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Estimating population prevalence of potential airflow obstruction using different spirometric criteria: a pooled cross-sectional analysis of persons aged 40–95 years in England and Wales

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ABSTRACT

Objectives: Consistent estimation of the burden of chronic obstructive pulmonary disease (COPD) has been hindered by differences in methods, including different spirometric cut-offs for impaired lung function. The impact of different definitions on the prevalence of potential airflow obstruction, and its associations with key risk factors, is evaluated using cross-sectional data from two nationally representative population surveys.

Design: Pooled cross-sectional analysis of Wave 2 of the UK Household Longitudinal Survey and the Health Survey for England 2010, including 7879 participants, aged 40–95 years, who lived in England and Wales, without diagnosed asthma and with good-quality spirometry data. Potential airflow obstruction was defined using self-reported physician-diagnosed COPD; a fixed threshold (FT) forced expiratory volume in 1 s/forced vital capacity (FEV_1/FVC) ratio <0.7 and an age-specific, sex-specific, height-specific and ethnic-specific lower limit of normal (LLN). Standardised questions elicited self-reported information on demography, smoking history, ethnicity, occupation, respiratory symptoms and cardiovascular disease.

Results: Consistent across definitions, participants classed with obstructed airflow were more likely to be older, currently smoke, have higher pack-years of smoking and be engaged in routine occupations. The prevalence of airflow obstruction was 2.8% (95% CI 2.3% to 3.2%), 22.2% (21.2% to 23.2%) and 13.1% (12.2% to 13.9%) according to diagnosed COPD, FT and LLN, respectively. The gap in prevalence between FT and LLN increased in older age groups. Sex differences in the risk of obstruction, after adjustment for key risk factors, was sensitive to the choice of spirometric cut-off, being significantly higher in men when using FT, compared with no significant difference using LLN.

Conclusions: Applying FT or LLN spirometric cut-offs gives a different picture of the size and distribution of the disease burden. Longitudinal studies examining differences in unscheduled hospital admissions and risk of death between FT and LLN may inform the choice as to the best way to include spirometry in assessments of airflow obstruction.

Strengths and limitations of this study

- Estimates of the burden of chronic obstructive pulmonary disease using spirometry data collected in epidemiological studies are inconsistent through differences in methods, including different spirometric cut-offs.
- Our study combined two nationally representative samples of adults living in England and Wales, with standardised protocols and objective measurements of lung function, and a wide range of clinically relevant conditions including self-reported respiratory symptoms (chronic cough and phlegm) and breathlessness.
- Consistent definitions and up-to-date reference equations were used, providing baseline data for monitoring purposes in the UK, and for facilitating comparison with international studies.
- Prevalence estimates were based on prebronchodilator lung function measurements, and so are likely to overestimate true prevalence.

INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is characterised by a progressive decline in lung function.[1 2] In total, 2.9 million deaths were attributed to COPD in 2010, making it the third leading global cause of death.[3] The National Outcomes Strategy for COPD estimated that 835 000 people living in the UK are currently diagnosed with COPD, with a further 2.2 million being undiagnosed.[4] COPD is the second leading cause of emergency hospital admission and is one of the most costly diseases in terms of acute hospital care in England.[4]

Healthcare budgeting is often contingent on the estimated burden of disease. Spirometry, the mainstay of lung function assessment, has been used in nationally representative surveys to estimate the COPD burden in terms of prevalence, associated comorbidities and mortality. Estimation of the disease burden has been hindered, however, by differences in methods, including spirometric cut-offs.[5–8] Fixed thresholds (FTs) use cut-offs for lung function measurements (eg, forced expiratory volume in 1 s/forced vital capacity (FEV_1/FVC) ratio <0.7) regardless of age, sex, height and ethnicity.[9] An additional threshold for per cent-of-predicted FEV_1 (expected for persons of a given age, sex, height and ethnicity) is also commonly used for severity classification. In contrast, a lower limit of normal (LLN) cut-off uses a statistical definition of abnormal/normal (eg, below/above the lower 5th centile of the distribution of age-specific, sex-specific, height-specific and ethnic-specific FEV_1/FVC values from a healthy, lifelong non-smoking population).[10]

At present, applying FTs such as FEV_1/FVC <0.7 is the standard approach. However, the European Respiratory Society (ERS) Task Force on epidemiology recently advocated using the LLN in epidemiological studies as FTs overestimate airflow obstruction in older populations, due to the physiological reduction of FEV_1/FVC with age, and underestimate in young adults, compared with LLN.[11–16] The controversy over FT versus LLN thresholds is well known with no signs of a consensus among expert groups being agreed.[17–21]

Partly as a result of this controversy, the COPD epidemiological database shows heterogeneity in definitions and consequential estimates of the disease burden.[5 22] Two nationally representative samples, Wave 2 (2010–2012) of the UK Household Longitudinal Survey (UKHLS, 'Understanding Society') and the Health Survey for England (HSE) 2010, collected lung function data using identical measurement protocols and specialist equipment, providing an opportunity to increase statistical precision by combining both data sets. Therefore, the primary objective of the present study was to compare the prevalence of 'potential' airflow obstruction according to FT and LLN thresholds among persons aged 40–95 years living in England and Wales: potential in the sense that the administration of bronchodilators to measure the extent of reversibility in airflow obstruction was not used. As a secondary aim, we compared the sensitivity of associations with risk factors including age, sex, smoking history and socioeconomic position. Using the same variables, we also examined the characteristics associated with spirometry in connection with self-reported physician-diagnosed COPD.

METHODOLOGY

Study design and setting

The UKHLS and HSE selected participants using stratified multistage probability sampling designs.[23] Self-reported health information, risk factors and demographics were collected through face-to-face interviews, followed by a visit from a trained nurse during which lung function was measured. Response rates for the Wave 2 interview (among individuals issued) and nurse visit (among eligible participants in the Wave 2 interview) were 61% and 59%, respectively, in UKHLS. In HSE 2010, interview (among the estimated total number of adults in sampled households) and nurse-visit (adults in co-operating households) response rates were 59% and 57%. Sampling methods are described elsewhere.[24–26] Eligible participants gave written consent to participate in spirometry.

Questionnaire and procedures

Participants were excluded from spirometry for the following safety reasons: pregnancy; had in the past 3 months abdominal/chest surgery, a heart attack, detached retina or eye or ear surgery; admitted to hospital with a heart complaint in the preceding month; a resting pulse rate >120 bpm or currently taking medications for the treatment of tuberculosis. Spirometry, without bronchodilator use, was conducted using NDD EasyOne PCC spirometers (NDD Medical Technologies, Zurich, Switzerland). Quality control was summarised in a session grade based on the number of technically acceptable blows and their reproducibility. Grades A (three acceptable manoeuvres, two highest FVC and FEV_1 within 100 mL), B (three acceptable manoeuvres, two highest FVC and FEV_1 within 150 mL) and C (two or three acceptable manoeuvres within 200 mL) were considered good quality. Full details on measurement procedures are available elsewhere.[25–27]

The highest values for FEV_1 and for FVC, from at least three and up to eight blows, were used. Age-specific, sex-specific, height-specific and ethnic-specific predicted values and z-scores (FEV_1, FVC and FEV_1/FVC) were computed using the ERS Global Lungs Initiative (GLI 2012, http://www.lungfunction.org) reference equations. These have been prepared by an international collaboration based on data spanning 26 countries from >70 000 healthy individuals across four ethnic groups (Caucasian, African-American, and North-East Asian and South-East Asian), valid for persons aged 3–95 years[28 29] and have been shown to fit contemporary Australasian spirometric data.[30]

FT and LLN spirometric cut-offs

Using FTs, we applied the 2007 Global Initiative for Chronic Obstructive Lung Disease (GOLD) classification,[31] which was designed for use with postbronchodilator spirometry: potential airflow obstruction was defined as FEV_1/FVC <0.7 (FT). Disease stage was defined by the reduction in FEV_1 relative to per cent-of-predicted values as follows: stage I (FEV_1/FVC <0.7 and FEV_1 ≥80% of predicted); stage II (FEV_1/FVC <0.7 and FEV_1 50–79% of predicted) and stage III+ (FEV_1/FVC <0.7 and FEV_1 <50% of predicted).[32] Participants with FEV_1/FVC ≥0.7 were defined as non-obstructed.

