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BMJ Open Respiratory Research

Predicting risk of COPD in primary care: development and validation of a clinical risk score

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ABSTRACT

Objectives: To develop and validate a clinical risk score to identify patients at risk of chronic obstructive pulmonary disease (COPD) using clinical factors routinely recorded in primary care.

Design: Case–control study of patients containing one incident COPD case to two controls matched on age, sex and general practice. Candidate risk factors were included in a conditional logistic regression model to produce a clinical score. Accuracy of the score was estimated on a separate external validation sample derived from 20 purposively selected practices.

Setting: UK general practices enrolled in the Clinical Practice Research Datalink (1 January 2000 to 31 March 2006).

Participants: Development sample included 340 practices containing 15 159 newly diagnosed COPD cases and 28 296 controls (mean age 70 years, 52% male). Validation sample included 2259 cases and 4196 controls (mean age 70 years, 50% male).

Main outcome measures: Area under the receiver operator characteristic curve (c statistic), sensitivity and specificity in the validation practices.

Results: The model included four variables including smoking status, history of asthma, and lower respiratory tract infections and prescription of salbutamol in the previous 3 years. It had a high average c statistic of 0.85 (95% CI 0.83 to 0.86) and yielded a sensitivity of 63.2% (95% CI 63.1 to 63.3) and specificity 87.4% (95% CI 87.3 to 87.5).

Conclusions: Risk factors associated with COPD and routinely recorded in primary care have been used to develop and externally validate a new COPD risk score. This could be used to target patients for case finding.

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KEY MESSAGES

▸ Opportunities to diagnose chronic obstructive pulmonary disease (COPD) in primary care are frequently missed.
▸ Data routinely recorded in primary care can be used to identify patients with undiagnosed COPD.
▸ We report the development and external validation of a clinical risk score for COPD in primary care, providing important information for the future development of risk prediction models for COPD that may be used to stratify patients for case finding.

INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is the third leading cause of mortality.[1] However, population studies suggest that 50–80% of the disease burden remains undiagnosed.[2][3] A recent analysis of UK primary healthcare records showed that opportunities to diagnose COPD are frequently missed with up to 85% of patients presenting within 5 years of their diagnosis with indicative symptoms and clinical events.[4] There is now a drive to identify such patients in order to instigate early management and reduce disease progression.[5][6] A variety of screening tools have been proposed and evaluated including symptom-based questionnaires,[7] and use of handheld[8] and diagnostic spirometry.[9] However, mass screening is likely to be costly and a more targeted approach is required to improve their efficiency.

Several clinical prediction models have been developed to identify individuals at risk of undiagnosed COPD. These include two developed in the USA using administrative claims data,[10][11] one in Denmark using primary and secondary care data,[12] and most recently in Scotland using routine primary healthcare data.[13] The first three models are unlikely to be implementable in a UK or similar primary care setting because of differences in healthcare structures as well as the included predictor variables, many of which are not routinely recorded. The Scottish model while likely to be implementable only considered a very limited number of potential risk factors and was not externally validated.[13]

We report the development and external validation of a clinical prediction model that provides a score for identifying patients at high risk of undiagnosed COPD in primary care.

METHOD
Study design
Electronic primary care records were available from a matched case–control data set obtained from the General Practice Research Database (GPRD; now the Clinical Practice Research Datalink). Cases with incident COPD were matched by age, sex and general practice with controls without COPD (1:2).

Risk score derivation and external validation
Description of dataset
The GPRD is a computerised database of longitudinal anonymised patient records from a representative sample of 480 general practices across the UK, covering approximately 6% of the population.[14]

Selection of cases and controls
Cases consisted of all patients aged ≥35 years on 1st April 2006 with a new diagnosis of COPD recorded between 1 January 2000 and 1 April 2006 (see online supplementary table S1 for clinical codes). Cases had at least 3 years of up-to-standard data (ie, data entry meeting set quality standards) prior to the date of COPD diagnosis (index date). Controls had no diagnosis of COPD, were registered on the index date and also had at least 3 years of up-to-standard data.

Identification of candidate risk factors
Risk factors associated with newly diagnosed COPD were identified from published epidemiological studies. Studies were identified from Medline, Embase and Google Scholar using 'COPD' (and relevant synonyms) and 'risk factor' as Medical Subject Headings and free text. From 544 articles we identified 46 candidate risk factors that were likely to be routinely recorded in primary care (see online supplementary table S2). The final list included smoking history, comorbidities (including asthma, ischaemic heart disease and depression), lower respiratory tract infections (LRTIs) and upper respiratory tract infections, respiratory symptoms (including cough, dyspnoea, wheeze and sputum production), systemic symptoms (including unintentional weight loss, chronic fatigue, and poor sleep), body mass index and health service use including medication prescriptions (salbutamol, oral prednisolone and antibiotics for a LRTI) and number of previous primary care consultations.

