Online supplement

Undiagnosed and over-diagnosed COPD using post-bronchodilator spirometry in primary healthcare settings: a systematic review and meta-analysis

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Methods S1. Search strategy

Found at PROSPERO registration CRD42022295832

MEDLINE (OVID) and Embase were searched systematically including MeSh terms/keywords “COPD”, "Diagnostic errors", “under-diagnosis”, “over-diagnosis” and “mis-diagnosis”.

Database 1:

Embase Classic+Embase <1947 to 2022 January 04>

exp chronic obstructive lung disease/ or obstructive airway disease/
(COPD or chronic obstructive lung disease* or chronic obstructive pulmonary disease* or COAD or chronic obstructive airway disease* or airflow obstruction, chronic or Airflow Obstructions, Chronic or Chronic Airflow Obstruction* or pulmonary disease, chronic obstructive).tw,kw.
1 or 2
exp diagnostic error/ or exp false negative result/ or exp false positive result/ or exp missed diagnosis/
(misdiagnos* or underdiagnos* or under-diagnos* or overdiagnos* or over- diagnos* or mis-diagnos*).tw,kw.
4 and 5
3 and 6
limit 7 to "humans only (removes records about animals)"

Database 2:

Ovid MEDLINE(R) UI_04.20.01.001 and Epub Ahead of Print, In-Process, In-Data-Review & Other Non-Indexed Citations and Daily <1946 to January 04, 2022>

pulmonary disease, chronic obstructive/ or asthma-chronic obstructive pulmonary disease overlap syndrome/ or bronchitis, chronic/ or pulmonary emphysema/
(COPD or chronic obstructive lung disease* or chronic obstructive pulmonary disease* or COAD or chronic obstructive airway disease* or airflow obstruction, chronic or Airflow Obstructions, Chronic or Chronic Airflow Obstruction* or pulmonary disease, chronic obstructive).tw,kf.
1 or 2
Diagnostic Errors/
(misdiagnos* or underdiagnos* or under-diagnos* or overdiagnos* or over- diagnos* or mis-diagnos*).tw,kf.
4 or 5
3 and 6
limit 7 to "humans only (removes records about animals)"

Results S1. Data extraction table – adults in general ≥40 years

Table S1. Undiagnosed COPD§ and its over-diagnosis using post-BD spirometry: cross-sectional studies in primary healthcare setting

Author year citation		**Study name Location**	**Participant Number† (%eligible‡), Sampling, Selection, Number/type of GP practices**	**Gender Age [mean (SD) years]**	**Prevalence of spirometrically-defined COPD [%, (n/N)] §**		**Underdiagnosis in COPD sub-population [%, (n/N)] §**	**Undiagnosed COPD in studied population [%, (n/N)] *§**		**Overdiagnosis in population labelled with COPD [%, (n/N)] §**
Utsugi et al. 2016 [1]		NW Tokyo, Japan	N=950 (98.0%) Consecutive adults 40-75 years without prior lung disease; 13 urban GP clinics	49.5% male 64.9 (8.7) years	12.7% (121/950)		□	12.7% (121/950)		NA
Weiss, G et al. 2014 [2]		Salzburg, Austria	N=775 (7.9%) Adults >40 years old attending 30 randomly selected GP clinics	41.8% male 58.5 (0.4) years	16.8% (130/775) ‖		90% (117/130) ‖	15.1% (117/775) ‖		76.8% (43/56) GOLD Stage II-IV
Siatkowska, H et al. 2010 [3]		Bytom district Poland	N=1,026 (41.8%) Convenience; Adults ≥18 years Single GP clinic at the Mining Complex of "Unia Bracka" Foundation	48% male 48.8 (16.3) years (68.5% >40y)	6.0% (62/1026) 8.1% (n=57) if >40 years)		95.2% (59/62) ‖	5.75% (59/1026) ‖		NA
Bednarek, M et al. 2008 [4]		Sierpc, Poland	N=1960 (87.1%) Consecutive Adults >40 years Single GP practice (urban/rural)	39.0% males 56.7 (12) years	9.3% (183/1960) §		81.4% (149/183) §‖	7.6% (149/1960) §‖		NA

Definitions of abbreviations: COPD, Chronic obstructive pulmonary disease; GOLD, Global Initiative for Chronic Obstructive Lung Disease; GP, general practitioner; LLN, lower limit of normal at the 5th percentile; NA, not available; SD, standard deviation

§ Spirometrically-defined COPD using the GOLD criterion of post-bronchodilator forced expiratory ratio <0.70, except for one study that solely used the LLN.[4]

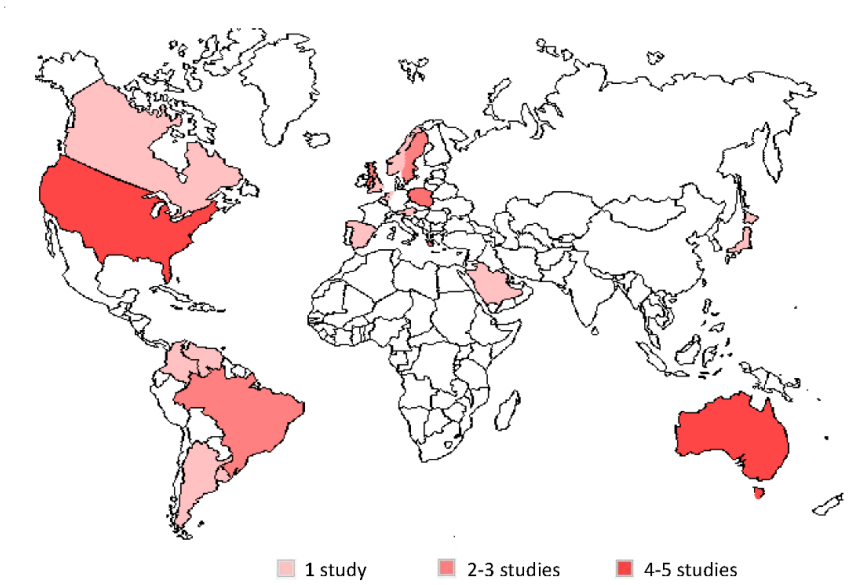
‡ All % eligible figures were calculated, except when mentioned in the discussion text by Tinkelman et al.[5]