Participants with FEV_1/FVC<LLN (below the lower 5th centile of the distribution of z-scores) were defined as obstructed (LLN). To examine possible heterogeneity among participants with FEV_1/FVC<LLN, disease stage

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was defined by FEV_1 relative to LLN as follows: stage I ($FEV_1/FVC<LLN$ and $FEV_1 \geq LLN$) and stage II ($FEV_1/FVC<LLN$ and $FEV_1<LLN$).[33] Participants with $FEV_1/FVC \geq LLN$ were defined as non-obstructed. The fifth centile was chosen due to its established associations with respiratory symptoms and all-cause mortality.[34]

Physician-diagnosed COPD

In UKHLS, disease status was ascertained through questions asking "Has a doctor or other health professional ever told you that you have [disease]?" Diagnosed COPD was defined as a positive response to either chronic bronchitis or emphysema. In HSE, diagnosed COPD was defined as a positive response to the question "Did a doctor ever tell you that you had chronic bronchitis, emphysema or COPD?"

Risk factors, measurements of lung function and comorbidities

Key subgroups were defined by age (40–54, 55–64, 65–74, 75–95); sex; smoking status (current, former, never); pack-years of cigarette smoking (a cumulative total reflecting the amount and duration of consumption, with 1 pack-year equating to an average of 20 cigarettes smoked/day for 1 year) and socioeconomic position, defined by the National Statistics Socio-Economic Classification (NS-SEC), grouped into professional, intermediate and routine occupations.

FEV_1, FVC and FEV_1/FVC, on a continuous scale, were expressed as per cent-of-predicted values. Additional variables included current use of respiratory medicine; area of residence (urban/rural); body mass index (weight in kilograms divided by the square of height in metres), grouped into normal weight (18.5–24.9 kg/m^2), overweight (25–29.9 kg/m^2) and obese ($\geq$30 kg/m^2); diagnosed diabetes; poor self-rated health and reported cardiovascular disease (stroke, angina, myocardial infarction). In HSE, participants were asked to name any long-standing illness: respiratory diseases were identified using *International Classification of Diseases, Tenth Revision* codes J00-J99. In the HSE, presence of respiratory symptoms was defined as usually coughing first thing in the morning, for at least 3 months/year, and bringing up phlegm from the chest most days for three consecutive months in a year. In the HSE, participants with some limitation of activity due to breathlessness during daily living were identified by a score of 3+ on the Medical Research Council (MRC) dyspnoea scale. Exposure to passive smoking in the HSE was measured by reported number of hours/week currently exposed to cigarette smoke (0, 1–9 and ≥10 h).

Statistical analyses

A lower age limit was used of 40 years due to the low prevalence of non-asthma airflow obstruction in the youngest age groups.[35] As bronchodilators were not used, we excluded participants who reported diagnosed asthma.[34 36–38] Five sets of analyses were conducted across the categories of diagnosed COPD, FT and LLN. First, participants' characteristics (demographics, risk factors, comorbidities and per cent-of-predicted FEV_1, FVC and FEV_1/FVC) were summarised as means, accompanied by SD, or as counts accompanied by percentages. Participants were counted under each relevant definition. Participants with/without obstruction were compared using the χ^2 test and analysis of variance for categorical and continuous variables, respectively.[39]

Second, prevalence estimates were computed for a subset of sociodemographic variables defined by age, sex, smoking status, pack-years of cigarette smoking and NS-SEC. Third, in the absence of a gold standard, we calculated the sensitivity and specificity of each spirometric criterion, using the alternative cut-off as the reference standard.[40]

Fourth, regression analyses were performed using age, sex, pack-years of smoking and NS-SEC as independent variables with airflow obstruction as outcome. Current smoking status could not be entered in the same model as pack-years due to significant collinearity. The dependent variable based on FTs had four categories: non-obstructed, stage I, stage II and stage III+. The LLN-derived outcome had three categories: non-obstructed, stage I and stage II. In each case, multinomial logistic regression was used to estimate relative risk ratios (RRRs), with non-obstructed as the reference category. Multinomial logistic regression generalises logistic regression to outcomes with more than two possible discrete outcomes. The RRR is interpreted as the relative risk of one outcome in relation to the reference category for a specified category of an independent variable compared with the reference.[41 42] Diagnosed COPD was analysed as a binary outcome (not reported/reported): logistic regression was therefore used to estimate ORs.[39 41] The overall association for independent variables with >2 categories was computed using the adjusted Wald test. The likelihood ratio test was used to estimate the statistical significance of interaction terms: non-significant terms were excluded, and models refitted with only the main effects.

Fifth, to examine risk factors associated with possible underdiagnosis, a four-category outcome variable was created combining diagnosed COPD and spirometric criteria as follows: (1) neither diagnosed nor spirometrically defined obstruction; (2) physician-diagnosed COPD but no obstructive spirometry; (3) spirometrically defined but no diagnosed COPD and (4) both diagnosed and obstructive spirometry.[43] FT and LLN cut-offs were analysed separately. RRRs generated from multinomial logistic regressions were used to examine associations between the same set of risk factors listed above and the composite dependent variable.

Participants with missing values on covariates were excluded from relevant analyses. Tests of statistical significance were based on two-sided probability ($p<0.05$). Data set preparation was performed in SPSS V.20.0 (SPSS IBM Inc, Chicago, Illinois, USA), Stata V.13.1

(StataCorp, College Station, Texas, USA) and R (V.3.0.3; R Foundation, http://www.r-project.org). Analysis was conducted in Stata accounting for the complex design of both surveys, using the appropriate weighting variables and primary sampling units. Both datasets are available via the UK Data Service (http://www.ukdataservice.ac.uk).

Sensitivity analyses

Analyses were initially undertaken excluding participants with reported diagnosed asthma and then repeated including those with asthma. In accordance with the previous UK National Institute for Health and Care Excellence (NICE) recommendations,[44] comparisons between FT and LLN were rerun defining only the subset of FT participants with FEV_1 <80% of predicted (ie, stage II+) as having obstructed airflow.

RESULTS

The analytical sample comprised 7879 participants (5936 and 1943 from UKHLS and HSE, respectively) aged 40–95 years, who resided in England and Wales, did not report diagnosed asthma, had valid values of height and ethnicity and provided good-quality spirometry. Response flow charts for the UKHLS and HSE are provided in online supplementary figures S1 and S2, respectively. Excluded participants were more likely to be older, engaged in routine occupations and self-reported respiratory symptoms (data not shown). Differences between the UKHLS and HSE in terms of sex ratio, age, smoking history, NS-SEC and objective measurements of lung function were not materially important (see online supplementary table S1).