Data extraction
Clinical codes for each variable were identified using the CPRD medical and product dictionaries and the NHS Clinical Terminology Browser V.1.04.[15] Data on demographic characteristics, smoking, comorbidities, respiratory symptoms and health service use were extracted over the specified period (see online supplementary table S2). Data recorded within 60 days prior to the index date were excluded since a clinical suspicion of COPD could have influenced clinical activity during this period.[10] Smoking status closest to the COPD diagnosis date (or matched time point) was used to reflect likely clinical practice.

Sample size and creation of derivation and validation data sets
The data set was split into a development and external validation sample (while preserving matching of cases and controls) by purposively selecting 20 general practices that reflected the full range of practice and population characteristics where the risk score would be applicable. These practices each had at least 200 individuals to ensure validation statistics were estimated with high precision.

Model development
Both the unadjusted and adjusted association between each factor and COPD were estimated using conditional logistic regression (to account for matching of cases and controls). Risk factors were included in the model based on statistical significance (adjusted OR≥1.5 and p value <0.05) and clinical understanding, with the aim to achieve a parsimonious and clinically acceptable model. The final model was simplified by including only four risk factors that had the highest adjusted ORs and were most likely to be recorded in a range of primary care settings.

Missing smoking status was accounted for by including a missing value category in the regression model. Patients in primary care often have unknown smoking status and the model in practice may be applied to such patients. Missing data for other factors was assumed indicative of their true absence. Risk scores were computed for each individual by combining the estimated regression log ORs (β coefficients) from the final model with the individual's risk factor values.

External validation and model performance
The accuracy of the risk score was evaluated in each of the 20 validation practices by producing the corresponding receiver operator characteristic (ROC) curve and estimating the area under it (c statistic). To summarise the average performance across the 20 practices, the c statistic estimates were synthesised in a random effects meta-analysis. We also summarised the heterogeneity in performance by estimating a 95% interval for the range of potential c statistics.[16]

A score threshold to define 'high risk' was selected by optimising the balance between the sensitivity and positive predictive value (PPV), assuming a prevalence of undiagnosed COPD of 5.5% in the general population.[17] We divided the total number screened by the

Table 1 General characteristics of participants in the development sample

| | Controls (n=28 296) | | Cases (n=15 159) | | | |
	N	(%)	N	(%)	Unadjusted OR	(95% CI)
Mean age (SD)	69.7	(10.8)	69.7	(10.9)	–	
Males	14 655	(51.8)	7849	(51.8)	–	
Socioeconomic quintile*						
1	5035	(17.8)	2698	(17.8)	–	
2	4156	(14.7)	2237	(14.8)	–	
3	5079	(17.9)	2733	(18.0)	–	
4	6386	(22.6)	3429	(22.6)	–	
5	7640	(27.0)	4062	(26.8)	–	
Smoking status†						
Never	14 693	(51.9)	2758	(18.2)	1	
Former	6013	(21.3)	4671	(30.8)	4.79	(4.49 to 5.10)
Current	4831	(17.1)	6961	(45.9)	8.99	(8.43 to 9.59)
Missing	2759	(9.8)	769	(5.1)	1.37	(1.23 to 1.51)
BMI†						
<18.5	5810	(20.5)	2917	(19.2)	0.80	(0.76 to 0.85)
18.5–25	8651	(30.6)	5232	(34.5)	1	
25–30	9299	(32.9)	4475	(29.5)	0.79	(0.75 to 0.83)
>30	4536	(16.0)	2535	(16.7)	0.93	(0.87 to 0.98)

Unadjusted OR for association with COPD.
Unadjusted ORs for age, sex and socioeconomic status of general practice were not estimated as cases and controls were matched on these variables.
*1=least deprived.
2
3
4
5=most deprived.
Based on Index of Multiple Deprivation score of general practice electoral ward.
†Closest to diagnosis.
BMI, body mass index; COPD, chronic obstructive pulmonary disease.

number of true positives to derive the number-needed-to-screen (NNS) to detect a single case of COPD. The number of diagnostic assessments needed to detect a single case of COPD was estimated as the reciprocal of the PPV.

RESULTS

Development sample: population characteristics

15 159 newly diagnosed COPD cases and 28 296 controls from 340 general practices were included in the development sample (tables 1 and 2). Mean age was 70 years and 52% were male. Cases and controls were matched and therefore identical in age, sex, and socioeconomic status of registered practice. 27% were current smokers, 25% ex-smokers and 40% had never smoked. A significantly higher proportion of cases than controls had a positive smoking history (77% vs 38%, respectively). All co-morbidities except hyperlipidaemia and diabetes mellitus were more common in cases than in controls. This was also true for respiratory and systemic symptoms, including fatigue and poor sleep, as well as health service use.