□ Percentage undiagnosed in the COPD sub-population was 100% as the population excluded patients with a history of COPD (1 of total of 7 studies)

‖ Data needed to be deduced and calculated from the figures given (by the present authors). Calculations not shown but available upon request

Results S2. Description of included studies

Figure S1. Map of countries from which data has been sourced for this systematic review.



Numbers include countries that comprised studies of mixed origin (n=2)

Figure S2. Descriptive features for all studies (n=26), by risk category

Author, year	Continent	Country	Diagnosis	Criterion	Sample_size
Case series					
Fisk, 2019	Europe	Wales	GP records	GOLD	Adequate
Ghattas, 2013	North America	United States	GP records	GOLD	Inadequate
Walters, 2011	Australia/Oceania	Australia	GP records	GOLD	Adequate
Zwar, 2011	Australia/Oceania	Australia	GP records	GOLD	Adequate
Sichletidis, 2007	Europe	Greece	GP records	GOLD	Adequate
Smokers with symptoms					
Liang, 2018	Australia/Oceania	Australia	GP records	GOLD	Adequate
Lokke, 2012	Europe	Scandinavia	GP records	GOLD	Adequate
Sandelowsky, 2011	Europe	Sweden	GP records	GOLD	Inadequate
Yawn, 2009	North America	United States	GP records	GOLD	Adequate
Smoking per se					
Stafyla, 2018	Europe	Greece	Self-reported	GOLD	Inadequate
Herrera, 2016	South America	South America	Self-reported	LLN/ GOLD	Adequate
Llordes, 2015	Europe	Spain	Self-reported	GOLD	Adequate
De Queiroz, 2012	South America	Brazil	Self-reported	GOLD	Adequate
Al Ghobain, 2011	Asia	Saudi Arabia	GP records	GOLD	Adequate
Hill, 2010	North America	Canada	Self-reported	GOLD	Adequate
Tinkelman, 2007	North America	Scotland & US	Self-reported	GOLD	Adequate
Any adult >40y					
Utsugi, 2016	Asia	Japan	GP records	GOLD	Adequate
Weiss, 2014	Europe	Austria	Self-reported	GOLD	Adequate
Siatkowska, 2010	Europe	Poland	GP records	GOLD	Adequate
Bednarek, 2008	Europe	Poland	Self-reported	LLN	Adequate
Inhalers incl. asthma					
Abramson, 2012	Australia/Oceania	Australia	GP records	GOLD	Adequate
Tinkelman, 2006	North America	Scotland & US	Self-reported	GOLD	Adequate
Asthma-COPD register					
Melbye, 2011	Europe	Norway	GP records	GOLD	Adequate
Medium-high COPD-risk					
Dirven, 2010	Europe	Netherlands	GP records	GOLD	Inadequate
Symptoms-risk factors					
Frank, 2006	Europe	England	GP records	GOLD	Adequate
Hamers, 2006	South America	Brazil	GP records	GOLD	Inadequate