Descriptive characteristics of the analytical sample according to physician-diagnosed COPD, FT and LLN are shown in online supplementary tables S2 and S3. Overall, 46.8% of participants were men, with mean age 57.6 years (SD 12.3), 16.6% were current smokers, 4.6% had >50 pack-years of cigarette smoking and 36.5% were engaged in professional occupations. Twelve (0.1%) and 265 (3.2%) participants had missing values for pack-years and NS-SEC, respectively. The prevalence of diagnosed COPD was similar between the sexes (p=0.349), but was higher for men using FT and LLN (both p<0.001). Participants with diagnosed COPD/obstructive spirometry were more likely to be older, currently smoke, have higher pack-years of smoking and be engaged in routine occupations (all p<0.001). Prevalence of diagnosed COPD was higher in HSE versus UKHLS (p<0.001), but survey-specific prevalence was similar for FT and for LLN. Participants with diagnosed COPD/obstructive spirometry were more likely to report respiratory symptoms (chronic cough and phlegm) and disease, current use of respiratory medications, cardiovascular disease, breathlessness, poor self-rated health and have, on average, lower (per cent-of-predicted) values of FEV_1, FVC and FEV_1/FVC. The prevalence of respiratory symptoms was 13.7%, 10.2% and 11.3% among participants classed as having airflow obstruction according to diagnosed COPD, FT and LLN, respectively; prevalence of having a score of 3+ on the MRC dyspnoea scale was 34.8%, 12.3% and 15.9%.

Prevalence of airflow obstruction

The prevalence of airflow obstruction was 2.8%, 22.2% and 13.1% using diagnosed COPD, FT and LLN, respectively (table 1). Using FTs, 11.6%, 8.9% and 1.7% of participants were classed as stage I, stage II and stage III+, respectively. LLN-derived obstruction was 6.6% (stage I) and 6.4% (stage II). For most subgroups, prevalence was highest for FT and lowest for diagnosed COPD, with LLN falling in between. The gap in prevalence between FT and LLN increased in older age groups. Prevalence among participants aged 40–54 years was 11.9% and 10.7% using FT and LLN, respectively. Prevalence among participants aged 75–95 was 45% and 17.2%.

Table 2 shows estimates of sensitivity and specificity for FT and LLN, using the alternative spirometric cut-off as the reference standard. When using LLN as reference, specificity—the percentage of participants classed as non-obstructed using LLN identified as non-obstructed using FT—decreased from 94.9% among participants aged 40–64 years to 74.4% among those aged 65–95.

Multivariate analyses of airflow obstruction

Table 3 shows the significant risk factors for diagnosed COPD, and the FT and LLN disease stage classifications (non-obstructed as reference category). For diagnosed COPD, the significant interaction between sex and age group (p=0.022) suggested no difference in odds between the sexes among participants aged 40–64 years, but higher odds among men aged 65–95. Using FTs, being male was associated with a significantly increased risk of airflow obstruction: RRR 1.35 (95% CI 1.16 to 1.58), RRR 1.35 (1.12 to 1.63) and RRR 1.72 (1.08 to 2.76) for stages I, II and III+, respectively. In contrast, sex differences were not significant using LLN: RRR 1.07 (0.88 to 1.31) for stage I and RRR 1.20 (0.96 to 1.50) for stage II.

Odds of diagnosed COPD increased significantly with age only in men (p=0.022 for the interaction term). Using non-obstruction as reference, RRRs increased significantly with age when using FTs (p<0.001 for each stage). The age-related difference using LLN was more marked for stage II (p=0.492 and p<0.001 for stages I and II, respectively). A dose-related increased risk with pack-years of cigarette smoking was observed across each definition (p<0.001). The difference between NS-SEC levels was more marked with diagnosed COPD (p=0.012) and the tightest FT and LLN definitions (FT: p=0.002 stage III+; LLN: p<0.001 stage II).

Combination of diagnosed COPD and spirometric cut-offs

The significant risk factors for the two four-category outcome variables created as a composite of diagnosed

Table 1 Prevalence of diagnosed COPD and potential airflow obstruction using FTs and LLN spirometric criteria, persons aged 40–95 years without diagnosed asthma, HSE 2010 and UKHLS Wave 2 (2010–2012)*

		Diagnosed-COPD†	FTs‡				LLN§		
	n	% (95% CI)	Obstructed % (95% CI)	Stage I % (95% CI)	Stage II % (95% CI)	Stage III+ % (95% CI)	Obstructed % (95% CI)	Stage I % (95% CI)	Stage II % (95% CI)
All	7879	2.8 (2.3 to 3.2)	22.2 (21.2 to 23.2)	11.6 (10.9 to 12.4)	8.9 (8.2 to 9.6)	1.7 (1.3 to 2.0)	13.1 (12.2 to 13.9)	6.6 (6.0 to 7.3)	6.4 (5.8 to 7.0)
Sex									
Males	3335	3.0 (2.3 to 3.6)	26.3 (24.8 to 27.9)	13.2 (12.1 to 14.4)	10.7 (9.6 to 11.8)	2.4 (1.8 to 3.0)	15.0 (13.7 to 16.4)	7.2 (6.2 to 8.1)	7.9 (6.9 to 8.9)
Females	4544	2.6 (2.0 to 3.1)	18.6 (17.4 to 19.9)	10.2 (9.2 to 11.2)	7.4 (6.5 to 8.2)	1.0 (0.7 to 1.4)	11.3 (10.3 to 12.3)	6.2 (5.4 to 6.9)	5.1 (4.4 to 5.9)
Age group									
40–54	3472	1.7 (1.3 to 2.2)	11.9 (10.7 to 13.1)	7.0 (6.1 to 7.9)	4.6 (3.8 to 5.4)	0.3 (0.1 to 0.6)	10.7 (9.6 to 11.9)	6.7 (5.7 to 7.6)	4.1 (3.3 to 4.9)
55–64	2072	3.4 (2.5 to 4.2)	24.2 (22.2 to 26.1)	12.6 (11.1 to 14.1)	9.5 (8.1 to 10.9)	2.0 (1.4 to 2.7)	14.2 (12.6 to 15.8)	6.5 (5.4 to 7.7)	7.7 (6.4 to 8.9)
65–74	1557	3.9 (2.8 to 5.0)	32.6 (30.1 to 35.1)	16.5 (14.6 to 18.5)	12.9 (11.1 to 14.6)	3.2 (2.1 to 4.2)	15.0 (13.0 to 17.0)	6.4 (5.1 to 7.7)	8.6 (7.0 to 10.2)
75–95	778	3.9 (2.0 to 5.8)	45.0 (41.1 to 48.8)	21.1 (18.0 to 24.2)	19.6 (16.6 to 22.6)	4.3 (2.5 to 6.0)	17.2 (14.2 to 20.1)	7.2 (5.2 to 9.2)	9.9 (7.6 to 12.3)
Smoking status									
Current	1198	4.7 (3.5 to 6.0)	37.0 (34.1 to 39.9)	14.5 (12.3 to 16.6)	18.2 (15.9 to 20.6)	4.2 (3.0 to 5.4)	29.8 (27.0 to 32.6)	13.5 (11.3 to 15.7)	16.2 (14.0 to 18.5)
Ex-regular	2547	3.6 (2.7 to 4.5)	26.8 (24.9 to 28.7)	14.1 (12.7 to 15.6)	10.5 (9.2 to 11.8)	2.2 (1.5 to 2.9)	14.5 (13.0 to 16.1)	7.2 (6.0 to 8.3)	7.4 (6.2 to 8.5)
Never	4134	1.6 (1.2 to 2.0)	14.7 (13.5 to 15.9)	9.2 (8.2 to 10.1)	5.0 (4.3 to 5.7)	0.5 (0.2 to 0.9)	6.8 (5.9 to 7.7)	4.1 (3.5 to 4.8)	2.7 (2.1 to 3.3)
Pack-years¶									
0–0.9	4299	1.6 (1.2 to 2.0)	14.8 (13.6 to 16.0)	9.3 (8.4 to 10.3)	5.0 (4.3 to 5.7)	0.5 (0.2 to 0.8)	6.7 (5.9 to 7.6)	4.1 (3.5 to 4.7)	2.6 (2.0 to 3.2)
1–19.9	1905	2.3 (1.5 to 3.1)	22.3 (20.3 to 24.3)	12.9 (11.3 to 14.5)	7.5 (6.2 to 8.8)	1.9 (1.1 to 2.6)	13.4 (11.7 to 15.1)	7.6 (6.3 to 8.9)	5.8 (4.6 to 7.0)
20–49.9	1318	5.0 (3.6 to 6.5)	36.8 (34.0 to 39.6)	15.7 (13.5 to 17.9)	18.1 (15.9 to 20.4)	2.9 (2.0 to 3.9)	25.4 (22.8 to 27.9)	11.6 (9.5 to 13.6)	13.8 (11.8 to 15.8)
50+	345	10.5 (7.0 to 14.1)	53.7 (48.0 to 59.4)	16.0 (12.0 to 20.1)	28.0 (23.0 to 32.9)	9.7 (6.2 to 13.2)	39.3 (33.5 to 45.0)	12.4 (8.7 to 16.2)	26.9 (21.6 to 32.1)
NS-SEC¶									
Professional	3050	1.9 (1.4 to 2.4)	17.1 (15.7 to 18.5)	10.4 (9.3 to 11.6)	5.7 (4.9 to 6.5)	1.0 (0.6 to 1.4)	9.1 (8.0 to 10.2)	5.6 (4.6 to 6.5)	3.6 (2.9 to 4.3)
Intermediate	1859	2.3 (1.6 to 3.0)	21.9 (19.9 to 23.9)	12.5 (10.9 to 14.1)	8.4 (7.0 to 9.7)	1.1 (0.5 to 1.7)	12.0 (10.5 to 13.5)	6.6 (5.4 to 7.8)	5.4 (4.3 to 6.5)
Routine	2705	4.0 (3.1 to 4.8)	26.6 (24.7 to 28.5)	11.6 (10.3 to 12.9)	12.3 (10.9 to 13.7)	2.7 (2.0 to 3.5)	17.4 (15.8 to 19.1)	7.7 (6.6 to 8.9)	9.7 (8.4 to 11.0)