Model results

The final model included history of smoking, asthma and salbutamol prescriptions and number of LRTIs in the previous 3 years (table 3). There was a significant drop in the model fit when removing asthma, salbutamol and LRTIs. The model was used to derive a clinical score ranging from 0 to 6.5 as shown below table 3. This had a c statistic in the development sample of 0.85 (95% CI 0.845 to 0.853). A more comprehensive model that incorporates additional variables, including symptoms, is provided in table 4.

External validation sample: population characteristics

A total of 2259 newly diagnosed cases and 4196 controls from 20 general practices were included in the validation sample (table 5). The mean age was 70 years, 50% were men, and 26.6% were current smokers. A greater proportion of participants in the validation sample than the development sample were from the lowest socioeconomic quintile (42.4% vs 26.8%, respectively).

External validation: discriminative ability

The final risk score had a c statistic of 0.84 (95% CI 0.83 to 0.85) in the validation sample when analysing the data from all 20 practices combined (ignoring clustering of patients within practices; figure 1). The c statistic in each of the validation practices separately was consistently high (figure 2) and a random effects meta-analysis (which takes into account clustering) produced a similar

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Table 2 Comorbidities, symptoms, and healthcare use of participants in the development sample

	Controls (n=28 296)		Cases (n=15 159)		Unadjusted	
	N	(%)	N	(%)	OR	(95% CI)
Comorbidities*						
Asthma	2438	8.6	5669	37.4	6.61	(6.23 to 7.02)
Ischaemic heart disease	5572	19.7	3560	23.5	1.31	(1.25 to 1.38)
Heart failure	687	2.4	847	5.6	2.50	(2.24 to 2.77)
Stroke	850	3.0	539	3.6	1.23	(1.10 to 1.37)
Hyperlipidaemia	3327	11.8	1660	11.0	0.93	(0.87 to 1.00)
Anaemia	1554	5.5	859	5.7	1.04	(0.95 to 1.14)
Pulmonary embolism	50	0.2	71	0.5	2.72	(1.89 to 3.91)
Deep vein thrombosis	139	0.5	107	0.7	1.44	(1.12 to 1.86)
Atrial fibrillation	980	3.5	690	4.6	1.37	(1.24 to 1.51)
Lung cancer	35	0.1	68	0.4	3.68	(2.45 to 5.55)
Cancer	3805	13.4	2098	13.8	1.05	(0.99 to 1.11)
Depression†	967	3.4	630	4.2	1.24	(1.12 to 1.38)
Anxiety†	2056	7.3	1816	12.0	1.77	(1.65 to 1.90)
Allergic rhinitis	1917	6.8	1152	7.6	1.13	(1.05 to 1.22)
Tuberculosis	421	1.5	365	2.4	1.66	(1.44 to 1.91)
Pulmonary tuberculosis	371	1.3	344	2.3	1.77	(1.52 to 2.06)
Chronic kidney disease	56	0.2	45	0.3	1.69	(1.11 to 2.60)
Helicobacter pylori	188	0.7	139	0.9	1.45	(1.16 to 1.81)
Gastric ulcer	545	1.9	472	3.1	1.63	(1.43 to 1.85)
Gastooesophageal reflux disease	1897	6.7	1229	8.1	1.25	(1.16 to 1.35)
Osteoporosis	713	2.5	569	3.8	1.58	(1.41 to 1.78)
Fractures	3862	13.6	2547	16.8	1.30	(1.23 to 1.38)
Diabetes	2167	7.7	1015	6.7	0.87	(0.81 to 0.94)
Rheumatoid arthritis	462	1.6	369	2.4	1.52	(1.32 to 1.75)
Lower respiratory tract infections†						
0	25 128	88.8	9344	61.6	1	
1	2205	7.8	2947	19.4	4.02	(3.76 to 4.29)
>1	963	3.4	2868	18.9	9.76	(8.93 to 10.66)
Upper respiratory tract infections†						
0	22 355	79.0	10 623	70.1	1	
1	3917	13.8	2702	17.8	1.47	(1.39 to 1.56)
>1	2024	7.2	1834	12.1	1.98	(1.85 to 2.13)
Allergy	7614	26.9	5045	33.3	1.40	(1.34 to 1.46)
Symptoms†						
Presentations with cough						
0	23 470	82.9	8180	54.0	1	
1	3072	10.9	3130	20.6	3.14	(2.96 to 3.34)
>1	1754	6.2	3849	25.4	7.12	(6.64 to 7.63)
Presentations with dyspnoea						
0	26 789	94.7	11 294	74.5	1	
1	1014	3.6	2220	14.6	5.57	(5.12 to 6.06)
>1	493	1.7	1645	10.9	9.01	(8.05 to 10.09)
Wheeze	456	1.6	1860	12.3	8.89	(7.96 to 9.94)
Sputum production	245	0.9	609	4.0	5.32	(4.52 to 6.26)
Weight loss	211	0.7	306	2.0	2.74	(2.30 to 3.28)
Fatigue	1550	5.5	1215	8.0	1.53	(1.42 to 1.66)
Poor sleep	977	3.5	810	5.3	1.59	(1.44 to 1,75)
Health service use†‡						
Antibiotic courses						
0	18 799	66.4	5150	34.0	1	
1	5361	18.9	3313	21.9	2.34	(2.21 to 2.47)
2	2127	7.5	2267	15.0	4.04	(3.76 to 4.34)
>2	2009	7.1	4429	29.2	8.64	(8.07 to 9.25)
Salbutamol	2492	8.8	7723	50.9	11.5	(10.8 to 12.2)
Prednisolone	1800	6.4	4358	28.7	6.17	(5.78 to 6.58)
GP consultations						
<5	5162	18.2	1156	7.6	1	
5–10	4618	16.3	1734	11.4	1.81	(1.66 to 1.98)
10–20	7677	27.1	3745	24.7	2.55	(2.36 to 2.77)
20–40	7610	26.9	5136	33.9	3.99	(3.68 to 4.32)
>40	3229	11.4	3388	22.3	6.91	(6.31 to 7.57)
Hospital referrals	703	2.5	687	4.5	2.08	(1.85 to 2.34)

