



Predictors of pneumonia in lower respiratory tract infections: 3C prospective cough complication cohort study

Michael Moore¹, Beth Stuart ¹, Paul Little¹, Sue Smith², Matthew J. Thompson³, Kyle Knox², Anne van den Bruel², Mark Lown¹ and David Mant²

Affiliations: ¹University of Southampton, Primary Care Medical Group, Aldermoor Health Centre, Southampton, UK. ²Nuffield Department of Primary Health Care Sciences, University of Oxford, Oxford, UK. ³Dept of Family Medicine, University of Washington, Seattle, WA, USA.

Correspondence: Michael Moore, University of Southampton, Aldermoor Health Centre, Aldermoor Close, Southampton, SO16 5ST, UK. E-mail: mvm198@soton.ac.uk

 @ERSpublications

Pulse oximetry probably has a role in the diagnosis of pneumonia in the community
<http://ow.ly/QpWc30fVM2j>

Cite this article as: Moore M, Stuart B, Little P, *et al.* Predictors of pneumonia in lower respiratory tract infections: 3C prospective cough complication cohort study. *Eur Respir J* 2017; 50: 1700434 [<https://doi.org/10.1183/13993003.00434-2017>].

ABSTRACT The aim was to aid diagnosis of pneumonia in those presenting with lower respiratory tract symptoms in routine primary care.

A cohort of 28 883 adult patients with acute cough attributed to lower respiratory tract infections (LRTIs) was recruited from 5222 UK practices in 2009–13. Symptoms, signs and treatment were recorded at presentation and subsequent events followed-up for 30 days by chart review. The predictive value of patient characteristics, presenting symptoms and clinical findings for the diagnosis of pneumonia in the first 7 days was established.

Of the 720 out of 28 883 (2.5%) radiographed within 1 week of the index consultation, 115 (16.0%; 0.40% of 28 883) were assigned a definite or probable pneumonia diagnosis. The significant independent predictors of radiograph-confirmed pneumonia were temperature >37.8°C (RR 2.6; 95% CI 1.5–4.8), crackles on auscultation (RR 1.8; 1.1–3.0), oxygen saturation <95% (RR 1.7; 1.0–3.1) and pulse >100·min⁻¹ (RR 1.9; 1.1–3.2). Most patients with pneumonia (99/115, 86.1%) exhibited at least one of these four clinical signs; the positive predictive value of having at least one of these signs was 20.2% (95% CI 17.3–23.1).

In routine practice, radiograph-confirmed pneumonia as a short-term complication of LRTI is very uncommon (one in 270). Pulse oximetry may aid the diagnosis of pneumonia in this setting.

This article has supplementary material available from erj.ersjournals.com

Received: Feb 28 2017 | Accepted after revision: Aug 16 2017

Ethical approval: Oxfordshire REC A 09/HO604/67; UKCRN portfolio registration number: 7647.

Support statement: NIHR Programme Grant for Applied Research RP-PG-0407-10098. This article presents independent research funded by the National Institute for Health Research (NIHR) under its Programme Grants for Applied Research Programme. The views expressed are those of the author(s) and not necessarily those of the NHS, the NIHR or the Department of Health. Funding information for this article has been deposited with the Crossref Funder Registry.

Conflict of interest: Disclosures can be found alongside this article at erj.ersjournals.com

Copyright ©ERS 2017. This version is distributed under the terms of the Creative Commons Attribution Licence 4.0.

Introduction

Acute uncomplicated respiratory tract infections are one of the commonest acute illnesses managed in primary care and a large proportion receive antibiotic treatment [1–3]. The updated Cochrane review of antibiotics for bronchitis reported only a small benefit from antibiotics (risk ratio for clinical improvement 1.07; 95% CI 0.99–1.15) [4], findings confirmed in the largest clinical trial to date [5]. Prescribing unnecessary antibiotics exposes patients to potential side effects and will drive the development of antibiotic resistance that is dominated by primary care prescribing of antibiotics [6]. However, patients and clinicians are concerned about more severe or prolonged illness and complications [7]. Although primary care clinicians have a high predictive value when making the clinical diagnosis of pneumonia [8], they will still miss up to two-thirds of radiographic pneumonia in those presenting with lower respiratory tract infection (LRTI): those with a milder illness spectrum [8]. Some authors have suggested that missed pneumonia is not clinically relevant, but the subgroup with unidentified pneumonia in the GRACE study did have a shortened illness following antibiotic treatment [9]. A clinical decision rule to assist diagnosis was derived from the GRACE study cohort [10] but the number of radiograph-confirmed pneumonia cases was limited by the study size and, in the context of a clinical trial, the participants may not be fully representative of the illness spectrum in routine primary care. We therefore report the findings from a large prospective clinical cohort of patients presenting with acute LRTI in primary care.