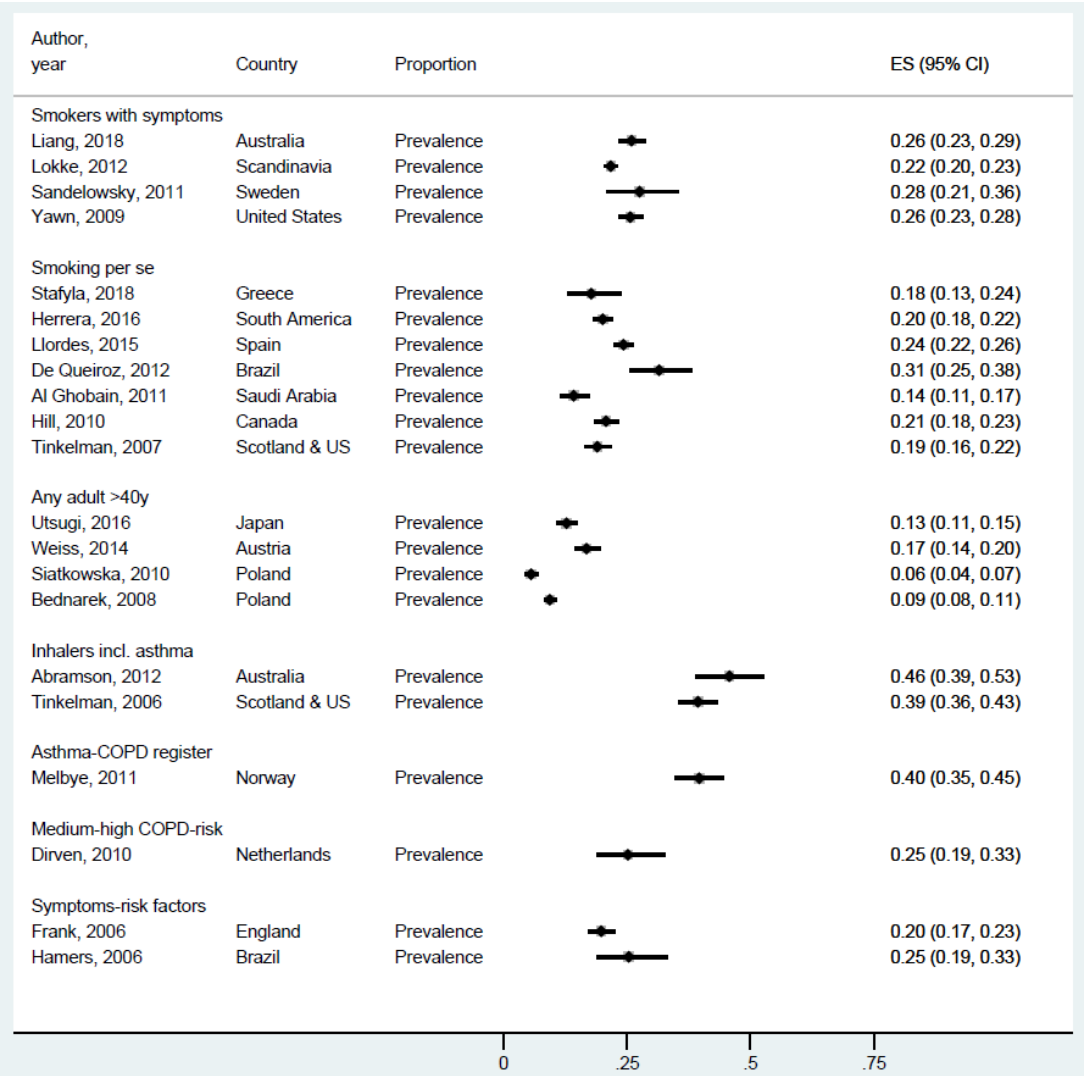
Note: The term "GP records" refer to the health records used in a variety of general practice, family health, and community health settings

For the cross-sectional prevalence studies, the health record was used to establish the diagnosis made by the treating clinician for all studies investigating symptomatic smokers (n=4) [6-9], adults with respiratory symptoms regardless of smoking (n=2) [10, 11], patients from an asthma/COPD register (n=1) [12] or determined to be medium-to-high COPD risk based on a screening questionnaire [13] (n=1). Conversely, the participants nominated themselves as having physician-diagnosed COPD in all [14-19] but one study of smokers regardless of symptoms [20] (n=7), with a mixture of health record or patient-reported diagnoses for the categories of any adult ≥ 40 years (n=4) [1-4] and inhaler-use including asthma (n=2) [5, 21]. For the case series (n=5), all PHC clinics used their health records to identify suitable patients who had been diagnosed and/or managed as having COPD.[22-26]

The studies calculated to have inadequate numbers undergoing post-BD spirometry to confidently calculate COPD prevalence in the population sample were roughly spread between study type and risk category (n=5, see Figure S4 and sample size calculations on pages 19-20).[8, 11, 13, 14, 23] These studies were included in the tables but not the Forest plots after the sensitivity analyses.

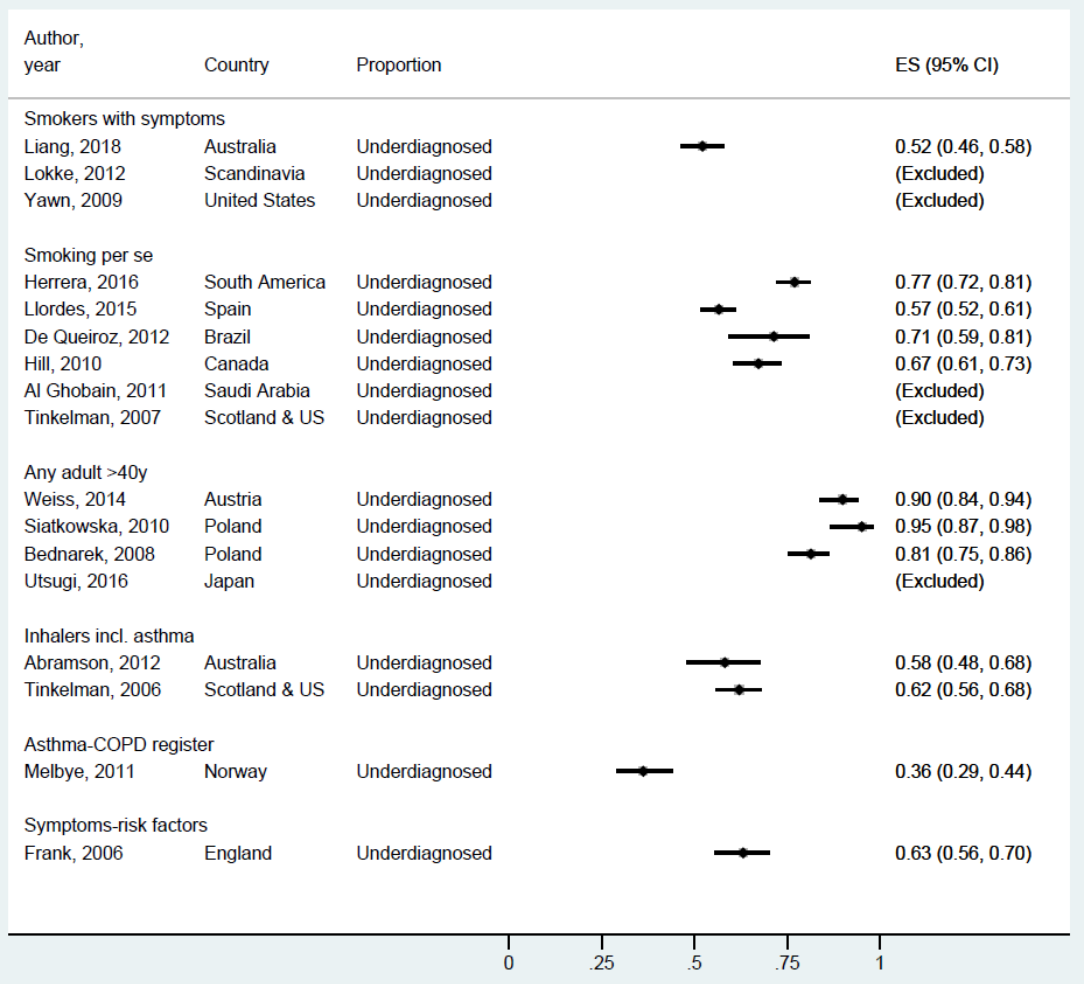
Results S3. Additional forest plots and descriptions of characteristics