Unadjusted OR for association with COPD.
*Ever previously diagnosed.
†Within 3 years of COPD diagnosis or equivalent matched time point for controls.
COPD, chronic obstructive pulmonary disease; GP, general practitioner.

Table 3 Adjusted ORs and regression coefficients (β) for risk factors included in the final risk model

	OR*	(95% CI)	β	(95% CI)
Smoking status				
Never	1		0	
Former	4.72	(4.35 to 5.12)	1.55	(1.47 to 1.63)
Current	11.7	(10.7 to 12.7)	2.46	(2.37 to 2.54)
Missing	2.44	(2.16 to 2.76)	0.89	(0.77 to 1.02)
Asthma	2.11	(1.93 to 2.31)	0.75	(0.66 to 0.84)
LRTI†				
0	1		0	
1	2.57	(2.36 to 2.81)	0.94	(0.86 to 1.03)
>1	4.29	(3.83 to 4.80)	1.46	(1.34 to 1.57)
Salbutamol†	6.91	(6.33 to 7.55)	1.93	(1.85 to 2.02)

As this model was developed using case-control data, the intercept term is not applicable and has therefore not been presented.
*Estimated using a multivariable conditional logistic regression model.
†Within 3 years of COPD diagnosis or equivalent matched time point for controls.
Risk score=(former smoker×1.55)+(current smoker×2.46) +(unknown smoking status×0.89)+(asthma×0.75)+(1 episode of LRTI×0.94)+(>1 episode of LRTI×1.46)+(salbutamol×1.93).
NB. Each variable can either take the value 0 (not present) or 1 (present).
For example, A former smoker with a history of asthma who presented with more than one lower respiratory tract infection in the past 3 years, and received salbutamol in the past 3 years would have the following risk score:
(1×1.55)+(0×2.46)+(0×0.89)+((1×0.75)+(0×0.94)+(1×1.46) +(1×1.93)=5.69.
COPD, chronic obstructive pulmonary disease; LRTI, lower respiratory tract infection.

summary c statistic of 0.85 (95% CI 0.83 to 0.86), with a 95% prediction interval of 0.80 to 0.90. The more comprehensive score had a marginally higher c statistic (0.87, 95% CI 0.86 to 0.87).

Table 6 summarises the performance of the final score across a range of thresholds in the validation sample. A score threshold ≥2.5 yielded a sensitivity of 63.2% (95% CI 63.1% to 63.3%) and specificity 87.4% (95% CI 87.3% to 87.5%). Assuming a 5.5% prevalence of undiagnosed COPD,[17] the score at our suggested threshold would have a PPV of 22.6%, NPV of 97.6%, and an overall screening yield of 3.5% when applied to patients over the age of 35 years. At this threshold the score would need to be applied to 29 patients, 5 of whom would require a clinical assessment, to identify one with COPD (figure 3).

DISCUSSION
Principal findings
We have developed and validated a clinical prediction model for identifying patients at high risk of COPD in primary care. Our clinical score incorporates smoking status, previous diagnosis of asthma and LRTIs, and prescriptions for salbutamol. The score showed good discrimination characteristics in the external validation population and our choice of optimal cut point yielded a relatively high sensitivity and specificity. It can

potentially detect about three out of every five patients with undiagnosed COPD while also being able to effectively rule out patients at low risk of disease. The score threshold, however, can be altered to either maximise sensitivity or specificity.

This builds on our previous published model (based on data from the Health Survey for England) which would require 19 patients to actively undertake a screening process (19 questionnaire responses and 7 clinical assessments) to identify one individual with COPD.[17] Our new clinical score, where we use routine data from primary care records, would significantly improve the efficiency of this process.