*Participants were included under each relevant definition. Bronchodilators were not used. Cell counts are unweighted; prevalence estimates were weighted.
†HSE: reported diagnosed COPD, bronchitis or emphysema; UKHLS: diagnosed bronchitis or emphysema.
‡FTs: obstruction (FT): FEV_1/FVC <0.7. Staging classification: stage I (FEV_1/FVC <0.7 and FEV_1 ≥80% of predicted); stage II (FEV_1/FVC <0.7 and FEV_1 50–79% of predicted); stage III+ (FEV_1/FVC <0.7 and FEV_1 <50% of predicted).
§LLN: obstruction (LLN): FEV_1/FVC<LLN. Staging classification: stage I (FEV_1/FVC<LLN and FEV_1>LLN); stage II (FEV_1/FVC<LLN and FEV_1<LLN).
¶Missing data: 12/7879 (0.2%) pack-years of cigarette smoking; 265/7879 (3.4%) NS-SEC.
COPD, chronic obstructive pulmonary disease; FEV_1, maximum expiratory volume in 1 s; FTs, fixed thresholds; FVC, forced vital capacity; HSE, Health Survey for England; LLN, lower limit of normal (below the lower 5th centile of z-scores); NS-SEC, National Statistics Socio-Economic Classification; UKHLS, UK Household Longitudinal Survey.

Table 2 Sensitivity and specificity of FTs and LLN spirometric criteria by age group, persons aged 40–95 years without diagnosed asthma, Health Survey for England 2010 and UK Household Longitudinal Survey Wave 2 (2010–2012)

	40–64 (n=5544)	65–95 (n=2335)	40–64 (n=5544)	65–95 (n=2335)
	FT using LLN as reference standard		LLN using FT as reference standard	
False positives (%)	5.1	25.6	0.4	0.0
False negatives (%)	2.5	0.0	28.0	57.6
Sensitivity	0.975	1.000	0.720	0.424
Specificity	0.949	0.744	0.996	1.000
PPV	0.720	0.424	0.975	1.000
NPV	0.996	1.000	0.949	0.744
κ coefficient	0.801	0.479	0.801	0.479
Likelihood ratio positive	18.98	3.90	200.65	N/A
Likelihood ratio negative	0.027	0.000	0.281	0.576
	FT (stage II+) using LLN as reference standard		LLN using FT (stage II+) as reference standard	
False positives (%)	1.3	8.9	6.3	5.2
False negatives (%)	49.2	26.7	16.0	39.1
Sensitivity	0.508	0.733	0.840	0.609
Specificity	0.987	0.911	0.937	0.948
PPV	0.840	0.609	0.508	0.733
NPV	0.937	0.948	0.987	0.911
κ coefficient	0.597	0.596	0.597	0.596
Likelihood ratio positive	38.82	8.28	13.27	11.67
Likelihood ratio negative	0.499	0.292	0.170	0.412

FTs, fixed thresholds; LLN, lower limit of normal (below the 5th centile of z-scores); NPV, negative predictive value; PPV, positive predictive value.

COPD and obstructive spirometry are shown in table 4. Relative to the reference category (neither doctor-diagnosed nor spirometrically defined airflow obstruction), the risk of reporting COPD in the absence of obstructive spirometry was significantly lower in men using either spirometric criterion (FT: RRR 0.53 (95% CI 0.32 to 0.87); LLN: RRR 0.56 (0.35 to 0.89)). The risk of having obstructed airflow using spirometry but with no diagnosed COPD—thereby indicating possible underdiagnosis—was significantly higher in men, and in older age groups, when using FT but not LLN. For both spirometric criterions, increases in risk with increasing pack-years of cigarette smoking, relative to the reference, was consistent across combinations of COPD/obstructive spirometry; the difference between NS-SEC levels was more marked for obstructive spirometry.

Sensitivity analyses

Repeating analyses by including 1183 participants with reported diagnosed asthma increased prevalence of diagnosed COPD, FT and LLN by 2–3 percentage points (see online supplementary figure S3), but showed similar patterns of association with risk factors. Diagnosed asthma was a strong predictor of diagnosed COPD and obstructive spirometry (p<0.001, data not shown). Narrowing FT-defined obstruction to the subset of FT participants with FEV_1 <80% of predicted (ie, stage II+) more than halved the FT-derived prevalence (22.2% vs 10.6%). Among participants aged 65–95 years, specificity using LLN as the reference standard was 74.4% and 91.1% for FT and FT stage II+, respectively (table 2). Patterns of association with risk factors using FT stage II+ were similar to those shown for FT.