Figure S3. Prevalence of spirometrically-defined COPD (ES) by risk category: cross-sectional studies



The cross-sectional prevalence studies calculated to have insufficient numbers of participants undergoing post-BD spirometry to accurately estimate COPD prevalence were spread quite evenly between study type and risk category (n=4, see sample size calculations in Results S4, page 17).[8, 11, 13, 14, 23] These 4 studies by Sandelowsky et al., Stafyla et al., Dirven et al., and Hamers et al. did not appear to be outliers in terms of COPD prevalence in their population studied.

Figure S4. Undiagnosed COPD but only amongst those with spirometrically-defined COPD (i.e. COPD underdiagnosis ES) by risk category: cross-sectional prevalence studies



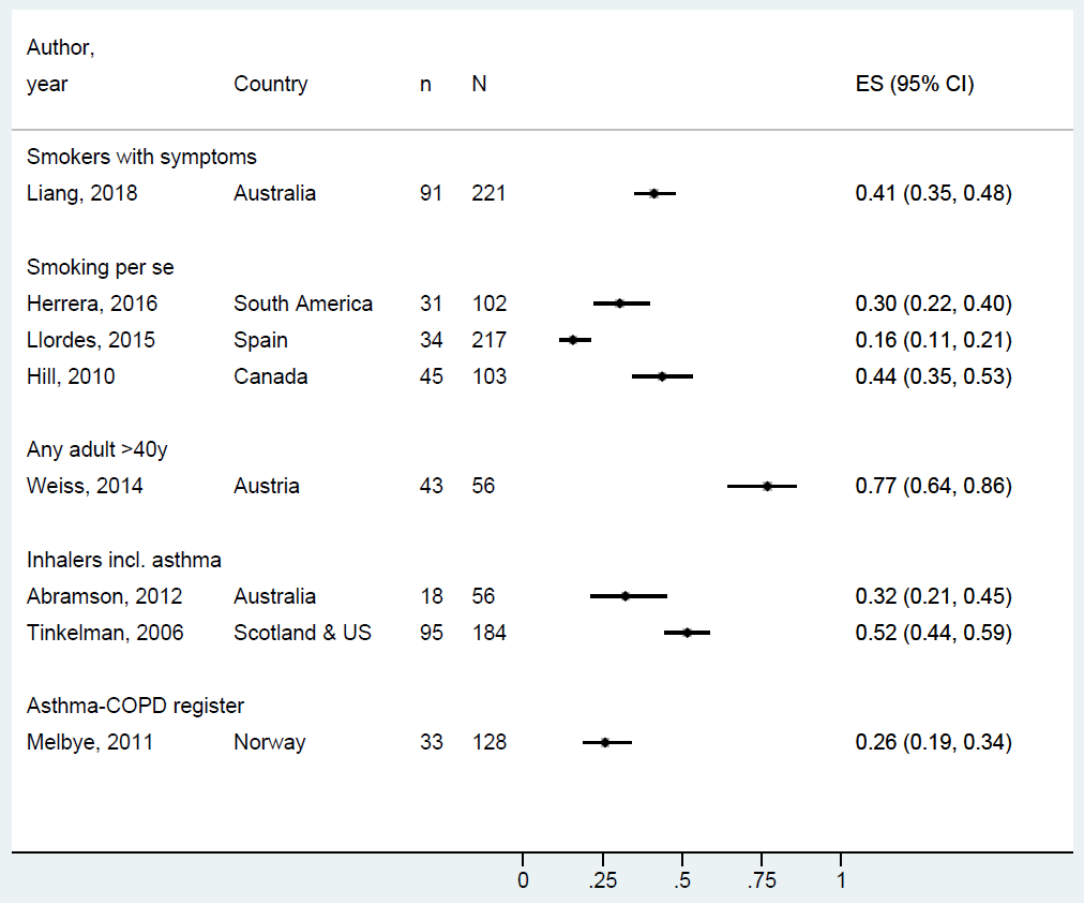
Among cross-sectional studies with adequate sample size, five intentionally did not recruit patients with a prior medical labelled diagnosis of COPD and/or lung disease so were automatically omitted from the Figure given 100% of cases of spirometrically-defined COPD were newly detected [7, 9, 19, 20]. PHC populations of adults >40 years with a relatively low overall COPD prevalence (6.0-16.8%) had a relatively high proportion with COPD under-diagnosis (between 81-95%, Table-S1). In contrast, a somewhat higher estimated 37-48% of symptomatic adults who had COPD confirmed in studies by post-BD spirometry had the diagnosis entered in their medical records (i.e., 52-63% were still under-diagnosed). Similarly, 38-42% of subjects taking inhalers for obstructive lung diseases and 63.8% of Norwegian subjects listed on an asthma-COPD registry who were found to have airflow obstruction on post-BD spirometry by researchers, were currently labelled as having COPD (i.e., 58-62% and 36.2% were under-diagnosed, respectively).