Our aim was to assess which clinical features are predictive of radiograph-confirmed pneumonia in those presenting with lower respiratory tract symptoms in routine primary care.

Methods

Key design features

This was a prospective cohort. Clinical presenting features and management strategies were documented using a structured clinical proforma at an index consultation. Review of medical records was performed to ascertain radiography findings, subsequent consultations with new or worsening illness, and hospitalisation or death during the next 30 days.

Participants

A cohort of 28 883 adult patients with acute cough attributed to LRTI was recruited from 5222 practices in 2009–13.

Inclusion criteria

Patients had to be aged 16 or over and presenting a new illness. We used a pragmatic definition of LRTI consistent with the Cochrane review of antibiotics for “bronchitis” [11]: acute cough (new or worsening cough for 3 weeks or less), presenting as the main symptom, and judged to be infective in origin by the physician.

Exclusion criteria

The exclusion criteria were other causes of acute cough (*e.g.* heart failure, acid reflux, fibrosing alveolitis, *etc.*); patients unable to fill out the diary (*e.g.* severe mental illness, dementia, mental impairment, *etc.*); the immune compromised; and those who had previously presented with the same episode of illness.

These criteria are also similar to those applied in several previous LRTI trials and cohort studies [5, 12–19].

Data collection

Clinical record form

A clinical data collection form was used by the physician in the acute consultation, collecting data on age, smoking history, prior duration of symptoms, nature and severity of symptoms (dry cough, productive cough, shortness of breath, coryza, fever, chills/shivering, chest pain, headache, muscles aches, sleep disturbance, confusion, diarrhoea, sputum colour), examination (respiratory rate, pulse, blood pressure, oxygen saturation, temperature, presence of wheeze, crepitations or bronchial breathing), a rating of the overall severity of the illness (VAS anchored from “well” to “very unwell”) and if antibiotics were prescribed.

Notes review

Data on radiography findings were collected at notes review. All reports were considered by the authors and rated as definite pneumonia, probable pneumonia, possible pneumonia, unlikely pneumonia and no pneumonia. Other diagnoses (TB and cancer) were also noted and differences were resolved by discussion to achieve consensus.

Outcome data were abstracted by practice staff overseen either by local research network staff or research staff from Oxford. The national deprivation index of the patient’s place of residence was derived from their

postcode. Data submitted by practices on paper forms were double entered by the data management team in Oxford, who also followed up data inconsistencies or missing data with individual practices. We have previously shown that clinical records can be assessed reliably using a very similar structured proforma [20].

Other data

Cardio- or cerebrovascular morbidities and lung comorbidities noted in the medical records were also documented. Lung comorbidity included acute and chronic obstructive airways disease (asthma, chronic obstructive pulmonary disease) or history of other significant lung disease requiring hospital investigation, and the use of steroids or bronchodilators. Vaccination status (pneumovax) was also recorded.

Sample size

The overall recruitment target of 28 000 patients was originally designed to achieve 80% power to identify predictive variables of adverse outcome following LRTI with an odds ratio of 3 ($\alpha=0.01$) on the assumption of an antibiotic prescribing rate of 50% and an event rate of 0.005.

Statistical analysis

Prediction of imparted risk of pneumonia

As the aim of this analysis was to assess the risk of pneumonia imparted by clinical features present at the index consultation, only radiographs completed within 7 days of the index consultation were included in the analysis. Participants were included as cases if the radiograph report was categorised as showing “definite”, “probable” or “possible” pneumonia. The explanatory variables assessed were patient characteristics (age, gender, social deprivation and medical history), presenting symptoms and clinical signs elicited by examination at the index consultation. Symptoms were included if reported as present, irrespective of their severity. Adjustment of crude relative risks for the effect of other variables, and for clustering by doctor, was done by logistic regression. Participants were included regardless of whether or not they were prescribed antibiotics (and relative risks were not adjusted for antibiotic prescribing).

Statistical modelling of diagnostic values

The diagnostic value of combining statistically predictive variables was assessed by including them in a statistical model, starting with the most predictive and then sequentially adding in the variables that most increased the area under the receiver operating curve (AUC). Goodness of fit was assessed by the Hosmer–Lemeshow test. Oxygen saturation is regarded as normal if in the range of 95–99% and so values were dichotomised at <95%. Temperature is regarded as normal up to 37.7°C and so values were dichotomised at $\geq 37.8^\circ\text{C}$, blood pressure values were selected to align with the CRB-65 score (confusion, respiratory rate ≥ 30 breaths·min⁻¹, blood pressure <90 mmHg (systolic) or ≤ 60 mmHg (diastolic), age ≥ 65 years). Tachycardia in adults is widely defined as >100 bpm and is consistent with previous diagnostic models.

