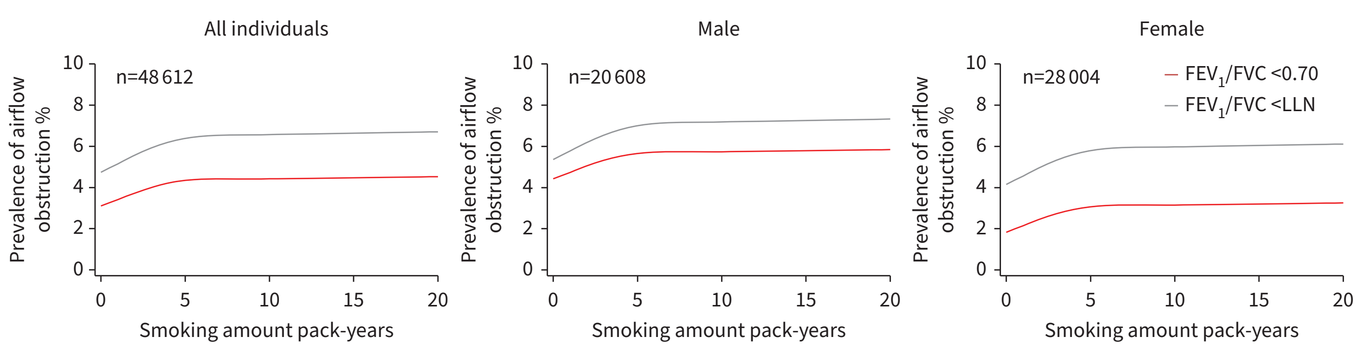

FIGURE 4 Prevalence of airflow obstruction according to smoking amount in young adults in Europe. Based on the Copenhagen City Heart Study (n=4083), European Community Respiratory Health Survey (n=7758), Trøndelag Health Study (HUNT) (n=1273), Copenhagen General Population Study (n=7178), LifeLines (n=24 911), LEAD (Lung, Heart, Social, Body) (n=3001), West Sweden Asthma Study (n=269) and Obstructive Lung Disease in Northern Sweden (n=139). FEV_1: forced expiratory volume in 1 s; FVC: forced vital capacity; LLN: lower limit of normal.

airflow obstruction according to FEV_1/FVC <LLN but not FEV_1/FVC <0.70, may represent a young at-risk group for COPD, other morbidity and early death [4, 17, 22]. In contrast, risk of morbidity and early death is lower when lung function is higher than normal [7, 8, 23–26], indicating the significance of optimising lung function not just for averting the onset of COPD but also for overall wellbeing, even in those with low–normal lung function [27]. Nonetheless, in the general population, it is not clear whether using FEV_1/FVC <LLN instead of FEV_1/FVC <0.70 would prove equally beneficial across the whole age range [28], or if the simultaneous use of both criteria with clinical findings would be better clinical practice. The finding for females is especially intriguing; to our knowledge, the clinical consequences of the higher discrepancy between airflow obstruction criteria compared to males have not been investigated, but should be the topic of future suitably designed studies. By using the LLN criterion, we would not expect an increase in prevalence with age in airway-healthy individuals, as the LLN is defined relative to age, and in each age group, the prevalence should theoretically remain ∼5%. However, our results indicate that the prevalence is significantly higher than 5% and increases with advancing age.

Strengths of the present study include a large sample size with young adults recruited from the general population representative of large parts of Europe. In addition, we were able to assess the prevalence using two different widely used airflow obstruction criteria according to smoking amount and sex.

A potential limitation is that post-bronchodilator airflow obstruction was not available, and we cannot determine how many have reversible or persistent airflow obstruction. However, pre-bronchodilator airflow obstruction has been shown to identify high-risk individuals with COPD before [28], and reversible airflow obstruction has been shown to increase risk of future COPD development [16].

