Primary care

Diagnostic value of C reactive protein in infections of the lower respiratory tract: systematic review
Victor van der Meer, Arie Knuijingh Neven, Peterhans J van den Broek, Willem J J Assendelft

Abstract

Objectives To evaluate the diagnostic accuracy of C reactive protein in detecting radiologically proved pneumonia and to evaluate how well it can discriminate between bacterial and viral infections of the lower respiratory tract.

Data sources Medline and Embase (January 1966 to April 2004), with reference checking.

Study selection We included articles comparing C reactive protein with a chest radiograph or with microbiological work-up as a reference test. Two authors independently assessed methodological items.

Results None of the studies met all validity criteria. Six studies used an infiltrate on chest radiograph as reference test. Sensitivities ranged from 10% to 98%, specificities from 44% to 99%. For adults, the relation of C reactive protein with an infiltrate (in a subgroup analysis of five studies) showed an area under the curve of 0.80 (95% confidence interval 0.75 to 0.85). In 12 studies, the relation of C reactive protein with a bacterial aetiology of infection of the lower respiratory tract was studied. Sensitivities ranged from 8% to 99%, specificities from 27% to 95%. These data were epidemiologically and statistically heterogeneous, so overall outcomes could not be calculated.

Conclusion Testing for C reactive protein is neither sufficiently sensitive to rule out nor sufficiently specific to rule in an infiltrate on chest radiograph and bacterial aetiology of lower respiratory tract infection. The methodological quality of the diagnostic studies is generally poor. The evidence not consistently and sufficiently supports a wide introduction of C reactive protein as a rapid test to guide antibiotics prescription.

Introduction

Infections of the lower respiratory tract are common in the community and comprise both acute bronchitis and pneumonia. Differentiating between these two diagnoses by history and physical examination is challenging. However, several studies show that making a diagnosis of pneumonia, defined as a new infiltrate on a chest radiograph, on the basis of clinical findings is difficult. Differentiation between pneumonia and acute bronchitis is important because of the therapeutic consequences. Bacterial pneumonia should be treated with antibiotics, whereas acute bronchitis is usually self limiting. Microbiological aetiology varies from 15-25% viral infection in radiologically proved pneumonia, to 15-40% viral infection in infection of the lower respiratory tract.

Although bacterial pneumonia occurs much less often than other infections of the lower respiratory tract, in studies more than 70% of acute infections of the lower respiratory tract are treated with antibiotics. These data call for additional information, in order to detect bacterial pneumonia and to differentiate between this diagnosis and other respiratory tract infections.

C reactive protein is often proposed as the solution of this clinical dilemma. This is a protein of the acute phase, synthesised by hepatocytes. Its production is stimulated mainly by interleukin 6, interleukin 1β, and tumour necrosis factor α in response to infection or tissue inflammation. Since its identification in 1930, C reactive protein has been studied as a screening device for inflammation, a marker for disease activity, and as a diagnostic adjunct. However, even though values of C reactive protein may reflect the severity of inflammation or tissue injury, its role in differentiating bacterial from viral infections is not proved. With the availability of rapid or bedside tests, particularly in general practice, determining its diagnostic value is of increasing importance. We assessed the value of C reactive protein in the detection of radiologically proved pneumonia. In addition, we evaluated whether C reactive protein can differentiate bacterial from viral infections of the lower respiratory tract.

Methods

We performed an electronic search according to the most recent recommendations. We searched the databases Medline (January 1966 to April 2004) and Embase (January 1980 to April 2004). This strategy included the medical subject headings and text words “C-reactive protein”, “pneumonia”, “acute bronchitis”, and “lower respiratory tract infection”, and the text words “C reactive protein” and “lower respiratory infection”. We included only articles in English. We applied methodological filters for Medline and Embase. We supplemented the search by reference checking. The complete search strategy is available from the first author (VvdM).

Selection of studies

On the basis of title and abstract, the first author (VvdM) selected full text articles. We aimed to include studies that compared C reactive protein with a chest radiograph (tackling our first research question), or microbiological work-up (discriminative value for bacterial and viral aetiology). We excluded articles concerning immunocompromised patients, patients treated in intensive care units, or patients with hospital acquired pneumonia. Data that were published twice or more often were selected only once.