Sensitivity analyses

Sensitivity analyses were carried out to assess the effect of varying three analytic parameters: 1) the definition of pneumonia (by excluding “possible” pneumonia); 2) the severity of symptoms (by including symptoms only if reported as severe); 3) the imputation of missing values for O₂ saturation (by assuming the extreme positions that all missing values were <95% or all were $\geq 95\%$). We did not impute missing data for every variable as levels of missingness were mostly low (see Supplementary table S1 for detail).

Results

Diagnosis of pneumonia

Of the cohort of 28 883 participants, 1782 had a chest radiograph within 30 days, 720 within the first 7 days. As would be expected, those referred for chest radiography were more unwell than the whole cohort: older, more likely to be a smoker, more severe by global assessment and more likely to have positive physical signs (see table 1).

The certainty of the diagnosis of pneumonia, assessed on the basis of the radiologist’s report, is shown in table 2. A “case” of pneumonia for the primary analysis included “definite pneumonia”, “probable pneumonia”, “possible pneumonia” and “cancer”; the only exclusions were “not pneumonia” and “unlikely pneumonia”; 115 cases of radiograph-diagnosed pneumonia were thereby included. The tuberculosis case was excluded because the radiograph was not within the first week.

Clinical features predicting radiograph-confirmed pneumonia

Table 3 shows that the characteristics of the individual patient (including age, gender, smoking habit and past medical history) do not provide useful diagnostic information in deciding who has, and has not, got

TABLE 1 Baseline characteristics of whole cohort and those having a chest radiograph within the first 7 days

	Whole cohort	Cohort referred for radiograph within 1 week
Age ≥60 years	10 903/28 883 (37.8%)	326/720 (45.3%)
Female	17 118/28 878 (59.3%)	352/719 (49.0%)
Duration of illness <7 days	14 006/28 883 (48.5%)	411/720 (57.1%)
Received pneumovax in the past 10 years	5301/28 883 (18.4%)	169/720 (23.5%)
Ever smoked	15 185/28 414 (53.4%)	431/708 (60.9%)
Any comorbidity	13 122/28 883 (45.4%)	359/720 (49.9%)
Lung comorbidity	7471/28 883 (25.9%)	195/720 (27.1%)
On steroids or bronchodilators	6547/27 570 (23.8%)	174/677 (25.7%)
Living in top decile deprivation area (most deprived)	5757/28 883 (19.9%)	146/720 (20.3%)
Symptoms		
Shortness of breath	18 533/28 764 (64.4%)	525/714 (73.5%)
Fever or chills	13 698/28 836 (47.5%)	352/718 (49.0%)
Chest pain	10 666/28 811 (37.0%)	317/715 (44.3%)
Confusion	1861/28 865 (6.5%)	49/720 (6.8%)
Coryza	15 736/28 785 (54.7%)	318/714 (44.5%)
Headache	13 267/28 798 (46.1%)	293/715 (41.0%)
Muscle aches	10 517/28 801 (36.5%)	270/714 (37.8%)
Diarrhoea	2513/28 857 (8.7%)	68/718 (9.5%)
Sputum		
Purulent	18 246/28 879 (63.2%)	408/720 (56.7%)
Bloody/rusty	1026/28 879 (3.6%)	100/720 (13.9%)
Clinical examination		
Severity assessment ≥5/10	11 936/28 883 (41.3%)	430/720 (59.7%)
Respiratory rate ≥24·min ⁻¹	2904/28 766 (10.1%)	117/718 (16.3%)
Temperature ≥37.8°C	1663/28 862 (5.8%)	76/720 (10.6%)
Pulse ≥100·min ⁻¹	2819/28 871 (9.8%)	115/720 (16.0%)
Oxygen saturation <95%	1719/23 778 (7.2%)	100/632 (15.8%)
SBP ≤90 mmHg or DBP ≤60 mmHg	2198/28 883 (7.6%)	68/720 (9.4%)
Crackles	12 287/28 875 (42.6%)	402/720 (55.8%)
Bronchial breathing	2173/28 870 (7.5%)	83/720 (11.5%)
Wheeze	7084/28 873 (24.5%)	218/720 (30.3%)

SBP: systolic blood pressure; DBP: diastolic blood pressure.

pneumonia. Similarly, table 4 shows that presenting symptoms are equally unhelpful, including shortness of breath and sputum colour.