Table S2. Undiagnosed COPD in primary healthcare settings: characteristics

Author year citation	Study design	Study name Location	Characteristics for those underdiagnosed
Liang, J et al. [2018]	CS	RADICALS study Australia	Younger age; current smokers; less symptomatic (mMRC, SGRQ); milder disease (better FEV_1/FVC) (p <0.001)
Stafyla, E et al. [2018]	CS	Thessaly, Central Greece	Younger patients; current smokers; fewer symptoms (mMRC ≥2 and total CCQ); not COPD stage or group
Herrera, A.C et al. [2016]	CS	PUMA study (PLATINO) 4 countries South America	Afro-Latin Americans; those obese; less severe airflow obstruction; no previous exacerbations; no GP visit in the past year; saw GP but not the specialist; no dyspnoea/ wheeze (univariable)
Utsugi et al. [2016]	CS	NW Tokyo, Japan	Predominantly men (19.1 versus 6.5%); older adults, higher pack-years (p<0.001)
Abramson, M.J. et al. [2012]	CS §	SPIRO-GP, VIC Australia	Qualitative review suggests some GPs use spirometry as a smoking cessation aid rather than for diagnosing COPD; influenced by funding arrangements and time constraints
De Queiroz, M,C et al. [2012]	CS	Brazil, South America	Fewer symptoms (less expectoration, wheezing, dyspnoea and activity limitation (MRC score)); males and higher FEV_1 and FEV_1/FVC did not reach statistical significance
Lokke, A et al. [2012]	CS	Denmark, Sweden	Female, younger age, higher BMI, less symptomatic, fewer pack-years (not smoking status)
Hill, K et al. [2010]	CS	Ontario CAN	Less likely to have ≥2 respiratory symptoms (39% vs 74%); been prescribed respiratory medication (39% vs 88%) and to have undergone previous spirometry (27% vs 85%)

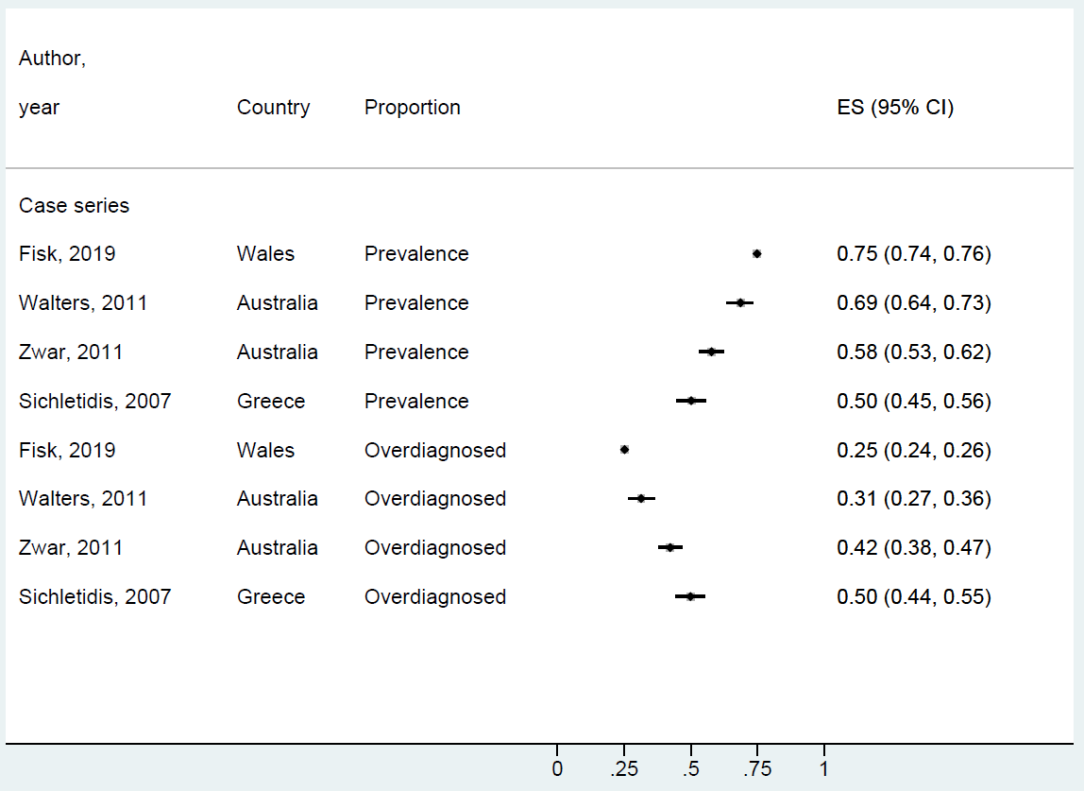
Definitions of abbreviations: ACO, asthma-COPD overlap; CCQ, clinical COPD questionnaire; COPD, Chronic obstructive pulmonary disease; CS, cross-sectional prevalence study; MRC, Medical Research Council dyspnoea score; mMRC, modified MRC dyspnoea score; OLDs, obstructive lung diseases; PC, primary care; SGRQ, St Georges Respiratory Questionnaire (50-items)

Figure S5. COPD over-diagnosis among those with doctor-labelled COPD (ES) by risk category: cross-sectional prevalence studies



A pooled estimate was not reported as the degree of heterogeneity (I-squared) for each subgroup was >75% and/or the 95% confidence intervals of all studies within a risk category did not clearly overlap. The abbreviation 'N' refers to the number of participants in the study with doctor-labelled COPD.