Additional tables and the results of the test performance of C reactive protein are on bmj.com
Primary care

Quality assessment
We used the guidelines of the Cochrane methods group on systematic reviews of screening and diagnostic tests to assess the quality of the studies.\(^1\) Table A on bmj.com shows how we used these guidelines. Lijmer et al defined four methodological criteria that overestimate the accuracy of a diagnostic test if these standards are not applied.\(^2\) We used these Lijmer criteria to test robustness in the sensitivity analysis.\(^2\)

Two authors (VvdM and AKN) independently assessed study quality. Disagreements were solved after discussion of the study details.

Data extraction
We constructed cross tables for calculating sensitivity and specificity for different cut-off points and extracted cut-off points for C reactive protein values. We aimed to extract three cross tables for three different values per study. If this was not possible on the basis of the reported data, we contacted the authors and asked them to provide the required additional data. All studies with quantitative information were eligible for statistical analysis.

Statistical analysis
We used the x statistic as a measure of agreement on quality assessment.\(^3\) For all studies, we extracted sensitivity, specificity, and positive and negative likelihood ratios for different cut-off points. We applied a statistical model for summarising performances of diagnostic tests that was based on that of Midgette et al.\(^4\) We calculated Spearman’s correlation of true positive rates and true negative rates. We calculated areas under the curve for each study to follow inverse correlation. We used a DerSimonian-Laird \(\chi^2\) test to test heterogeneity of these areas under the curve.\(^5\)\(^6\) We drew a summary receiver operating characteristic curve if data were homogeneous. We investigated the possibility of subgroup analysis and reported outcomes. We based a priori defined subgroups on age, setting, and sex.

We performed a sensitivity analysis by pooling separately the studies that met all four Lijmer criteria and those that did not.

Results
Figure 1 summarises the search strategy and selection of the identified studies. Of the 165 citations in Medline and 340 citations in Embase, we retrieved 22 full text copies on the basis of title and abstract. Reference checking retrieved one additional citation in Embase, which meant that 17 studies were included for quality assessment (n=17). Of the 12 studies dealing with our second research question, we obtained sufficient quantitative data to calculate sensitivity, specificity, and likelihood ratios for eight studies (n = 1096). Four authors were not able to provide additional data, because these data were not available any more.\(^7\)\(^8\)\(^9\)\(^10\) One did not respond.\(^10\)

Sensitivities ranged from 8% to 99%, specificities from 27% to 95%. Spearman’s correlation coefficient was \(-0.33, P < 0.01 (\chi^2\) test). Subgroup analysis in children (six studies providing 16 data points) resulted in a Spearman’s \(\rho\) of \(-0.82, P = 0.40 (\chi^2\) test).\(^11\)\(^12\)\(^13\)\(^14\)\(^15\)\(^16\) Figure 3 shows the summary receiver operating characteristic curve of this homogeneous subgroup. The area under the curve is 0.80 (95% confidence interval 0.75 to 0.85). Subgroups based on setting or sex could not be analysed, since they were too small (setting) or not available (lack of information on sex).

Bacterial aetiology
Of the 12 studies dealing with our second research question, we obtained sufficient quantitative data to calculate sensitivity, specificity, and likelihood ratios for eight studies (n = 1096). Four authors were not able to provide additional data, because these data were not available any more.\(^7\)\(^8\)\(^9\)\(^10\) One did not respond.\(^10\)

Sensitivities ranged from 8% to 99%, specificities from 27% to 95%. Spearman’s \(\rho\) for these eight studies was \(-0.49, P < 0.01 (\chi^2\) test). Subgroup analysis in children (six studies providing 16 data points) resulted in a Spearman’s \(\rho\) of \(-0.65, P < 0.01 (\chi^2\) test).\(^11\)\(^12\)\(^13\)\(^14\)\(^15\)\(^16\) A summary receiver operating characteristic curve for children could not be drawn because of statistical heterogeneity. We could not perform subgroup analysis based on setting or sex because none of the studies was conducted in primary care and data on sex were not available.

None of the studies fulfilled all four of the Lijmer criteria, so it was not possible to compare studies of different methodological quality.