However, table 4 also shows that clinical examination findings are diagnostically useful with four (temperature >37.8°C, crackles on auscultation, pulse >100 and blood O₂ saturation) all having significant independent predictive value. The strongest clinical sign predictive of pneumonia was a temperature >37.8°C (RR 2.6; 95% CI 1.5–4.8). The other predictive signs were pulse >100·min⁻¹ (RR 1.9; 1.1–3.2), crackles on auscultation (RR 1.8; 1.1–3.0) and oxygen saturation <95% (RR 1.7; 1.0–3.1).

Sensitivity analyses and statistical modelling

Excluding the “possible pneumonia” from the model reduced the number of pneumonia cases to 106, but the same four variables were identified as the only statistically significant predictors of pneumonia.

TABLE 2 Attribution of diagnosis reported on radiographs for all reports and those taken within the first 7 days

	All radiographs	Radiographs within first 7 days
Not pneumonia	1539 (86.4%)	601 (83.5%)
Definitely pneumonia	184 (10.3%)	89 (12.4%)
Probable pneumonia	28 (1.6%)	16 (2.2%)
Possible pneumonia	18 (1.0%)	9 (1.3%)
Cancer	4 (0.2%)	1 (0.1%)
Tuberculosis	1 (0.1%)	0
Unlikely pneumonia	8 (0.5%)	4 (0.6%)

TABLE 3 Patient characteristics predicting radiographic pneumonia on chest radiograph

	Proportion of patients with pneumonia		Radiograph within 1 week		Adjusted risk ratio [#] for pneumonia on radiograph [¶]	
	Characteristic present	Characteristic absent	Risk ratio for pneumonia on radiograph		Risk ratio	p-value
			Risk ratio (95% CI)	p-value		
Age ≥60 years	56/326 (17.2%)	59/394 (15.0%)	1.15 (0.82–1.60)	0.422		
Female	59/352 (16.8%)	56/367 (15.3%)	1.10 (0.79–1.54)	0.538		
Received pneumovax <10 years earlier	27/169 (16.0%)	88/551 (16.0%)	1.00 (0.67–1.49)	0.999		
Ever smoked	68/431 (15.8%)	46/277 (16.6%)	0.95 (0.67–1.34)	0.769		
Any comorbidity	60/359 (16.7%)	55/361 (15.2%)	1.10 (0.78–1.53)	0.589		
Lung comorbidity	33/195 (16.9%)	82/525 (15.6%)	1.08 (0.75–1.57)	0.670		
On steroids or bronchodilators	32/174 (18.4%)	78/503 (15.5%)	1.19 (0.82–1.72)	0.371		
Living in top decile deprivation area (most deprived)	18/115 (15.7%)	128/605 (21.2%)	0.73 (0.46–1.17)	0.188		

[#]: risk ratio adjusted for those variables that were significantly associated with the outcome in the univariate model; [¶]: these columns are empty because none of the univariate analyses were significant.

TABLE 4 Clinical symptoms and examination findings at presentation predicting radiographic pneumonia on chest radiography