Figure S6. Prevalence of spirometrically-defined COPD and overdiagnosis of doctor-labelled COPD: case series



Of 5 COPD case series, those with adequate participant numbers to estimate the prevalence of spirometrically-defined COPD in their studied population who underwent spirometry testing have been included in this sensitivity analysis (n=4).

Table S3. "Over-diagnosed" COPD in primary healthcare settings: characteristics

Author year citation	Study design	Study name Location	Characteristics for those over-diagnosed
Fisk et al. [2019]	Case series	Welsh COPD Primary Care Audit, UK	More likely to be female, overweight; have asthma-ever; be a never smoker; be coded as having mild (compared with mod-severe) COPD, bronchitis or emphysema
Abramson, M.J. et al. [2012]	CS §	SPIRO-GP, VIC Australia	Qualitative review suggests that some GPs may be overconfident in their diagnostic skills, influenced by funding arrangements and time constraints
Zwar, N.A et al. [2011]	Case series §	PELICAN study, NSW Australia	Younger patients; higher number of co-morbidities; having a practice manager (but not nurse) was protective
Walters, J.A et al. [2011]	Case series	TAS Australia	Younger patients; those less likely to be breathless and have activity limitation (MRC, BDI and SGRQ); currently employed; overweight; with allergic rhinitis/hay fever
Hill, K et al. [2010]	CS	Ontario CAN	Patients over-diagnosed had fewer respiratory symptoms
Tinkelman, D.G et al. [2006]	CS	Aberdeen UK and Denver US	Those over-diagnosed were prescribed less respiratory medication than those with true COPD/ACO (6.9% compared with 22.5%)

Definitions of abbreviations: ACO, asthma-COPD overlap; BDI, baseline dyspnoea index; COPD, Chronic obstructive pulmonary disease; CS, cross-sectional prevalence study; GP, general practitioner

§ Data are from the cross-sectional baseline assessment of a cluster randomized controlled trial prior to randomization

Results S4. Risk of bias assessment

Description of items – JBI checklist for prevalence studies

- Appropriate sample frame
    - Large number of urban GP practices, or smaller number of urban/rural GP practices
- Appropriate sampling
    - All subjects of sampling frame were included or random probabilistic sampling of a defined subset
    - If used, clustering sampling has been specified
    - Not a convenience sample
- Adequate sample size
    - Large national survey
    - Sample size calculation [n=(z^2p(1-p))/d^2], for 10% prevalence and 95% confidence (1.96^2*0.1*0.9)/0.0225^2
- Sufficient subject and setting details
- Minimal coverage bias
    - Approximate response rates across all subgroups
- Minimal measurement or classification bias (valid methods)
    - Outcomes assessed based on existing definitions or diagnostic criteria or validated tools
    - Not observer reported or self-reported scales for the outcome
- Reliable measurement
    - Trained staff collecting data; quality control by pulmonologist; same protocols
- Appropriate statistical analysis
    - Percentages given with confidence intervals (yellow if absent)
    - Numerator and denominator clearly reported
- Adequate response rate
    - Modest number of dropouts / refusals (>10% participation for random sampling; >70% non-random non-convenience samples)
    - Plus either
        - discussion about response rate and reasons for non-response
        - [if low] comparison of sociodemographic characteristics between those participating and non-participating (// coverage bias)

Table S4. Risk of bias – cross-sectional prevalence studies

Cross-sectional studies	Sample frame appropriate?	Study sampling appropriate?	Sample size adequate?	Subjects and settings details?	Analysis of sufficient coverage?	Valid identification methods?	Condition measured reliably?	Statistical results appropriate?	Response rate adequate?
Liang et al. 2018 [6]					n/a				
Melbye et al. 2011 [12]									
Hamers et al. 2006 [11]									
Weiss et al. 2014 [2]									
Utsugi et al. 2016 [1]									
Dirven et al. 2010 [13]									
Hill et al. 2010 [18]									
Herrera et al. 2016 [15]									
Bednarek et al. 2008 [4]									
Frank et al. 2006 [10]									
Al Ghobain et al. 2011 [20]									
De Queiroz et al. 2012 [17]									
Stafyla et al. 2018 [14]									
Siatkowska et al. 2010 [3]									
Tinkelman et al. 2006 [5]					n/a				
Tinkelman et al 2007 [19]					n/a				
Yawn et al. 2009 [9]									
Abramson et al. 2012 [21]									
Lokke et al. 2012 [7]									
Llordes et al. 2015 [16]									
Sandelowsky et al. 2011 [8]									
Key: Green = yes; Red = no; Yellow = unclear or intermediate									

Table S5. Risk of bias – COPD case series

COPD case series	Clear inclusion criteria?	Condition measured reliably?	Valid identification methods?	Consecutive inclusion?	Complete inclusion?	Clear demographic reporting?	Clear clinical information?	Clear setting / population details?	Statistical results appropriate?
Fisk et al. 2019 [22]									
Ghattas et al. 2013 [23]									
Zwar et al. 2011 [25]					n/a				
Walters et al. 2011 [24]					n/a				
Sichletidis et al. 2007 [26]					n/a				
Key: Green = yes; Red = no; Yellow = unclear or intermediate									

