**Predictors of pneumonia in lower respiratory tract infections: 3C prospective Cough Complication Cohort study**

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**Abstract**

**Objective:** To aid diagnosis of pneumonia in those presenting with lower respiratory tract symptoms in routine primary care.

**Methods:** A cohort of 28883 adult patients with acute cough attributed to LRTI 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 seven days was established.

**Results:** Of the 720/28883 (2.5.%) x-rayed within one week of the index consultation,115 (16.0%; 0.40% of 28883) were assigned a definite or probable pneumonia diagnosis. The significant independent predictors of X ray confirmed pneumonia were temperature >37.8 degrees (RR 2.6; 95%CI 1.5-4.8), crackles on auscultation (RR1.8; 1.1-3.0), oxygen saturation<95% (RR1.7; 1.0-3.1) and pulse >100/min (RR1.9; 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).

**Clinical Implications.** In routine practice, x-ray confirmed pneumonia as a short term complication of LRTI is very uncommon (1 in 270). Pulse oximetry may aid the diagnosis of pneumonia in this setting.

*255 words*

**Introduction**

Acute uncomplicated respiratory tract infections are one of the commonest acute illness managed in primary care and a large proportion receive antibiotic treatment[1-3]. The updated Cochrane review of antibiotics for bronchitis reported only small benefit from antibiotics (risk ratio for clinical improvement 1.07; 95% CI 0.99 to 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 which 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 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 x-ray 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.

**Objective:** To assess which clinical features are predictive of x-ray confirmed pneumonia in those presenting with lower respiratory tract symptoms in routine primary care.

**Method**

**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 x-ray findings, subsequent re-consultations with new or worsening illness, and hospitalisation or death during the next 30 days.

**Participants**

A cohort of 28883 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 three weeks or less), presenting as the main symptom, and judged to be infective in origin by the physician.

***Exlusion criteria****:* other cause 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); immune compromised; previously presented with the same episode of illness.

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

**Data collection*.***

***Clinical Record Form (CRF).*** 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 x-ray 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 cerebro-vascular morbidities and lung co-morbidities noted in the medical records were also documented. Lung co-morbidity included acute and chronic obstructive airways disease (asthma COPC) 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 28000 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 x-rays completed within 7 days of the index consultation were included in the analysis. Participants were included as cases if the x-ray 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-operator 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 and so values were dichotomised at > 37.8°C, blood pressure values were selected to align with the CRB 65 score. Tachycardia in adults is widely defined as >100bpm 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 >95%). We did not impute missing data for every variable as levels of missingness were mostly low - see Appendix Table 1 for detail).

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**Results.**

**Diagnosis of pneumonia**

Of the cohort of 28,883 participants, 1782 had a chest x-ray within 30 days, 720 within the first 7 days. As would be expected, those referred for chest x-ray were more unwell compared to 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).

Table 1

Baseline characteristics of whole cohort and those having a chest x-ray within the first 7 days

|  |  |  |
| --- | --- | --- |
|  | Whole cohort | Cohort referred for xray within one 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 illness <7 days | 14,006/28,883 (48.5%) | 411/720 (57.1%) |
| Received pneumovax <10y | 5,301/28,883 (18.4%) | 169/720 (23.5%) |
| Ever smoked | 15,185/28,414 (53.4%) | 431/708 (60.9%) |
| Any co-morbidity | 13,122/28,883 (45.4%) | 359/720 (49.9%) |
| Lung co-morbidity | 7,471/28,883 (25.9%) | 195/720 (27.1%) |
| On steroids or bronchodilators | 6,547/27,570 (23.8%) | 174/677 (25.7%) |
| Living in top decile deprivation area (most deprived) | 5,757/28,883 (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 | 1,861/28,865 (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 | 2,513/28,857 (8.7%) | 68/718 (9.5%) |
| Sputum: purulent | 18,246/28,879 (63.2%) | 408/720 (56.7%) |
| bloody/rusty | 1,026/28,879 (3.6%) | 100/720 (13.9%) |
|  |  |  |
| *Clinical examination* |  |  |
| Severity assessment > 5/10 | 11,936/28,883 (41.3%) | 430/720 (59.7%) |
| Resp rate > 24/min | 2,904/28,766 (10.1%) | 117/718 (16.3%) |
| Temp > 37.8°C | 1,663/28,862 (5.8%) | 76/720 (10.6%) |
| Pulse > 100/min | 2,819/28,871 (9.8%) | 115/720 (16.0%) |
| O2sat < 95% | 1,719/23,778 (7.2%) | 100/632 (15.8%) |
| SBP< 90 or DBP < 60 mmHg | 2,198/28,883 (7.6%) | 68/720 (9.4%) |
| Crackles | 12,287/28,875 (42.6%) | 402/720 (55.8%) |
| Bronchial breathing | 2,173/28,870 (7.5%) | 83/720 (11.5%) |
| Wheeze | 7,084/28,873 (24.5%) | 218/720 (30.3%) |