	Proportion of patients with pneumonia		Radiograph within 1 week				Adjusted risk ratio [#] for pneumonia on radiograph in imputed dataset	
	Characteristic present	Characteristic absent	Risk ratio for pneumonia on radiograph		Adjusted risk ratio [#] for pneumonia on radiograph		Risk ratio (95% CI)	p-value
			Risk ratio (95% CI)	p-value	Risk ratio (95% CI)	p-value		
Symptoms								
Shortness of breath	90/525 (17.1%)	22/189 (11.6%)	1.47 (0.95–2.28)	0.081				
Fever or chills	73/352 (20.7%)	40/366 (10.9%)	1.90 (1.33–2.71)	<0.001	1.32 (0.92–1.91)	0.134	1.31 (0.78–2.22)	0.307
Chest pain	57/317 (18.0%)	55/398 (13.8%)	1.30 (0.93–1.83)	0.129				
Confusion	13/49 (26.5%)	102/671 (15.2%)	1.75 (1.06–2.87)	0.029	1.46 (0.63–3.39)	0.378	1.84 (0.86–3.94)	0.117
No coryza	64/396 (16.2%)	47/318 (14.8%)	1.09 (0.77–1.55)	0.613				
Headache	56/293 (19.1%)	56/422 (13.3%)	1.44 (1.03–2.02)	0.035	1.21 (0.84–1.73)	0.320	1.39 (0.85–2.25)	0.186
Muscle aches	52/270 (19.3%)	59/444 (13.3%)	1.45 (1.03–2.04)	0.030	0.93 (0.58–1.51)	0.780	1.16 (0.70–1.94)	0.559
Diarrhoea	13/68 (19.1%)	101/650 (15.5%)	1.23 (0.73–2.07)	0.435				
Sputum								
Purulent	71/408 (17.4%)	44/312 (14.1%)	1.23 (0.87–1.74)	0.234				
Bloody/rusty	18/100 (18.0%)	97/620 (15.7%)	1.07 (0.85–1.35)	0.547				
Clinical examination								
Severity assessment ≥5/10	78/430 (18.1%)	37/290 (12.8%)	1.42 (0.99–2.04)	0.057				
Respiratory rate ≥24 min ⁻¹	26/117 (22.2%)	89/601 (14.8%)	1.50 (1.02–2.22)	0.041	1.01 (0.51–1.98)	0.980	0.81 (0.44–1.46)	0.481
Temperature ≥37.8°C	29/76 (38.2%)	86/644 (13.4%)	2.86 (2.02–4.04)	<0.001	2.37 (1.62–3.46)	<0.001	2.65 (1.46–4.81)	0.001
Pulse ≥100 min ⁻¹	31/115 (27.0%)	84/605 (13.9%)	1.94 (1.35–2.78)	<0.001	1.45 (1.00–2.11)	0.046	1.90 (1.12–3.24)	0.018
Oxygen saturation <95%	26/100 (26.0%)	76/532 (14.3%)	1.82 (1.23–2.69)	0.003	1.42 (0.99–2.05)	0.042	1.73 (0.98–3.06)	0.050
SBP ≤90 mmHg or DBP ≤60 mmHg	13/68 (19.1%)	102/652 (15.2%)	1.22 (0.73–2.06)	0.450				
Crackles			2.15 (1.47–3.16)	<0.001	1.69 (1.11–2.58)	0.009	1.82 (1.12–2.97)	0.015
Bronchial breathing			1.33 (0.84–2.11)	0.229				
Wheeze			1.02 (0.71–1.46)	0.929				

[#]: risk ratio adjusted for those variables that were significantly associated with the outcome in the univariate model. SBP: systolic blood pressure; DBP: diastolic blood pressure.

Similarly, excluding all but severe symptoms from the analysis did not change the finding that no symptom, including symptoms suggesting viral illness (coryza, headache and muscle ache), had significant diagnostic value. Imputing missing values for O₂ saturation had little impact on the assessed relative risk or on the statistical model (see below).

Clinicians traditionally give more weight to lateralising (asymmetric) symptoms. Treating wheeze and bronchial breathing as categorical (none/unilateral/bilateral) does not add precision: they remain nonsignificant in the univariate analysis and are not included in the final model.

Crackles as a yes/no variable was significant with an RR of 1.82 (95% CI 1.12–2.97). If this is treated as a categorical variable, the RRs are 1.89 (95% CI 1.25–2.86) for unilateral crackles and 1.51 (95% CI 0.96–2.38) for bilateral crackles. So it is true that unilateral is more predictive than bilateral. However, the AUC model with temperature plus unilateral crackles is still 0.65 (same as using crackles yes/no when you round to two decimal places) and the AUC for the full four-variable model remains 0.68. However, this is helpful information for the clinician since adding more weight to unilateral crackles is appropriate even if it does not add overall to the predictive power of the model.

The added diagnostic value achieved by combining the four significantly predictive clinical signs is shown in table 5 in terms of the AUC. Raised temperature alone achieved an AUC of 0.59 (95% CI 0.55–0.63). Adding crackles and O₂ saturation both significantly improved the AUC, but the improvement from adding raised pulse to the model was nonsignificant. The AUC achieved by considering all four variables was 0.68 (95% CI 0.62–0.74). As stated above, the impact of imputing missing values for O₂ saturation was negligible at either extreme. The Hosmer–Lemeshow test indicated that both the two-item and the four-item models fitted the data well ($p=0.993$).

Diagnostic performance in clinical practice

Table 6 shows the diagnostic performance of the predictive variables in clinical practice in those referred for radiography. Relying on temperature alone has very poor sensitivity; to achieve 83.5% sensitivity, it is necessary to consider all four predictive variables (*i.e.* if patients were only referred for radiography or prescribed antibiotics if they had at least one of these variables, about one in six would be missed). The positive predictive value of this decision threshold is 20.2% (*i.e.* one in five people radiographed who has at least one of these symptoms has pneumonia).

Discussion

Principal findings

The confirmation of pneumonia by radiography within 7 days of consultation is uncommon in adults presenting in primary care with LRTI 115 out of 28 883 (0.4%). The significant independent predictors of pneumonia in those receiving a chest radiograph within 1 week of consultation were temperature >37.8°C, crackles on auscultation, oxygen saturation <95% and pulse >100·min⁻¹. Most patients with pneumonia (99/115, 86.1%) exhibited at least one of these four clinical signs. The positive predictive value of having at least one sign was 20.2% (95% CI 17.3–23.1).