DISCUSSION

Consistent estimation of the COPD burden has been hindered by differences in methods, including disagreement among experts over the choice of FT versus LLN spirometric cut-offs.[5–8] In this study, we combined two nationally representative surveys, with standardised protocols and objective lung function measurements, to evaluate the impact of different definitions on the prevalence of potential airflow obstruction, and its associations with key risk factors. Participants with diagnosed COPD/obstructive spirometry were more likely to be older, currently smoke, have higher pack-years of cigarette smoking, be in lower socioeconomic groups and report the presence of respiratory symptoms (chronic cough and phlegm), cardiovascular disease, breathlessness and poor self-rated health. Among persons aged 40–95 years without physician-diagnosed asthma, prevalence was 2.8%, 22.2% and 13.1%, according to diagnosed COPD, FT and LLN, respectively. The gap in prevalence between FT and LLN increased in older age groups. When using LLN as the reference standard, specificity for FT decreased from 94.9% among participants aged 40–64 years to 74.4% among participants aged 65–95, corresponding to false-positive rates of 5.1% and 25.6%, respectively. Sex differences in the risk of

Table 3 Results of logistic and multinomial logistic regressions for reported diagnosed COPD and potential airflow obstruction using FTs and LLN spirometric criteria among persons aged 40–95 years, HSE 2010 and UKHLS Wave 2 (2010–2012)*

			FTs‡			LLN§	
			Non-obstructed as reference			Non-obstructed as reference	
Characteristics	N	Diagnosed-COPD† OR (95% CI)	Stage I RRR (95% CI)¶	Stage II RRR (95% CI)¶	Stage III+ RRR (95% CI)¶	Stage I RRR (95% CI)¶	Stage II RRR (95% CI)¶
Sex							
Females**	4372	1.00	1.00	1.00	1.00	1.00	1.00
Males	3231	0.60 (0.34 to 1.05)	1.35 (1.16 to 1.58)	1.35 (1.12 to 1.63)	1.72 (1.08 to 2.76)	1.07 (0.88 to 1.31)	1.20 (0.96 to 1.50)
p Value		0.075	<0.001	0.002	0.024	0.503	0.107
Age group							
40–54**	3416	1.00	1.00	1.00	1.00	1.00	1.00
55–64	2022	1.66 (1.07 to 2.58)	2.00 (1.63 to 2.45)	2.13 (1.65 to 2.73)	6.05 (2.82 to 12.99)	0.92 (0.72 to 1.18)	1.57 (1.20 to 2.06)
65–74	1451	0.96 (0.54 to 1.70)	2.85 (2.30 to 3.53)	3.01 (2.32 to 3.89)	10.11 (4.55 to 22.49)	0.83 (0.63 to 1.09)	1.56 (1.16 to 2.12)
75+	714	1.20 (0.39 to 3.70)	4.72 (3.66 to 6.07)	6.67 (5.00 to 8.90)	22.26 (9.45 to 52.44)	1.06 (0.74 to 1.51)	2.20 (1.52 to 3.17)
p Value		0.104	<0.001	<0.001	<0.001	0.492	<0.001
Pack-years††							
0–0.9**	4165	1.00	1.00	1.00	1.00	1.00	1.00
1–19.9	1835	1.38 (0.88 to 2.17)	1.61 (1.34 to 1.93)	1.66 (1.29 to 2.15)	3.82 (1.80 to 8.14)	1.94 (1.51 to 2.49)	2.22 (1.58 to 3.12)
20–49.9	1269	2.91 (1.91 to 4.45)	2.30 (1.86 to 2.85)	4.56 (3.64 to 5.72)	5.91 (2.81 to 12.45)	3.39 (2.61 to 4.41)	5.43 (3.98 to 7.41)
50+	334	5.64 (3.45 to 9.22)	2.34 (1.63 to 3.35)	6.83 (4.85 to 9.63)	17.27 (7.88 to 37.84)	4.50 (2.96 to 6.84)	11.20 (7.59 to 16.52)
p Value		<0.001	<0.001	<0.001	<0.001	<0.001	<0.001
NS-SEC††							
Professional**	3047	1.00	1.00	1.00	1.00	1.00	1.00
Intermediate	1855	1.03 (0.68 to 1.58)	1.18 (0.97 to 1.45)	1.34 (1.04 to 1.72)	1.01 (0.51 to 2.00)	1.14 (0.88 to 1.48)	1.35 (0.99 to 1.85)
Routine	2701	1.61 (1.13 to 2.31)	1.07 (0.89 to 1.29)	1.82 (1.47 to 2.26)	2.30 (1.36 to 3.88)	1.28 (1.01 to 1.63)	2.18 (1.67 to 2.85)
p Value		0.012	0.246	<0.001	0.002	0.123	<0.001
Sample							
UKHLS**	5675	1.00	1.00	1.00	1.00	1.00	1.00
HSE	1928	2.22 (1.60 to 3.07)	0.95 (0.79 to 1.14)	0.97 (0.79 to 1.20)	0.99 (0.62 to 1.59)	1.05 (0.82 to 1.33)	0.99 (0.77 to 1.26)
p Value		<0.001	0.587	0.798	0.967	0.716	0.913
Males×age group							
40–54¶	1319	1.00	–	–	–	–	–
55–64	876	1.16 (0.54 to 2.45)	–	–	–	–	–
65–74	664	3.21 (1.40 to 7.39)	–	–	–	–	–
75+	372	2.61 (0.67 to 10.22)	–	–	–	–	–
p Value		0.022	–	–	–	–	–

*Participants were included under each relevant definition. Bronchodilators were not used. Cell counts are unweighted; ORs and RRRs estimated using survey weights.
†HSE: reported diagnosed COPD, bronchitis or emphysema; UKHLS: diagnosed bronchitis or emphysema.
‡FTs: stage I (FEV_1/FVC <0.7 and FEV_1 ≥80% of predicted); stage II (FEV_1/FVC <0.7 and FEV_1 50–79% of predicted); stage III+ (FEV_1/FVC <0.7 and FEV_1 <50% of predicted). Reference category: FEV_1/FVC ≥0.7.
§LLN: stage I (FEV_1/FVC<LLN and FEV_1>LLN); stage II (FEV_1/FVC<LLN and FEV_1<LLN). Reference category: FEV_1/FVC≥LLN.
¶The RRR is interpreted as the relative risk of one outcome in relation to the reference category for a specified category of an independent variable compared with the reference category for that independent variable. Using FT stage I as an example, the RRR for men versus women is interpreted as the relative risk for FT stage I versus non-obstruction for men compared with the analogous relative risk for women, adjusted for the other variables in the model.
**Reference category.
††Missing data: 12/7879 (0.2%) pack-years of cigarette smoking; 265/7879 (3.4%) NS-SEC.
COPD, chronic obstructive pulmonary disease; FEV_1, maximum expiratory volume in 1 s; FTs, fixed thresholds; FVC, forced vital capacity; HSE, Health Survey for England; LLN, lower limit of normal (below the 5th centile of z-scores); NS-SEC, National Statistics Socio-Economic Classification; OR, odds ratio; RRR; relative risk ratios; UKHLS, UK Household Longitudinal Survey.

Table 4 Results of multinomial logistic regressions for combined outcome variable based on diagnosed COPD and potential airflow obstruction using FTs and LLN spirometric criteria among persons aged 40–95 years, HSE 2010 and UKHLS Wave 2 (2010–2012)*