. 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 x-ray diagnosed pneumonia were thereby included. The tuberculosis case was excluded because the x-ray was not within the first week.

**Table 2 Attribution of diagnosis reported on xrays for all reports and those taken within the first 7 days.**

|  |  |  |
| --- | --- | --- |
|  | All X-rays | X-rays 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%) |
| TB | 1 (0.1%) | 0 |
| Unlikely pneumonia | 8 (0.5%) | 4 (0.6%) |

**Clinical features predicting x-ray 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 pneumonia. Similarly, Table 4 shows that presenting symptoms are equally unhelpful, including shortness of breath and sputum colour.

**Table 3 Patient characteristics predicting radiographic pneumonia on chest x-ray**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | X-ray within one week | | | | | |
|  | **Proportion of patients with pneumonia** | | **Risk ratio for pneumonia on x-ray** | | **Adjusted risk ratio\* for pneumonia on x-ray** | |
|  | *Characteristic +* | *Characteristic -* | *Risk ratio* | *p* | *Risk ratio* | *P* |
| 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 <10y | 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 co-morbidity | 60/359 (16.7%) | 55/361 (15.2%) | 1.10 (0.78, 1.53) | 0.589 |  |  |
| Lung co-morbidity | 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 |  |  |

However, Table 4 also shows that clinical examination findings are diagnostically useful with four (temperature>37.8, 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 degrees (RR 2.6; 95%CI 1.5-4.8). The other predictive signs were pulse >100/min (RR1.9; 1.1-3.2), crackles on auscultation (RR1.8; 1.1-3.0), and oxygen saturation<95% (RR1.7; 1.0-3.1).

**Table 4 Clinical symptoms and examination findings at presentation predicting radiographic pneumonia on chest x-ray**

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  |  |  | X-ray within one week | | | |  |  | |
|  | **Proportion of patients with pneumonia** | | **Risk ratio for pneumonia on x-ray** | | **Adjusted risk ratio\* for pneumonia on x-ray** | | **Adjusted risk ratio\* for pneumonia on x-ray in imputed dataset** | | |
|  | *Characteristic +* | *Characteristic -* | Risk ratio | *P* | Risk ratio | *p* | Risk ratio | | *p* |
| *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 |  |  |  | |  |
| Resp rate > 24/min | 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 |
| Temp > 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 | 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 |
| O2sat < 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 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 |  |  |  | |  |

**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. 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 nor 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 non-significant 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% 1.25, 2.86) for unilateral crackles and 1.51 (0.96, 2.38) for bilateral crackles.  So it is true that unilateral is more predictive than bilateral.  However the AUROC a model with temperature plus unilateral crackles is still 0.65 (same as using crackles yes/no when you round to 2 decimal places) and the AUROC for the full 4 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 area under the receiver-operator curve (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 non-significant. The AUC achieved by considering all 4 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 2 item and 4 item models fitted the data well (p= 0.993).