Strengths and limitations

The main strengths of the study are 1) the power of the study due to the substantial size of the cohort of more than 28 000 participants; 2) the follow-up using notes review was very high; 3) the study included

TABLE 5 Area under the receiver operating curve (AUC) of successive statistical models combining the significantly predictive clinical signs

Predictive variables	AUC (95% CI)	p-value when compared to previous model	AUC in imputed dataset assuming all missing oxygen values are >95% (95% CI)	AUC in imputed dataset assuming all missing oxygen values are <95% (95% CI)
Temperature	0.59 [0.55–0.63]		0.59 [0.55–0.63]	0.59 [0.55–0.63]
Temperature + crackles	0.65 [0.60–0.70]	0.001	0.65 [0.60–0.70]	0.65 [0.60–0.70]
Temperature + crackles + oxygen saturation	0.67 [0.61–0.73]	0.095	0.67 [0.61–0.73]	0.67 [0.61–0.72]
Temperature + crackles + oxygen saturation + pulse	0.68 [0.62–0.74]	0.208	0.67 [0.62–0.72]	0.67 [0.62–0.73]

TABLE 6 Sensitivity, specificity and predictive values

	Within the subset of patients radiographed within 7 days [#]				
	n (%) of cohort	Sensitivity	Specificity	NPV	PPV
Temperature	76 (10.6%)	25.2%	92.2%	86.6%	38.2%
Temperature + crackles					
1 of the 2	418 (58.1%)	76.5%	45.5%	91.1%	21.1%
Both	61 (8.5%)	21.7%	94%	86.3%	41%
Temperature + crackles + oxygen saturation					
1 or more	448 (62.2%)	80%	41.2%	91.5%	20.5%
2 or more	116 (16.1%)	33.9%	87.3%	87.4%	33.6%
3 (all three)	15 (2.1%)	7%	98.8%	84.8%	53.3%
Temperature + crackles + oxygen saturation + pulse					
None	243 (33.8%)	86.1%	36.5%	93.2%	20.5%
1 or more	475 (66.0%)	83.5%	37.4%	92.2%	20.2%
2 or more	166 (23.1%)	41.7%	80.5%	87.9%	28.9%
3 or more	46 (6.4%)	19.1%	96.0%	86.2%	47.8%
4 (all 4)	7 (1.0%)	3.48%	99.5%	84.4%	57.1%

NPV: negative predictive value; PPV: positive predictive value. [#]: n=720.

patients from routine consultations and was designed for very easy recruitment, to create little or no selection bias and a large generalisable cohort; 4) those recruiting for the study represented a wide range of practices and doctors; 5) the diagnosis of chest infections used clinical criteria similar to the Cochrane review [4] and in other studies in primary care [5, 12–14, 21]; 6) the clinical characteristics of included participants were similar to prior trials and observational cohorts in primary care [5, 10, 22] (approximately 20% with lung comorbidity, 70% with sputum, prior illness duration 1 week).

The main limitation was that in routine practice those selected for chest radiography represented only a small sample from the full cohort 1782 out of 28883 (6%) and those selected were more unwell and at high risk of pneumonia; in those radiographed within the first 7 days the prior probability of pneumonia was 16% (115/720). The expected prior probability of pneumonia in a community cohort is 5–6% [8, 21]. So this represents both a higher risk of pneumonia in those radiographed and overall a lower probability of radiograph-confirmed pneumonia in the whole cohort of 0.4%. The model derived in this selected data set is likely to exaggerate the positive predictive values and we had no comparable confirmatory data set to further test the model. Other limitations were in the absence of prior training or standardisation of recorded history or clinical signs and we had no quality assurance for examination findings, but conversely this means that these results are likely to be generalisable to the routine clinical settings. Patients were recruited at the busiest times of the year, and as with other studies of acute infection [23, 24] documentation of the details of those not approached was poor due to time pressures on the consultation. Although nearly 20% of individuals had missing data for oxygen saturation, the sensitivity analyses that imputed missing values for the model and substituted extreme values for the missing data did not alter the inferences.