		FTs†			LLN‡		
		Neither diagnosed nor obstructive spirometry as reference			Neither diagnosed nor obstructive spirometry as reference		
Characteristics	n	Diagnosed alone RRR (95% CI)§	Obstructive spirometry alone RRR (95% CI)§	Diagnosed and obstructive spirometry RRR (95% CI)§	Diagnosed alone RRR (95% CI)§	Obstructive spirometry alone RRR (95% CI)§	Diagnosed and obstructive spirometry RRR (95% CI)§
Sex							
Females¶	4372	1.00	1.00	1.00	1.00	1.00	1.00
Males	3231	0.49 (0.31 to 0.79)	1.31 (1.16 to 1.49)	2.23 (1.34 to 3.71)	0.52 (0.34 to 0.81)	1.05 (0.90 to 1.23)	2.15 (1.25 to 3.71)
p Value		0.003	<0.001	0.002	0.004	0.543	0.006
Age-group							
40–54¶	3416	1.00	1.00	1.00	1.00	1.00	1.00
55–64	2022	1.26 (0.76 to 2.09)	2.08 (1.76 to 2.46)	4.06 (2.11 to 7.79)	1.34 (0.83 to 2.16)	1.09 (0.90 to 1.33)	2.91 (1.49 to 5.68)
65–74	1451	1.47 (0.84 to 2.55)	3.05 (2.56 to 3.63)	4.78 (2.38 to 9.57)	1.27 (0.74 to 2.15)	1.02 (0.82 to 1.27)	3.12 (1.53 to 6.36)
75+	714	1.95 (0.69 to 5.51)	5.89 (4.76 to 7.29)	7.55 (3.35 to 17.02)	1.60 (0.67 to 3.81)	1.42 (1.08 to 1.87)	3.47 (1.43 to 8.40)
p Value		0.388	<0.001	<0.001	0.535	0.085	<0.001
Pack-years**							
0–0.9¶	4165	1.00	1.00	1.00	1.00	1.00	1.00
1–19.9	1835	1.08 (0.61 to 1.92)	1.67 (1.42 to 1.96)	2.84 (1.30 to 6.23)	1.16 (0.68 to 2.00)	2.02 (1.63 to 2.50)	2.58 (1.10 to 6.01)
20–49.9	1269	3.05 (1.68 to 5.54)	3.18 (2.70 to 3.74)	6.70 (3.35 to 13.40)	2.98 (1.72 to 5.16)	4.23 (3.44 to 5.20)	5.74 (2.70 to 12.20)
50+	334	3.94 (1.70 to 9.13)	4.15 (3.13 to 5.49)	18.50 (8.41 to 40.70)	3.87 (1.81 to 8.29)	6.83 (4.98 to 9.37)	17.23 (7.37 to 40.28)
p Value		<0.001	<0.001	<0.001	<0.001	<0.001	<0.001
NS-SEC**							
Professional¶	3047	1.00	1.00	1.00	1.00	1.00	1.00
Intermediate	1855	0.76 (0.45 to 1.30)	1.20 (1.02 to 1.41)	1.84 (0.87 to 3.87)	0.83 (0.50 to 1.40)	1.19 (0.97 to 1.47)	1.57 (0.72 to 3.44)
Routine	2701	0.93 (0.59 to 1.48)	1.31 (1.12 to 1.53)	3.65 (1.89 to 7.06)	1.08 (0.70 to 1.67)	1.54 (1.27 to 1.87)	3.37 (1.70 to 6.68)
p Value		0.612	0.002	<0.001	0.632	<0.001	<0.001
Sample							
UKHLS¶	5675	1.00	1.00	1.00	1.00	1.00	1.00
HSE	1928	2.38 (1.54 to 3.69)	0.94 (0.81 to 1.09)	1.92 (1.21 to 3.05)	2.21 (1.46 to 3.35)	0.96 (0.79 to 1.16)	2.13 (1.31 to 3.48)
p Value		<0.001	0.420	0.006	<0.001	0.664	0.002

*Participants were included under each relevant definition. Bronchodilators were not used. Cell counts unweighted; RRRs estimated using survey weights.
†FTs: obstruction (FT): FEV_1/FVC <0.7. Diagnosed COPD: HSE: reported diagnosed chronic bronchitis, emphysema, or COPD; UKHLS: diagnosed bronchitis or emphysema.
‡LLN: obstruction (LLN): FEV_1/FVC<LLN. Diagnosed COPD: HSE: reported diagnosed chronic bronchitis, emphysema, or COPD; UKHLS: diagnosed bronchitis or emphysema.
§The RRR is interpreted as the relative risk of one outcome in relation to the reference category for a specified category of an independent variable compared with the reference category for that independent variable. Using diagnosed alone as an example, the RRR for men versus women is interpreted as the relative risk for diagnosed alone versus neither diagnosed nor objective spirometry for men compared with the analogous relative risk for women, adjusted for the other variables in the model.
¶Reference category.
**Missing data: 12/7879 (0.2%) pack-years of cigarette smoking; 265/7879 (3.4%) NS-SEC.
COPD, chronic obstructive pulmonary disease; FEV_1, maximum expiratory volume in 1 s; FTs, fixed thresholds; FVC, forced vital capacity; HSE, Health Survey for England; LLN, lower limit of normal (below the 5th centile of z-scores); NS-SEC, National Statistics Socio-Economic Classification; RRR; relative risk ratios; UKHLS, UK Household Longitudinal Survey.

obstructed airflow, after adjustment for potential confounders, were sensitive to spirometric criteria, being higher among men for FT, compared with no difference using LLN.

Strengths and limitations

Analyses were based on nationally representative samples, with identical measurement protocols and specialist equipment for collecting lung function data. Combining the HSE and UKHLS data sets increased statistical precision for spirometry-based estimates, particularly for population subgroups, and allowed detailed analyses to be conducted. Predicted values and z-scores were obtained from the ERS GLI 2012 reference equations,[28] facilitating inclusion of older participants, non-white populations and comparability with international studies. Our study has a number of limitations. Reversibility in airflow obstruction could not be assessed due to bronchodilators not being used. Spirometry-based prevalence, therefore, may be overestimated. Analysis of the National Health and Nutrition Examination Survey (NHANES) 2007–2010 showed that FT and LLN prevalence estimates among US adults aged 40–79 years decreased, in relative terms, by approximately one-third after administration of bronchodilators.[45] Although recent guidelines from NICE[46] and ERS[13] recommend use of postbronchodilator spirometry to confirm the presence of airflow obstruction, debate continues over its use in epidemiological settings, with the arguments against including ethical issues such as possible side effects and contraindications.[47] Potential misclassification of disease status through bronchodilators not being used was reduced by excluding participants with physician-diagnosed asthma. Some participants in the analytical sample, however, may be undiagnosed asthmatics. On the other hand, the disease burden may be underestimated through excluding participants with poor-quality spirometry. Participation in spirometry, and achievement of good-quality standards among participants with any spirometry data, was higher among participants of younger age, engaged in professional/managerial occupations, non-smokers and with no physician-diagnosed COPD. Lower survey participation rates among sociodemographic groups at higher risk of airflow obstruction (eg, older persons, lower socioeconomic groups) would also have led to an underestimation of true prevalence. These limitations, however, are unlikely to affect comparisons across definitions, but may have led to an underestimate of risk associations. The list of health conditions in the UKHLS interview programme included chronic bronchitis and emphysema but not COPD, leading to potential underestimation of self-reported physician-diagnosed COPD.

Comparisons with previous studies

Earlier analyses of HSE data[36 38 48] used older reference equations[49 50] applicable only to white, younger populations. Nevertheless, estimates of prevalence and their substantive conclusions of higher prevalence using FT versus LLN, with a widening gap in prevalence in older age groups, and sex differences when using FT but not LLN were similar to ours: confirming findings reported in the USA,[45] Europe,[51] Korea,[16] internationally,[12] and in recent literature reviews.[6 52] A further strength of our study was the wide range of clinically relevant conditions examined in the context of disease staging, with higher prevalence of respiratory symptoms, respiratory and cardiovascular diseases, breathlessness and poor self-rated health among participants in the tightest definitions of FT and LLN obstruction, confirming similar findings in the USA.[53 54] While recent guidelines[13 46 55] recommend adopting multidimensional definitions of respiratory disease, our study outcomes were defined only using spirometry. While we acknowledge the merits of a multidimensional approach, and agree that neither spirometric cut-off is able to fully characterise the complex diagnostic features of COPD,[56] our primary aim was to use up-to-date survey data to evaluate differences in prevalence according to FT and LLN thresholds, to provide baseline data for monitoring purposes in the UK, and promote comparability with international studies. Current recommendations regarding symptom criteria are less specific than those for spirometry. We chose, therefore, to examine the associations between disease staging assessed only using spirometry and presence of respiratory symptoms, rather than broaden the definition of disease.