**Table 5 Area under the receiver-operator 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 O2 values are >95%** | **AUC in imputed dataset assuming all missing O2 values are <95%** |
| 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 sat | 0.67  (0.61, 0.73) | 0.095 | 0.67  (0.61, 0.73) | 0.67  (0.61, 0.72) |
| Temperature + crackles+oxygen sat  +pulse | 0.68  (0.62, 0.74) | 0.208 | 0.67  (0.62, 0.72) | 0.67  (0.62, 0.73) |

**Diagnostic performance in clinical practice**

Table 6 shows the diagnostic performance of the predictive variables in clinical practice in those referred for x-ray. 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 x-ray or prescribed antibiotics if they had at least one of these variables, about 1 in 6 would be missed). The positive predictive value of this decision threshold is 20.2% (i.e. 1 in 5 people x-rayed who has at least one of these symptoms has pneumonia).

**Table 6 Sensitivity, specificity and predictive values**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  | **Within the subset of patients x-rayed within 7 days (n=720)** | | | | |
| N (%) of cohort | Sensitivity | Specificity | NPV | PPV |
| Temperature | 76 (10.6%) | 25.2% | 92.2% | 86.6% | 38.2% |
|  |  |  |  |  |  |
| Temp+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% |
| Temp+Crackles+O2 sat |  |  |  |  |  |
| 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% |
| Temp+Crackles+O2 sat + 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% |

**Discussion**

**Principal findings**

The confirmation of pneumonia by x-ray within seven days of consultation is uncommon in adults presenting in primary care with LRTI 115/28883 (0.4%). The significant independent predictors of pneumonia in those receiving a chest x-ray within one week of consultation were temperature >37.8 degrees, crackles on auscultation, oxygen saturation<95% and pulse >100/min. 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 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 22]; 6) the clinical characteristics of included participants were similar to prior trials and observational cohorts in primary care[5, 10, 21] (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 x-ray represented only a small sample from the full cohort 1782/28883 (6%) and those selected were more unwell and at high risk of pneumonia; in those x-rayed 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, 22]. So this represents both a higher risk of pneumonia in those x-rayed and overall a lower probability of x-ray confirmed pneumonia in the whole cohort of 0.4%. The model derived in this selected data set is likely to exaggerate 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 generaliseable to the routine clinical settings. Patients were recruited at the busiest times of 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 which imputed missing values for the model and extreme values for the ROC 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 sub-optimally[10]. A new model was derived, items of history and physical examination with independent diagnostic value were absence of runny nose and presence of breathlessness, crackles and diminished breath sounds on auscultation, tachycardia (>100/min), and fever (temperature ≥37.8°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 ED 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 ED 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/min), and fever (temperature ≥37.8°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 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 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 x-rays and that and 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 x-ray.

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**Appendix Table 1**

**Summary of missing data**

|  |  |  |
| --- | --- | --- |
|  | Number missing (N=28,883) | Proportion data missing |
| Reconsultation within 30 days | 0 | 0% |
| Hospitalisation/death | 24 | 0.1% |
| Antibiotic strategy | 0 | 0% |
| Age | 0 | 0% |
| Gender | 5 | 0.02% |
| Duration illness | 0 | 0% |
| Received pneumovax | 0 | 0% |
| Smoking status | 469 | 1.6% |
| Any co-morbidity | 0 | 0% |
| Lung co-morbidity | 0 | 0% |
| Steroid or bronchodilator use | 1,313 | 4.6% |
| Deprivation | 0 | 0% |
| *Symptoms* |  |  |
| Shortness of breath | 119 | 0.4% |
| Fever | 68 | 0.2% |
| Chills | 79 | 0.3% |
| Chest pain | 72 | 0.3% |
| Confusion | 18 | 0.1% |
| Coryza | 98 | 0.3% |
| Headache | 85 | 0.3% |
| Muscle aches | 82 | 0.3% |
| Diarrhoea | 26 | 0.1% |
| Sputum colour | 4 | 0.01% |
| *Clinical examination* |  |  |
| Severity assessment | 10 | 0.03% |
| Resp rate | 119 | 0.4% |
| Temp | 21 | 0.7% |
| Pulse | 12 | 0.4% |
| O2sat | 5100 | 17.7% |
| Blood pressure | 34 | 0.1% |
| Crackles | 8 | 0.03% |
| Bronchial breathing | 13 | 0.1% |
| Wheeze | 10 | 0.01% |