Comparison with the literature

There are many prediction models for pneumonia derived mainly from secondary care populations but only two previous studies have tested models in a primary care cohort [18, 25]. In one community cohort six models were tested in a cohort of 126 patients with a pneumonia incidence of 20% when only the model including CRP was found to be predictive [26]. In a second study using the much larger cohort of 2820 patients with evaluable radiographs existing models again performed suboptimally [10]. A new model was derived: items of history and physical examination with an independent diagnostic value were absence of runny nose and presence of breathlessness, crackles and diminished breath sounds on auscultation, tachycardia ($>100\text{-min}^{-1}$) and fever (temperature $\geq 37.8^\circ\text{C}$). Combination of these items (“symptoms and signs” model) resulted in an area under the curve of 0.70. In a systematic review and individual patient meta-analysis of diagnostic models for pneumonia six models were tested in a combined dataset (n=5308 pneumonia prevalence 12%) where the van Vugt model [10] had the combination of the highest pooled AUC and best calibration and was considered the best candidate for primary care use [27].

What then do our results add to the existing literature? Three items are shared with the model of van Vugt: presence of fever, tachycardia and crackles on chest examination. The presence of coryza was not

significant in the new model and there was no comparative measure of diminished breath sounds. Pulse oximetry was not recorded in the GRACE study but may be a relevant addition. In one retrospective cohort study in an emergency department population (n=1948 pneumonia prevalence 10%), pulse oximetry of <95% was a useful addition to a diagnostic decision rule including fever tachycardia and tachypnoea [28]. In a second retrospective cohort study also in the emergency department setting (n=4464 pneumonia prevalence 9%), older age and vital signs (fever, tachycardia, tachypnoea) and oxygen saturation were all independent predictors of a pneumonia diagnosis [29].

Clinical implications

The best current diagnostic model for pneumonia for use in a primary care setting is that derived by VAN VUGT [10], which includes absence of runny nose and presence of breathlessness, crackles and diminished breath sounds on auscultation, tachycardia ($>100\text{-min}^{-1}$) and fever (temperature $\geq 37.8^{\circ}\text{C}$). The addition of CRP to this model adds some diagnostic precision and is recommended in the NICE pneumonia guidelines [30]. However, CRP is not routinely measured and very few clinicians take any notice of clinical decision rules in everyday practice, particularly if they involve multiple variables and include subjective symptoms. In contrast, the four variables identified by this analysis are easily measured clinical signs. Although pulse oximetry is not routinely measured, it is a robust and inexpensive technology that is widely available. If antibiotic prescribing was restricted to people who had one or more of these signs, it could substantially reduce antibiotic prescribing for this condition. Clinicians should be aware that the model was derived in those with more severe symptoms referred for radiographs and that effective clinical safety-netting would be needed to cope with missed cases of pneumonia. Pulse oximetry probably has a place in the diagnosis of pneumonia in the community but this should be formally tested in a population with more comprehensive assessment of pneumonia by chest radiograph.