Comparison with existing literature
The first published risk model to identify patients with undiagnosed COPD was based on managed (predominantly secondary) care administrative claims data in the USA.[18] Using a case–control design, 19 health service utilisation characteristics were included, many of which are unlikely to be routinely recorded in primary care. In contrast we developed a more parsimonious model that uses routinely data recorded in primary care. Furthermore our study population had more complete data on smoking history. A further US model was developed using outpatient pharmacy data.[11] This incorporated respiratory and cardiovascular medications and antibiotics, and had a sensitivity of 60.6% and specificity of 70.5% when externally validated. Our risk score similarly included prior prescription of salbutamol as an important predictor. However, the ROC curve and c statistic for both US models were not reported, which makes it impossible to evaluate their discriminatory accuracy.

In Denmark Smidth et al[12] used administrative data on hospital admissions for lung disorders, respiratory prescriptions and lung function tests to develop a model to identify COPD. This had a much lower sensitivity (29.7–44.8%) but higher specificity (98.9%) than the score we developed. While it had a high PPV in the Dutch population (65.0–72.9%; based on an overall COPD prevalence of 9%), it would be difficult to administer in a UK or similar primary care setting where primary and secondary care data are currently poorly linked. This model also relies on prior diagnoses of emphysema and chronic bronchitis at hospital admissions and would miss a significant number of patients due to the low sensitivity and high proportion of false negative results.

Kotz et al[13] recently developed and internally validated a COPD risk model using routine longitudinal data from primary care in Scotland, including a very large (n=480 903 in the development cohort) and relatively young population (mean age 55.6 years). Their model demonstrated similar discrimination characteristics to our own (c statistic 0.85 (95% CI 0.84 to 0.85) in women and 0.83 (95% CI 0.83 to 0.84) in men), with good calibration. However, this has only been internally validated since the study population was randomly split into derivation and

Table 4 Adjusted ORs and regression coefficients (β) for variables included in a more comprehensive risk score

	OR*	(95% CI)	β	(95% CI)
Smoking status				
Never	1		0	
Former	4.36	(4.00 to 4.75)	1.47	(1.39 to 1.56)
Current	12.0	(10.97 to 13.12)	2.48	(2.40 to 2.57)
Missing	2.87	(2.52 to 3.26)	1.05	(0.92 to 1.18)
Asthma	1.89	(1.71 to 2.08)	0.64	(0.54 to 0.73)
LRTI†				
0	1		0	
1	1.81	(1.64 to 1.99)	0.59	(0.49 to 0.69)
>1	2.23	(1.96 to 2.54)	0.80	(0.67 to 0.93)
Presentations with cough†				
0	1		0	
1	1.42	(1.30 to 1.56)	0.35	(0.26 to 0.44)
>1	1.77	(1.59 to 1.97)	0.57	(0.46 to 0.68)
Presentations with dyspnoea†				
0	1		0	
1	3.17	(2.82 to 3.57)	1.16	(1.04 to 1.27)
>1	4.53	(3.89 to 5.28)	1.51	(1.36 to 1.66)
Wheeze†	1.86	(1.60 to 2.17)	0.62	(0.47 to 0.77)
Sputum production†	1.49	(1.17 to 1.90)	0.40	(0.16 to 0.64)
Unintended weight loss†	1.75	(1.33 to 2.31)	0.56	(0.29 to 0.84)
Antibiotic courses for a LRTI†				
0	1		0	
1	1.33	(1.23 to 1.44)	0.29	(0.21 to 0.37)
2	1.53	(1.38 to 1.70)	0.43	(0.32 to 0.53)
>2	1.80	(1.62 to 2.01)	0.59	(0.48 to 0.70)
Salbutamol†	4.19	(3.81 to 4.61)	1.43	(1.34 to 1.53)
Prednisolone†	1.53	(1.38 to 1.69)	0.42	(0.32 to 0.52)

As this model was developed using case-control data, the intercept term is not applicable and has therefore not been presented.
The c statistic for this model in the external validation sample was 0.87 (95% CI 0.86 to 0.87).
*Estimated using a multivariable conditional logistic regression model.
†Within 3 years of COPD diagnosis or equivalent matched time point for controls.
Risk score=(former smoker×1.47)+(current smoker×2.48)+(unknown smoking status×1.05)+(asthma×0.64)+(1 episode of LRTI×0.59)+ (>1 episode of LRTI×0.80)+(1 episode of cough×0.35)+(>1 episode of cough×0.57)+(1 episode of dyspnoea×1.16)+(>1 episode of dyspnoea×1.15)+(wheeze×0.62)+(sputum×0.40)+(unintended weight loss×0.56)+(1 antibiotic course×0.29)+(2 antibiotic course×0.43)+ (>2 antibiotic courses×0.59)+(salbutamol×1.43)+(prednisolone×0.42).
NB. Each variable can either take the value 0 (not present) or 1 (present).For example, A former smoker with a history of asthma who presented with more than one lower respiratory tract infection and episode of cough in the past 3 years, reported of unintended weight loss and received salbutamol and 2 course of antibiotics for a LRTI in the past 3 years would have the following risk score: (1×1.47)+(0×2.48)+(0×1.05)+(1×0.64)+(0×0.59)+(1×0.80)+(0×0.35)+(1×0.57)+(0×1.16)+(0×1.15)+(0×0.62)+(0×0.40)+(1×0.56)+(0×0.29) +(1×0.43)+(0×0.59)+(1×1.43)+(0×0.42)=5.9.
COPD, chronic obstructive pulmonary disease; LRTI, lower respiratory tract infection.