Implications

Recent UK studies used administrative primary care databases to report the number of diagnosed and treated patients, thereby missing undiagnosed cases. Such studies have reported prevalence below 2%.[57 58] The disparity in prevalence from clinical versus epidemiological studies led to the development of the COPD prevalence model, with the HSE 2001 used as input data, to more accurately estimate prevalence.[59] In accordance with previous NICE recommendations,[44] COPD is currently defined in the model as FT stage II+ (FEV_1/FVC <0.7 and FEV_1 <80% of predicted), with the logistic regression models showing sharp increases with age and a modifying effect of gender.[60 61] Similar to the findings reported by Jordan *et al*,[36] our study shows that the strength of association between risk factors and airflow obstruction varies according to spirometric criterion, with age and sex differences in risk being more marked for FT, and for FT stage II+, than LLN. In the absence of agreement among experts, policymakers, clinicians and researchers building the COPD epidemiological database, it is important to appreciate the sensitivity of estimates of the disease burden, and its distribution across sociodemographic groups, to differences in methods, including spirometric cut-offs.

The prevalence of reported physician-diagnosed COPD in our study was 2.8%, considerably lower than spirometry-based estimates, possibly indicating considerable under-recognition by participants and physicians. Using the tightest definitions, prevalence of physician-diagnosed COPD among participants with obstructive spirometry was 30.2% (FT stage III+) and 14.7% (LLN stage II). Similar low rates of physician diagnosis among participants meeting spirometric criteria have been reported in New Zealand.[62] Spirometrically defined airflow obstruction but no diagnosed COPD does not necessarily indicate underdiagnosis. Definitive diagnosis requires further information on all relevant clinical factors, particularly respiratory symptoms and smoking history, as well as postbronchodilator spirometry.

CONCLUSION

In summary, we have enhanced the COPD epidemiological database by evaluating the impact of different definitions on the prevalence of potential airflow obstruction and its associations with key risk factors and comorbidities. With no gold standard currently available, longitudinal studies examining differences in unscheduled hospital admissions and risk of death between FT and LLN may inform the choice as to the best way to include spirometric data in multidimensional assessments of airflow obstruction in clinical and epidemiological settings.

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Competing interests None.

Ethics approval Ethical approval for collecting biosocial data in UKHLS was obtained from the Oxfordshire A Research Ethics Committee (10/H0604/2); approval for HSE 2010 was obtained from the Oxfordshire B Research Ethics Committee (09/H0605/73).

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Data sharing statement Both datasets are available via the UK Data Service (http://www.ukdataservice.ac.uk). Statistical code is available from the corresponding author at s.scholes@ucl.ac.uk.

REFERENCES

1. Mannino DM, Buist AS. Global burden of COPD: risk factors, prevalence, and future trends. *Lancet* 2007;370:765–73.
2. Raherison C, Girodet PO. Epidemiology of COPD. *Eur Respir Rev* 2009;18:213–21.
3. Lozano R, Naghavi M, Foreman K, *et al*. Global and regional mortality from 235 causes of death for 20 age groups in 1990 and 2010: a systematic analysis for the Global Burden of Disease Study 2010. *Lancet* 2012;380:2095–128.
4. Department of Health. An Outcomes Strategy for COPD and asthma: NHS Companion Document. 2012. https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/216139/dh_128428.pdf
5. Atsou K, Chouaid C, Hejblum G. Variability of the chronic obstructive pulmonary disease key epidemiological data in Europe: systematic review. *BMC Med* 2011;9:7.
6. Rycroft CE, Heyes A, Lanza L, *et al*. Epidemiology of chronic obstructive pulmonary disease: a literature review. *Int J Chron Obstruct Pulmon Dis* 2012;7:457–94.
7. McLean S, Wild SH, Simpson CR, *et al*. Models for estimating projections for the prevalence and disease burden of chronic obstructive pulmonary disease (COPD): systematic review protocol. *Prim Care Respir J* 2013;22:S8–21.
8. Salvi SS, Manap R, Beasley R. Understanding the true burden of COPD: the epidemiological challenges. *Prim Care Respir J* 2012;21:249–51.
9. Pauwels RA, Buist AS, Calverley PM, *et al*. Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease. NHLBI/WHO Global Initiative for Chronic Obstructive Lung Disease (GOLD) Workshop summary. *Am J Respir Crit Care Med* 2001;163:1256–76.
10. Miller MR, Hankinson J, Brusasco V, *et al*. Standardisation of spirometry. *Eur Respir J* 2005;26:319–38.
11. Miller MR, Quanjer PH, Swanney MP, *et al*. Interpreting lung function data using 80% predicted and fixed thresholds misclassifies more than 20% of patients. *Chest* 2011;139:52–9.
12. Swanney MP, Ruppel G, Enright PL, *et al*. Using the lower limit of normal for the FEV1/FVC ratio reduces the misclassification of airway obstruction. *Thorax* 2008;63:1046–51.
13. Bakke PS, Ronmark E, Eagan T, *et al*. Recommendations for epidemiological studies on COPD. *Eur Respir J* 2011;38:1261–77.
14. Hansen JE, Sun XG, Wasserman K. Spirometric criteria for airway obstruction: use percentage of FEV1/FVC ratio below the fifth percentile, not < 70%. *Chest* 2007;131:349–55.
15. Roberts SD, Farber MO, Knox KS, *et al*. FEV1/FVC ratio of 70% misclassifies patients with obstruction at the extremes of age. *Chest* 2006;130:200–6.
16. Hwang YI, Kim CH, Kang HR, *et al*. Comparison of the prevalence of chronic obstructive pulmonary disease diagnosed by lower limit of normal and fixed ratio criteria. *J Korean Med Sci* 2009;24:621–6.
17. Quanjer PH, Cole TJ. COPD and GOLD stage I. *Chest* 2012;141:1122.
18. Enright P, Brusasco V. Counterpoint: should we abandon FEV(1)/FVC <0.70 to detect airway obstruction? Yes. *Chest* 2010;138:1040–2.
19. Quanjer PH, Enright PL, Miller MR, *et al*. The need to change the method for defining mild airway obstruction. *Eur Respir J* 2011;37:720–2.
20. Celli BR, Halbert RJ. Point: should we abandon FEV(1)/FVC <0.70 to detect airway obstruction? No. *Chest* 2010;138:1037–40.
21. Falaschetti E, Swanney MP, Crapo RO, *et al*. Diagnosis of COPD. *Thorax* 2007;62:924–5.
22. Halbert RJ, Natoli JL, Gano A, *et al*. Global burden of COPD: systematic review and meta-analysis. *Eur Respir J* 2006;28:523–32.
23. Mindell J, Biddulph JP, Hirani V, *et al*. Cohort profile: the health survey for England. *Int J Epidemiol* 2012;41:1585–93.
24. Joint Health Surveys Unit. The Health Survey for England 2010, Volume 1: Respiratory Health. In: Craig R, Mindell J. eds. *Respiratory health*. Leeds: NHS Information Centre, 2011. http://www.hscic.gov.uk/pubs/hse10report
25. Joint Health Surveys Unit. *The Health Survey for England 2010, Volume 2: Methods and Documentation*. Leeds: The Information Centre for Health and Social Care, 2011. http://www.hscic.gov.uk/catalogue/PUB03023/heal-surv-eng-2010-resp-heal-vol2-meth-rep.pdf
26. Lynn P. Sample design for Understanding Society. Understanding Society Working Paper Series: 2009-01. https://www.understandingsociety.ac.uk/research/publications/working-paper/understanding-society/2009-01.pdf
27. McFall SL, Petersen J, Kaminska O, *et al*. *Understanding Society—The UK Household Longitudinal Study: Waves 2 and 3 Nurse Health Assessment, 2010–2012 Guide to Nurse Health Assessment*. Colchester: University of Essex, 2012. https://www.understandingsociety.ac.uk/d/100/7251_User_Guide_Health_Assmt_w2_w3.pdf?1392855567
28. Quanjer PH, Stanojevic S, Cole TJ, *et al*. Multi-ethnic reference values for spirometry for the 3–95-yr age range: the global lung function 2012 equations. *Eur Respir J* 2012;40:1324–43.