References

- 1 Lee GC, Reveles KR, Attridge RT, *et al.* Outpatient antibiotic prescribing in the United States: 2000 to 2010. *BMC Med* 2014; 12: 96.
- 2 Gulliford MC, Dregan A, Moore MV, *et al.* Continued high rates of antibiotic prescribing to adults with respiratory tract infection: survey of 568 UK general practices. *BMJ Open* 2014; 4: e006245.
- 3 Hawker JI, Smith S, Smith GE, *et al.* Trends in antibiotic prescribing in primary care for clinical syndromes subject to national recommendations to reduce antibiotic resistance, UK 1995–2011: analysis of a large database of primary care consultations. *J Antimicrob Chemother* 2014; 69: 3423–3430.
- 4 Smith SM, Fahey T, Smucny J, *et al.* Antibiotics for acute bronchitis. *Cochrane Database Syst Rev* 2014; 3: CD000245.
- 5 Little P, Stuart B, Moore M, *et al.* Amoxicillin for acute lower-respiratory-tract infection in primary care when pneumonia is not suspected: a 12-country, randomised, placebo-controlled trial. *Lancet Infect Dis* 2013; 13: 123–129.
- 6 Goossens H, Ferech M, Vander Stichele R, *et al.* Outpatient antibiotic use in Europe and association with resistance: a cross-national database study. *Lancet* 2005; 365: 579–587.
- 7 Cornford CS. Why patients consult when they cough: a comparison of consulting and non-consulting patients. *Br J Gen Pract* 1998; 48: 1751–1754.
- 8 van Vugt SF, Verheij TJ, de Jong PA, *et al.* Diagnosing pneumonia in patients with acute cough: clinical judgment compared to chest radiography. *Eur Respir J* 2013; 42: 1076–1082.
- 9 Teepe J, Little P, Elshof N, *et al.* Amoxicillin for clinically unsuspected pneumonia in primary care: subgroup analysis. *Eur Respir J* 2016; 47: 327–330.
- 10 van Vugt SF, Broekhuizen BD, Lammens C, *et al.* Use of serum C reactive protein and procalcitonin concentrations in addition to symptoms and signs to predict pneumonia in patients presenting to primary care with acute cough: diagnostic study. *BMJ* 2013; 346: f2450.
- 11 Smith S, Fahey T, Smucny J, *et al.* Antibiotics for acute bronchitis. *Cochrane Database Syst Rev* 2014; 3: CD000245.
- 12 MacFarlane J, Macfarlane RM, Rose D, *et al.* 809 How common is pneumonia and other radiographic features in previously well adults who present in the community with acute lower respiratory tract illness? *Eur Respir J* 1999; 14: Suppl. 30, 116s.
- 13 MacFarlane J, Holmes W, Gard P, *et al.* Prospective study of the incidence, aetiology and outcome of adult lower respiratory tract illness in the community. *Thorax* 2001; 56: 109–114.
- 14 Little P, Rumsby K, Kelly J, *et al.* Information leaflet and antibiotic prescribing strategies for acute lower respiratory tract infection: a randomised controlled trial. *JAMA* 2005; 293: 3029–3035.
- 15 Butler J, Hofmann J, Cetron M, *et al.* The continued emergence of drug-resistant *Streptococcus pneumoniae* in the United States: an update from the Centers for Disease Control and Prevention Pneumococcal Sentinel Surveillance System. *J Infect Dis* 1996; 174: 986–993.
- 16 Butler C, Hood K, Verheij T, *et al.* Variation in antibiotic prescribing and its impact on recovery in patients with acute cough in primary care: prospective study in 13 countries. *BMJ* 2009; 338: b2242.
- 17 van Vugt S, Broekhuizen B, Lammens C, *et al.* Use of serum C reactive protein and procalcitonin concentrations in addition to symptoms and signs to predict pneumonia in patients presenting to primary care with acute cough: diagnostic study. *BMJ* 2013; 346: f2450.
- 18 Moore M, Stuart B, Coenen S, *et al.* Amoxicillin for acute lower respiratory tract infection in primary care: subgroup analysis of potential high-risk groups. *Br J Gen Pract* 2014; 64: e75–e80.
- 19 Little P, Stuart B, Hobbs R, *et al.* Antibiotic prescription strategies for acute sore throat: a prospective observational cohort study. *Lancet Infect Dis* 2014; 14: 213–219.

- 20 Little P, Stuart B, Francis N, *et al.* Effects of internet-based training on antibiotic prescribing rates for acute respiratory-tract infections: a multinational, cluster, randomised, factorial, controlled trial. *Lancet* 2013; 382: 1175–1182.
- 21 Macfarlane JT, Colville A, Guion A, *et al.* Prospective study of aetiology and outcome of adult lower-respiratory-tract infections in the community. *Lancet* 1993; 341: 511–514.
- 22 Butler CC, Hood K, Verheij T, *et al.* Variation in antibiotic prescribing and its impact on recovery in patients with acute cough in primary care: prospective study in 13 countries. *BMJ* 2009; 338: b2242.
- 23 Little P, Gould C, Williamson I, *et al.* Pragmatic randomised controlled trial of two prescribing strategies for childhood acute otitis media. *BMJ* 2001; 322: 336–342.
- 24 Little P, Stuart B, Hobbs FD, *et al.* Predictors of suppurative complications for acute sore throat in primary care: prospective clinical cohort study. *BMJ* 2013; 347: f6867.
- 25 Graffelman AW, le Cessie S, Knuistingh Neven A, *et al.* Can history and exam alone reliably predict pneumonia? *J Fam Pract* 2007; 56: 465–470.
- 26 Hopstaken RM, Muris JW, Knottnerus JA, *et al.* Contributions of symptoms, signs, erythrocyte sedimentation rate, and C-reactive protein to a diagnosis of pneumonia in acute lower respiratory tract infection. *Br J Gen Pract* 2003; 53: 358–364.
- 27 Schierenberg A, Minnaard MC, Hopstaken RM, *et al.* External validation of prediction models for pneumonia in primary care patients with lower respiratory tract infection: an individual patient data meta-analysis. *PLoS One* 2016; 11: e0149895.
- 28 Khalil A, Kelen G, Rothman RE. A simple screening tool for identification of community-acquired pneumonia in an inner city emergency department. *Emerg Med J* 2007; 24: 336–338.
- 29 Nolt BR, Gonzales R, Maselli J, *et al.* Vital-sign abnormalities as predictors of pneumonia in adults with acute cough illness. *Am J Emerg Med* 2007; 25: 631–636.
- 30 National Institute for Health and Care Excellence. Pneumonia in adults: diagnosis and management. Clinical guideline [CG191]. London, NICE, 2014.