For prevalence studies (Table S3), all eligible studies used valid "gold standard" identification methods, i.e., post-bronchodilator spirometry, and also appropriate definitions and population-specific reference values, although one used non-contemporary reference equations [3, 27]. However, the overall quality of the studies was moderate at best since many did not satisfy at least one of the required JBI criteria (in 13 of 21 studies). Specifically, some studies only included participants from a single GP practice [3, 4], a single primary care centre [16], or from 2 GP practices in which the population studied was not generalizable [10, 13], although most compared sociodemographic characteristics between participation and non-participation [4, 10, 16]. Five studies used convenience sampling [3, 9, 14, 17, 21] and one explained that most testing staff were not trained (35% of staff had spirometry training and only 20% of staff had undergone COPD-management training in the last 2 years)[6]. Of studies that sourced a population-based sample by random sampling, recruitment rates were as low as 1-6% [5] and 9.4% [6]; however, they were also low (≤15%) in some consecutive [10, 18] and non-consecutive samples [21].

The prevalence figures for COPD under-diagnosis were difficult to find in 4 studies [2, 3, 9, 13], and only one study provided 95% confidence intervals of the estimates [16]. Four studies had an insufficient sample size for those who underwent spirometry to be able to accurately determine the baseline COPD prevalence [8, 11, 13, 14] and one study was borderline on this [17] when assessed objectively [28, 29].

For the 5 COPD case series (Table S4), the one of a COPD registry that included all 8,957 COPD participants from half of the GP practices of Wales increased study reliability [22]; three recruited participants in a non-consecutive manner [24-26]; and although the final one recruited consecutive patients, it was underpowered to estimate the true COPD prevalence [23]. Like the prevalence studies, all studies were required to have used post-BD spirometry as a valid identification method, although only two specified that the spirometry was performed by trained testing staff [23, 25] and one study gave only limited clinical information and did not use contemporary spirometry standards [26].

Coverage bias arising from differing responses across subgroups was not addressed in any study but seemed irrelevant to these entire study populations.

Sample size calculations

An adequate sample size is important to ensure good precision of the final estimate.

These calculations retrospectively looked at the number of participants required to observe the prevalence found by the study researchers with predefined precision using the following formula [28, 29]

$$n = z^2 p(1-p)/d^2$$

n is the sample size,
Z is the statistic corresponding to level of confidence,
P is prevalence
d is precision (corresponding to effect size, assumed ¼ to 1/5 prevalence)

Cross-sectional prevalence studies (cases/N/ calculation = minimum n)	
Liang 2018.	272/1050: di (1.96^2*0.26*0.74)/0.065^2 = 175
Hill 2010	208/1003: di (1.96^2*0.207*0.793)/0.052^2 = 233
Herrera 2016.	309/1540: di (1.96^2*0.201*0.799)/0.050^2 = 247
Bednarek 2008.	183/1960: di (1.96^2*0.093*0.907)/0.023^2 = 613
Frank 2006.	163/825: di (1.96^2*0.198*0.802)/0.050^2 = 244
De Queiroz 2012.	63/200: di (1.96^2*0.315*0.685)/0.070^2 = 169
Stafyla 2018	33/186: di (1.96^2*0.178*0.822)/0.045^2 = **277 ‡**
Siatkowska 2010	57/1026: di (1.96^2*0.060*0.940)/0.015^2 = 962
Tinkelman 2006	235/597: di (1.96^2*0.394*0.606)/0.10^2 = 92
Tinkelman 2007	155/818: di (1.96^2*0.189*0.811)/0.05^2 = 236
Yawn 2009	308/1201: di (1.96^2*0.256*0.744)/0.064^2 = 179
Abramson 2012	91/199: di (1.96^2*0.457*0.543)/0.114^2 = 73
Lokke 2012	878/4049: di (1.96^2*0.217*0.783)/0.054^2 = 223
Llordes 2015	422/1738: di (1.96^2*0.243*0.757)/0.061^2 = 190
Sandelowsky	38/138: di (1.96^2*0.275*0.725)/0.069^2 = **160 ‡** di (1.96^2*0.275*0.725)/0.055^2 = 253
Al Ghobain 2011	71/501: di (1.96^2*0.142*0.858)/0.0355^2 = 371
Melbye 2011	149/376: di (1.96^2*0.396*0.604)/0.088^2 = 118
Hamers 2006	36/142: di (1.96^2*0.254*0.746)/0.056^2 **= 232 ‡**
Weiss 2014	130/775: di (1.96^2*0.168*0.832)/0.037^2 = 392
Heffler 2018	96/300: di (1.96^2*0.320*0.680)/0.071^2 = 165.8
Dirvan 2010	37/149: di (1.96^2*0.248*0.752)/0.055^2 **= 237 ‡**
Utsugi 2016	121/950: di (1.96^2*0.127*0.873)/0.028^2 = 543
‡ excluded from the Forest plots illustrating undiagnosed COPD, COPD underdiagnosis and COPD overdiagnosis, as the accuracy of baseline COPD prevalence is uncertain	