29. Quanjer PH, Brazzale DJ, Boros PW, *et al*. Implications of adopting the Global Lungs Initiative 2012 all-age reference equations for spirometry. *Eur Respir J* 2013;42:1046–54.
30. Hall GL, Thompson BR, Stanojevic S, *et al*. The Global Lung Initiative 2012 reference values reflect contemporary Australasian spirometry. *Respirology* 2012;17:1150–1.
31. Rabe KF, Hurd S, Anzueto A, *et al*. Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease: GOLD executive summary. *Am J Respir Crit Care Med* 2007;176:532–55.
32. COPD Guidelines Group of the Standards of Care Committee of the BTS. BTS guidelines for the management of chronic obstructive pulmonary disease. The COPD Guidelines Group of the Standards of Care Committee of the BTS. *Thorax* 1997;52 5):S1–28.
33. Ferguson GT, Enright PL, Buist AS, *et al*. Office spirometry for lung health assessment in adults: a consensus statement from the National Lung Health Education Program. *Chest* 2000;117:1146–61.
34. Vaz Fragoso CA, Concato J, McAvay G, *et al*. The ratio of FEV1 to FVC as a basis for establishing chronic obstructive pulmonary disease. *Am J Respir Crit Care Med* 2010;181:446–51.
35. Centers for Disease Control and Prevention (CDC). Deaths from chronic obstructive pulmonary disease—United States, 2000–2005. *MMWR Morb Mortal Wkly Rep* 2008;57:1229–32.
36. Jordan RE, Miller MR, Lam KB, *et al*. Sex, susceptibility to smoking and chronic obstructive pulmonary disease: the effect of different diagnostic criteria. Analysis of the Health Survey for England. *Thorax* 2012;67:600–5.
37. Bhatt SP, Sieren JC, Dransfield MT, *et al*. Comparison of spirometric thresholds in diagnosing smoking-related airflow obstruction. *Thorax* 2014;69:409–14.
38. Jordan RE, Cheng KK, Miller MR, *et al*. Passive smoking and chronic obstructive pulmonary disease: cross-sectional analysis of data from the Health Survey for England. *BMJ Open* 2011;1:e000153.
39. Woodward M. *Epidemiology study design and data analysis*. 2nd edn. Boca Raton, FL: Chapman & Hall/CRC, 2004.
40. Loong TW. Understanding sensitivity and specificity with the right side of the brain. *BMJ* 2003;327:716–9.
41. Rabe-Hesketh S, Skrondal A. *Multilevel and longitudinal modeling using Stata: volume II: categorical responses, counts, and survival*. 3rd edn. Stata Press, 2012.
42. UCLA Statistical Consulting Group. Multinomial Logistic Regression. http://www.ats.ucla.edu/stat/stata/dae/mlogit.htm
43. Hill K, Goldstein RS, Guyatt GH, *et al*. Prevalence and underdiagnosis of chronic obstructive pulmonary disease among patients at risk in primary care. *CMAJ* 2010;182:673–8.
44. Chronic obstructive pulmonary disease. National clinical guideline on management of chronic obstructive pulmonary disease in adults in primary and secondary care. *Thorax* 2004;59(Suppl 1):1–232.
45. Tilert T, Dillon C, Paulose-Ram R, *et al*. Estimating the U.S. prevalence of chronic obstructive pulmonary disease using pre- and post-bronchodilator spirometry: the National Health and Nutrition Examination Survey (NHANES) 2007–2010. *Respir Res* 2013;14:103.
46. National Institute for Health and Care Excellence (NICE). Chronic obstructive pulmonary disease: management of chronic obstructive pulmonary disease in adults in primary and secondary care. 2010. http://www.nice.org.uk/Guidance/CG101.
47. Quanjer PH, Stanojevic S, Swanney MP, *et al*. Recommendations for epidemiological studies on COPD. *Eur Respir J* 2012;39:1277–8.
48. Shahab L, Jarvis MJ, Britton J, *et al*. Prevalence, diagnosis and relation to tobacco dependence of chronic obstructive pulmonary disease in a nationally representative population sample. *Thorax* 2006;61:1043–7.
49. Quanjer PH, Tammeling GJ, Cotes JE, *et al*. Lung volumes and forced ventilatory flows. Report Working Party Standardization of Lung Function Tests, European Community for Steel and Coal. Official Statement of the European Respiratory Society. *Eur Respir J Suppl* 1993;16:5–40.
50. Falaschetti E, Laiho J, Primatesta P, *et al*. Prediction equations for normal and low lung function from the Health Survey for England. *Eur Respir J* 2004;23:456–63.
51. Maio S, Sherrill DL, MacNee W, *et al*. The European Respiratory Society spirometry tent: a unique form of screening for airway obstruction. *Eur Respir J* 2012;39:1458–67.
52. Mohamed Hoesein FA, Zanen P, Lammers JW. Lower limit of normal or FEV1/FVC <0.70 in diagnosing COPD: an evidence-based review. *Respir Med* 2011;105:907–15.
53. Mannino DM, Thorn D, Swensen A, *et al*. Prevalence and outcomes of diabetes, hypertension and cardiovascular disease in COPD. *Eur Respir J* 2008;32:962–9.
54. Ford ES, Wheaton AG, Mannino DM, *et al*. Elevated cardiovascular risk among adults with obstructive and restrictive airway functioning in the United States: a cross-sectional study of the National Health and Nutrition Examination Survey from 2007–2010. *Respir Res* 2012;13:115.
55. Vestbo J, Hurd SS, Agusti AG, *et al*. Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease: GOLD executive summary. *Am J Respir Crit Care Med* 2013;187:347–65.
56. Clini EM, Crisafulli E, Roca M, *et al*. Diagnosis of chronic obstructive pulmonary disease, simpler is better. Complexity and simplicity. *Eur J Intern Med* 2013;24:195–8.
57. Haughney J, Gruffydd-Jones K, Roberts J, *et al*. The distribution of COPD in UK general practice using the new GOLD classification. *Eur Respir J* 2014;43:993–1002.
58. Simpson CR, Hippisley-Cox J, Sheikh A. Trends in the epidemiology of chronic obstructive pulmonary disease in England: a national study of 51 804 patients. *Br J Gen Pract* 2010;60:277–84.
59. Walford H, Ramsey L. COPD Prevalence Modelling Briefing Document. 2011. http://www.apho.org.uk/resource/view.aspx?RID=111137
60. Nacul LC, Soljak M, Meade T. Model for estimating the population prevalence of chronic obstructive pulmonary disease: cross sectional data from the Health Survey for England. *Popul Health Metr* 2007;5:8.
61. Nacul L, Soljak M, Samarasundera E, *et al*. COPD in England: a comparison of expected, model-based prevalence and observed prevalence from general practice data. *J Public Health (Oxf)* 2011;33:108–16.
62. Shirtcliffe P, Weatherall M, Marsh S, *et al*. COPD prevalence in a random population survey: a matter of definition. *Eur Respir J* 2007;30:232–9.

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Notes