validation samples. Furthermore only a very limited range of risk factors were considered (age, sex, smoking status, socioeconomic status and history of asthma) and important predictors such as respiratory infections were not. They constructed separate models for men and women since they found an interaction between smoking status and sex. We also stratified our model by sex and repeated our analysis but found the ORs to be broadly similar to those in the non-stratified model.

A variety of screening questionnaires have also been evaluated. For example Price et al[7] assessed the accuracy of a case finding questionnaire which included items on respiratory symptoms, smoking, and allergies and showed good discrimination characteristics.[8] This and other questionnaire-based tools can only be used in either face-to-face consultations or distributed by mail or online.

If used in a population with a 5.5% prevalence of undiagnosed COPD, 26 patients would need to be screened to identify one case of COPD. Our model has the advantage of being applicable in both face-to-face consultations as well as integrated with clinical information systems and used at a practice level to identify whole groups of high-risk patients who could be invited to screening sessions. With the latter approach, only five patients would need to be invited for assessment to identify one case of COPD, thus improving its efficiency fivefold over the use of current screening questionnaires.

Strengths
We used data from a large primary care population and explored a wide range of risk factors, focusing on those routinely recorded in primary care. Both aspects help

Table 5 Characteristics of subjects in the external validation sample (derived from 20 general practices)

	Controls (n=4196)		Cases (n=2259)	
	N	(%)	N	(%)
Mean age (SD)	69.8	(11.0)	70.0	(11.1)
Males	2110	(50.3)	1133	(50.2)
Socioeconomic quintile*				
1	475	(11.3)	258	(11.4)
2	561	(13.4)	313	(13.9)
3	1072	(25.5)	574	(25.4)
4	308	(7.3)	159	(7.0)
5	1780	(42.4)	955	(42.3)
Smoking status				
Never	1858	(44.3)	374	(16.6)
Former	799	(19.0)	674	(29.8)
Current	751	(17.9)	966	(42.8)
Missing	788	(18.8)	245	(10.8)
Body mass index				
<18.5	1234	(29.4)	623	(27.6)
18.5–25	1098	(26.2)	643	(28.5)
25–30	1246	(29.7)	624	(27.6)
>30	618	(14.7)	369	(16.3)

*1=least deprived, 5=most deprived. Based on the Index of Multiple Deprivation score of electoral ward,

ensure this clinical score will be widely applicable in primary care in the UK and other similar health systems. The score was also validated in a number of non-randomly selected practices allowing for assessment of the heterogeneity of its performance.

Weaknesses

Ideally we would like to have used previously undiagnosed COPD cases identified by case-finding/screening to derive our risk score since their characteristics may
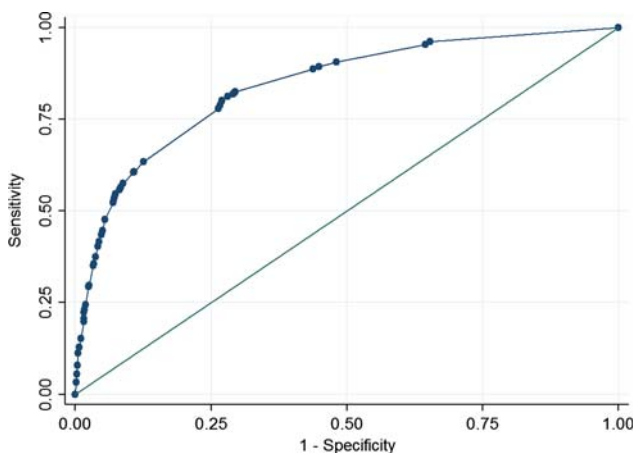
Figure 1 Receiver under the operator characteristic (ROC) curve for the test accuracy of the final risk score in the entire external validation sample (c statistic=0.84, 95% CI 0.83 to 0.85), ignoring clustering of patients within practices. Each point on the graph represents the performance (sensitivity and specificity) of the risk score at specific thresholds.