COPD case series (cases/N/ calculation = minimum n)		
	Zwar 2011	257/445: di (1.96^2*0.578*0.422)/0.145^2 = 45
	Walters 2011	234/341: di (1.96^2*0.686*0.314)/0.172^2 = 28
	Sichletidis 2007	160/319: di (1.96^2*0.501*0.499)/0.125^2 = 61.5
	Fisk 2019	6702/8957: di (1.96^2*0.748*0.252)/0.166^2 = 26.3
	Ghattas 2013	28/80: di (1.96^2*0.35*0.65)/0.078^2 = **143 ‡**
	‡ excluded from the Forest plot on COPD overdiagnosis as the accuracy of baseline COPD prevalence is uncertain	

References

1 Utsugi H *et al.* (2016) Associations of lifelong cigarette consumption and hypertension with airflow limitation in primary care clinic outpatients in Japan. Respir Investig **54:** 35-43

2 Weiss G *et al.* (2014) Detection of chronic obstructive pulmonary disease in primary care in Salzburg, Austria: findings from the real world. Respiration **87:** 136-143

3 Siatkowska H *et al.* (2010) [Chronic obstructive pulmonary disease patients in the general practice]. Pneumonol Alergol Pol **78:** 112-120

4 Bednarek M *et al.* (2008) Prevalence, severity and underdiagnosis of COPD in the primary care setting. Thorax **63:** 402-407

5 Tinkelman DG *et al.* (2006) Misdiagnosis of COPD and asthma in primary care patients 40 years of age and over. J Asthma **43:** 75-80

6 Liang J *et al.* (2018) Diagnosing COPD and supporting smoking cessation in general practice: evidence-practice gaps. The Medical journal of Australia **208:** 29-34

7 Lokke A *et al.* (2012) Detection of previously undiagnosed cases of COPD in a high-risk population identified in general practice. COPD **9:** 458-465

8 Sandelowsky H *et al.* (2011) The prevalence of undiagnosed chronic obstructive pulmonary disease in a primary care population with respiratory tract infections - a case finding study. BMC family practice **12:** 122

9 Yawn B *et al.* (2009) Prevalence of COPD among symptomatic patients in a primary care setting. Current medical research and opinion **25:** 2671-2677

10 Frank TL *et al.* (2006) The diagnostic accuracies of chronic obstructive pulmonary disease (COPD) in general practice: The results of the MAGIC (Manchester Airways Group Identifying COPD) study. Prim Care Respir J **15:** 286-293

11 Hamers R *et al.* (2006) Chronic obstructive pulmonary disease in Brazilian primary care: Diagnostic competence and case-finding. Prim Care Respir J **15:** 299-306

12 Melbye H *et al.* (2011) Asthma, chronic obstructive pulmonary disease, or both? Diagnostic labeling and spirometry in primary care patients aged 40 years or more. International journal of chronic obstructive pulmonary disease **6:** 597-603

13 Dirven JA *et al.* (2010) COPD screening in general practice using a telephone questionnaire. COPD **7:** 352-359

14 Stafyla E *et al.* (2018) Missed diagnosis and overtreatment of COPD among smoking primary care population in Central Greece: old problems persist. International journal of chronic obstructive pulmonary disease **13:** 487-498

15 Casas Herrera A *et al.* (2016) COPD Underdiagnosis and Misdiagnosis in a High-Risk Primary Care Population in Four Latin American Countries. A Key to Enhance Disease Diagnosis: The PUMA Study. PLoS One **11:** e0152266

16 Llordes M *et al.* (2015) Prevalence, Risk Factors and Diagnostic Accuracy of COPD Among Smokers in Primary Care. COPD **12:** 404-412

17 Queiroz MC *et al.* (2012) Underdiagnosis of COPD at primary health care clinics in the city of Aparecida de Goiania, Brazil. J Bras Pneumol **38:** 692-699

18 Hill K *et al.* (2010) Prevalence and underdiagnosis of chronic obstructive pulmonary disease among patients at risk in primary care. CMAJ **182:** 673-678

19 Tinkelman DG *et al.* (2007) COPD screening efforts in primary care: what is the yield? Prim Care Respir J **16:** 41-48

20 Al Ghobain M *et al.* (2011) Prevalence of chronic obstructive pulmonary disease among smokers attending primary healthcare clinics in Saudi Arabia. Ann Saudi Med **31:** 129-133

21 Abramson MJ *et al.* (2012) Accuracy of asthma and COPD diagnosis in Australian general practice: a mixed methods study. Prim Care Respir J **21:** 167-173

22 Fisk M *et al.* (2019) Inaccurate diagnosis of COPD: the Welsh National COPD Audit. Br J Gen Pract **69:** e1-e7

23 Ghattas C *et al.* (2013) Over diagnosis of chronic obstructive pulmonary disease in an underserved patient population. International journal of chronic obstructive pulmonary disease **8:** 545-549

24 Walters JA *et al.* (2011) Factors associated with misdiagnosis of COPD in primary care. Prim Care Respir J **20:** 396-402

25 Zwar NA *et al.* (2011) Predictors of accuracy of diagnosis of chronic obstructive pulmonary disease in general practice. The Medical journal of Australia **195:** 168-171

26 Sichletidis L *et al.* (2007) The validity of the diagnosis of chronic obstructive pulmonary disease in general practice. Prim Care Respir J **16:** 82-88

27 Quanjer PH *et al.* (1993) 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 **16:** 5-40

28 Daniel WW. (1999) Biostatistics: A Foundation for Analysis in the Health Sciences. 7th Ed, edn 7th: John Wiley & Sons

29 Pourhoseingholi MA *et al.* (2013) Sample size calculation in medical studies. Gastroenterol Hepatol Bed Bench **6:** 14-17