Another potential limitation is that we were unable to explore the role of nonsmoking-related risk factors in airflow obstruction, particularly air pollution. Emerging evidence suggests that air pollution plays an increasingly significant role in lung health, a trend that is likely to become more pronounced as smoking prevalence continues to decline [29, 30]. Given the heterogeneity in prevalence estimates across cohorts, environmental exposures may contribute substantially to these differences. Future studies should investigate the impact of air pollution in a European context, where the CADSET collaboration is well-positioned to lead such efforts.

Lastly, since we are a large consortium, we only had access to summary data due to local legislation, and are restricted in some forms of analyses. However, in the present study we were interested in ascertaining the prevalence of airflow obstruction in younger European adults, which was successfully accomplished.

Clinical implications of this study underscore the importance of recognising airflow obstruction in younger adults. With up to 8% of individuals aged 20–40 years found to have airflow obstruction, evaluating obstructive lung disease remains relevant in this age group, particularly among those with a history of smoking and respiratory symptoms. A key challenge in clinical practice is the substantial underdiagnosis of obstructive lung disease [31, 32]. Many patients receive a diagnosis and start treatment too late, often when severe airflow obstruction has already developed and symptoms have become disabling, resulting in less effective treatment outcomes and a poorer prognosis. This may also explain why undiagnosed and untreated patients experience significant healthcare utilisation, along with increased morbidity and mortality [33–35]. Early diagnosis could improve treatment potential and reduce the overall disease burden [36].

Furthermore, the general population nature of the cohorts included enabled us to study young adults between the ages of 20 and 40 years, a group studied relatively little in COPD research. In doing so, we provide data suggesting that there needs to be greater awareness of the potential presence of airflow obstruction in younger adults and further study to understand its prognostic significance. As a result, we may be able to offer clinical diagnostic evaluation and begin treatment to hinder progression for obstructive lung disease at an earlier stage.

In summary, we found that up to 8% of adults aged 20–40 years across Europe have airflow obstruction. This study highlights the need for awareness of obstructive lung disease in the young, which in turn could have implications for prevention, early diagnosis, and treatment of airway disease in young adults.

Data availability: Additional data regarding technical details, statistical code and derivative data are available from the corresponding author. Data access for further analyses is possible through direct collaborative agreement or through locally managed access arranged through the study's principal investigator.

Provenance: Submitted article, peer reviewed.

Ethics statement: Each study obtained written informed consent from their participants and ethical approval from the relevant regulatory boards. Links to each study can be found at https://europeanlung.org/cadset/.

Author contributions: Y. Çolak and S. Afzal conceptualised the study, formulated the original draft and figures, and had full access to all the data in the study and final responsibility for the decision to submit for publication. Y. Çolak, J.P. Allinson and S. Afzal contributed to writing. Y. Çolak and S. Afzal performed the statistical analyses. Y. Çolak, S. Afzal, J.P. Allinson, D. Jarvis, R. Breyer-Kohansal, M-K. Breyer, S.A. Aalberg Vikjord, A. Langhammer, R. Faner, M. van den Berge, H. Backman, E. Rönmark, J.M. Vonk, B.I. Nwaru and B.G. Nordestgaard contributed to the curation, preparation and contribution of data from the respective population-based cohorts. P. Lange is a principal investigator of the Copenhagen City Heart Study. D. Jarvis is a principal investigator of the European Community Respiratory Health Study. A. Langhammer is a principal investigator of the HUNT study. B.G. Nordestgaard is a principal investigator of the Copenhagen General Population Study. M. van den Berge is a principal investigator of the LifeLines study. R. Breyer-Kohansal and M-K. Breyer are principal investigators of the Austrian LEAD study. E. Rönmark is a principal investigator of the OLIN study. B.I. Nwaru is a principal investigator of the West Sweden Asthma Study. J.A. Wedzicha, R. Faner, E. Melén and A. Agustí set up and lead CADSET, a pan-European, multicentre Clinical Research Collaboration (CRC) endorsed by the European Respiratory Society. R. Faner contributed towards the CRC registry curation and administration. All authors contributed to the scientific content of the manuscript, critically reviewed it, and approved the final version.

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