differ from incident cases identified clinically. We used a coded diagnosis of COPD for our case definition. However, there is good evidence that COPD is misdiagnosed and underdiagnosed in primary care,[19] a proportion of patients are likely to have undergone spirometry of variable quality,[20] and this may have led to some misclassification of our cases and controls. Unfortunately there was insufficient spirometry data in our data set to validate the diagnosis. Quint et al[21] recently demonstrated that clinical codes specific for COPD and emphysema have a high PPV for validated COPD. We used clinical codes for COPD that were recommended by the GPRD (now CPRD) at the time of our analysis. Although these largely overlapped with those recommended by Quint et al they also included codes specific for chronic bronchitis, which would not necessarily constitute a diagnosis of COPD (although may increase the likelihood of the development of airflow obstruction and risk of mortality).[22]

The mean age of our study population (70 years) was older than patients who would typically be targeted for case finding. Age and sex, which are likely to be predictors of COPD, could not be incorporated in the model because of the matched case-control data. This also prevented us from examining calibration performance in the validation practices. Another limitation of the matched case–control design is that c statistics are generally downwardly biased when estimated in such data.[23 24] Therefore, it is possible the true c statistic may be closer to 1 on application.

Some of the variables we explored, such as hospitalisations were poorly recorded, and may actually be significant predictors of COPD. In addition the absence of a risk factor could be secondary to under-recording. However, we aimed to produce a model that would be implementable in a common primary care setting drawing on routinely recorded data. If clinical coding improves over time some of these variables may need to be revisited as potential predictors and considered for inclusion in future revised models. Finally, our clinical score may not be applicable in health settings where exposure to risk factors other than cigarette smoking (eg, biomass fuels) is a significant cause of COPD.

Implications for clinicians, policymakers and research

Our clinical score once further validated, could be used by clinicians in primary care to stratify patients by risk of COPD. This could be achieved primarily with the aid of developed software applications that would automate the calculations. Since the model was based entirely on routinely collected data it could also be integrated into primary care clinical information systems to use data on risk factors to stratify all eligible patients. Patients predicted to be at high risk of COPD could then be referred for a clinical assessment including confirmatory spirometry testing.

However, further work is needed to validate or adapt this preliminary model in other populations, notably in
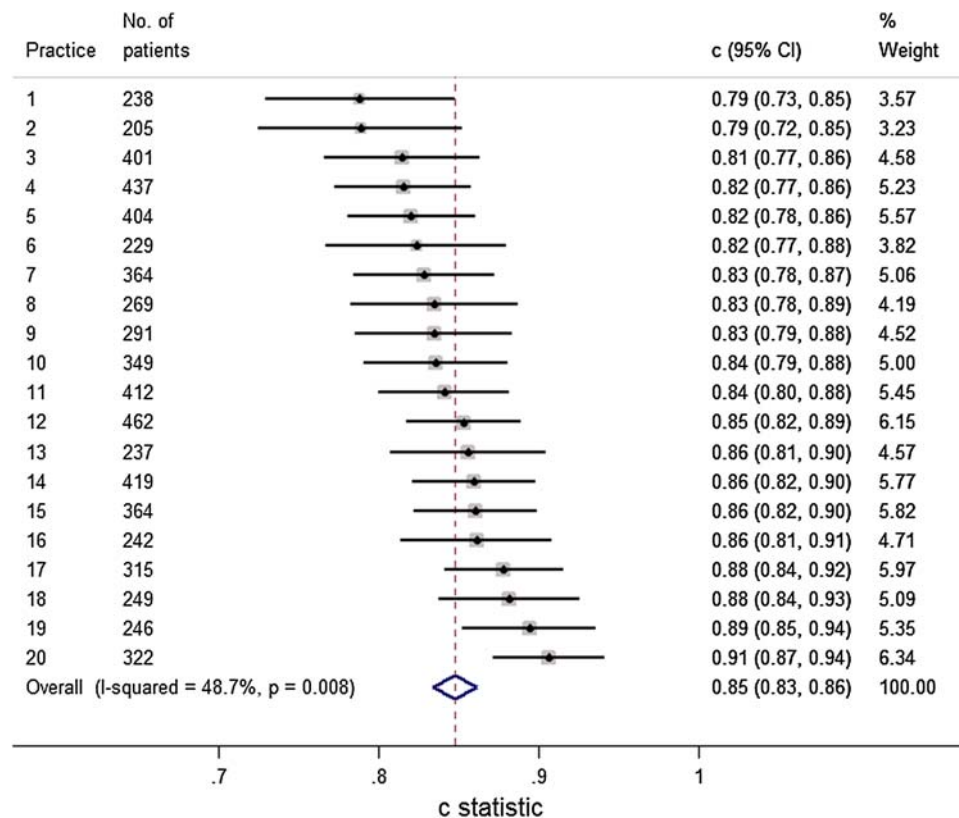
Figure 2 Random effects meta-analysis of the c statistics obtained for the final risk score when applied in each of the 20 validation practices separately. The summary result is the estimate of the average c statistic across the validation practices.

Table 6 Test accuracy of the final risk score in the external validation sample

Score threshold	Discrimination characteristics					Application of the score assuming 5.5% prevalence of undiagnosed COPD				
	Sensitivity (%)	Specificity (%)	Correctly classified (%)	LR+	LR–	PPV (%)	NPV (%)	Screening yield (%)	NNS	Clinical assessments per case detected
0	100	0	35.0	1	–	5.5	–	5.50	19	19
0.5	96.1	34.7	56.2	1.47	0.11	7.9	99.3	5.29	19	13
1	90.6	51.9	65.5	1.88	0.18	9.9	99.0	4.98	21	11
1.5	89.4	55.1	67.1	1.99	0.19	10.4	98.9	4.92	21	10
2	81.2	71.9	75.2	2.89	0.26	14.4	98.5	4.47	23	7
2.5	63.2	87.4	79.0	5.02	0.42	22.6	97.6	3.48	29	5
3	55.8	91.9	79.3	6.89	0.48	28.6	97.3	3.07	33	4
3.5	47.6	94.6	78.1	8.80	0.55	33.9	96.9	2.62	39	3
4	40.4	95.8	76.4	9.57	0.62	35.8	96.5	2.22	45	3
4.5	23.2	98.3	72.0	13.5	0.78	44.0	95.6	1.28	79	3
5	20.6	98.4	71.2	13.1	0.81	44.3	95.5	1.13	89	3
5.5	11.3	99.5	68.6	21.5	0.89	55.8	95.1	0.62	161	2
6	5.53	99.7	66.7	18.9	0.95	50.9	94.8	0.30	329	2
6.5	3.23	99.8	65.0	19.4	0.97	52.5	94.7	0.18	563	2

Correctly classified= proportion of participants with disease status correctly classified.
LR, likelihood ratio (ie, the ratio by which the pretest probability is altered by a positive or negative test result);
NPV, negative predictive value (proportion of all participants with a negative test who are disease free);
NNS, number-needed-to-screen (the number of patients or patient records the risk score would need to be applied to) to identify one patient with COPD; NPV, negative predictive value (proportion of all subjects with a negative test who are disease free); PPV, positive predictive value (proportion of all participants with a positive test who have disease); Screening yield, proportion of all patients subjected to the risk score who would be correctly identified as having COPD.
COPD, chronic obstructive pulmonary disease.

Figure 3 Screening test accuracy of the final risk score at a threshold of ≥2.5 when applied to 100 patients aged ≥35 years in primary care with an assumed prevalence of undiagnosed chronic obstructive pulmonary disease (COPD) of 5%.

- Patient with COPD referred for further assessment
- Patient with COPD not referred
- Patient without COPD referred
- Patient without COPD
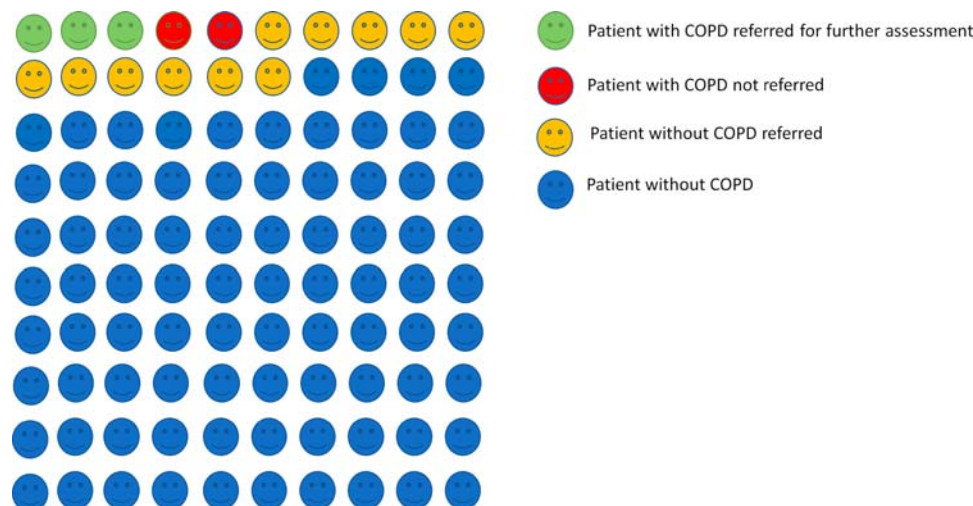
case finding trials that have enrolled patients with previously undiagnosed COPD. This includes examining our matching factors (age, sex and socioeconomic deprivation) as potential predictors. The cost-effectiveness of targeting patients at different thresholds should also be evaluated. Future studies should also address the impact of this tool on use and outcomes in general practice.

Conclusion

Our risk score shows promising accuracy and increased efficiency over current methods for identifying patients with COPD in primary care. Use of an externally validated score could be used for risk stratification so that high-risk patients can be efficiently identified and referred for confirmatory spirometry. However, evidence that early identification of COPD results in improved patient outcomes must be robustly assessed before screening for COPD can be recommended as part of routine practice.

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