---

**Table 1**

<table>
<thead>
<tr>
<th>Study characteristics</th>
<th>Medline (n=165)</th>
<th>Embase (n=340)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Potentially relevant studies</td>
<td>Full text copies retrieved (n=22)</td>
<td>Relevant study from reference checking (n=1)</td>
</tr>
<tr>
<td>Excluded on basis of title and abstract (n=483)</td>
<td>All relevant studies (n=23)</td>
<td>Studies not fulfilling inclusion criteria (n=5), published twice (n=1)</td>
</tr>
<tr>
<td>All relevant studies (n=23)</td>
<td>Studies included for quality assessment (n=17)</td>
<td>Studies without usable quantitative information (n=4)</td>
</tr>
<tr>
<td>Studies included for quality assessment (n=17)</td>
<td>Studies included for quantitative analysis (n=13)</td>
<td></td>
</tr>
</tbody>
</table>

**Fig 1** Flow of studies through the stages of the review

**Test performance**

The results of the test performance of C reactive protein with regard to the detection of an infiltrate on a chest radiograph or to the detection of a bacterial aetiology of lower respiratory tract infection are shown in table B on bmj.com and figure 2.

Detection of an infiltrate
With respect to our first research question, we derived 17 data points out of six studies (n = 1178; the number is determined by the number of patients contributing to a data point). Sensitivities ranged from 10% to 98%, specificities from 44% to 99%. Sensitivity and specificity were inversely related: Spearman’s correlation coefficient was \(-0.33, P < 0.01 (\chi^2\) test). Subgroup analysis in adults (five studies providing 14 data points) resulted in a Spearman’s \(\rho\) of \(-0.82, P = 0.40 (\chi^2\) test).\(^11\)\(^12\)\(^13\)\(^14\)\(^15\)\(^16\) Figure 3 shows the summary receiver operating characteristic curve of this homogeneous subgroup. The area under the curve is 0.80 (95% confidence interval 0.75 to 0.85). Subgroups based on setting or sex could not be analysed, since they were too small (setting) or not available (lack of information on sex).

Bacterial aetiology
Of the 12 studies dealing with our second research question, we obtained sufficient quantitative data to calculate sensitivity, specificity, and likelihood ratios for eight studies (n = 1096). Four authors were not able to provide additional data, because these data were not available any more.\(^7\)\(^8\)\(^9\)\(^10\) One did not respond.\(^10\)

Sensitivities ranged from 8% to 99%, specificities from 27% to 95%. Spearman’s \(\rho\) for these eight studies was \(-0.49, P < 0.01 (\chi^2\) test). Subgroup analysis in children (six studies providing 16 data points) resulted in a Spearman’s \(\rho\) of \(-0.65, P < 0.01 (\chi^2\) test).\(^11\)\(^12\)\(^13\)\(^14\)\(^15\)\(^16\) A summary receiver operating characteristic curve for children could not be drawn because of statistical heterogeneity. We could not perform subgroup analysis based on setting or sex because none of the studies was conducted in primary care and data on sex were not available.

None of the studies fulfilled all four of the Lijmer criteria, so it was not possible to compare studies of different methodological quality.
Table 1: Quality assessment of the 17 studies

<table>
<thead>
<tr>
<th>Detection of infiltrate</th>
<th>Blind measurement*</th>
<th>Avoidance of verification bias*</th>
<th>Spectrum of the disease*</th>
<th>Avoidance of selection bias</th>
<th>Independent interpretation</th>
<th>Avoidance of treatment paradox</th>
<th>Setting*</th>
<th>Duration of illness</th>
<th>Demographic information (age)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Flanders et al 2004†</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>?</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Almirall et al 2004††</td>
<td>†</td>
<td>†</td>
<td>†</td>
<td>†</td>
<td>†</td>
<td>†</td>
<td>†</td>
<td>†</td>
<td>†</td>
</tr>
<tr>
<td>Hopstaken et al 2003††</td>
<td>†</td>
<td>†</td>
<td>†</td>
<td>†</td>
<td>†</td>
<td>†</td>
<td>†</td>
<td>†</td>
<td>†</td>
</tr>
<tr>
<td>Melbye et al 1992†</td>
<td>–</td>
<td>+</td>
<td>?</td>
<td>†</td>
<td>†</td>
<td>+</td>
<td>†</td>
<td>†</td>
<td>+</td>
</tr>
<tr>
<td>Babu et al 1989†</td>
<td>†</td>
<td>†</td>
<td>†</td>
<td>†</td>
<td>†</td>
<td>†</td>
<td>†</td>
<td>†</td>
<td>†</td>
</tr>
<tr>
<td>Melbye et al 1988††</td>
<td>†</td>
<td>†</td>
<td>†</td>
<td>†</td>
<td>†</td>
<td>†</td>
<td>†</td>
<td>†</td>
<td>†</td>
</tr>
</tbody>
</table>

Discrimination between viral and bacterial aetiology

<p>| | | | | | | | | | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Almirall et al 2004†</td>
<td>††</td>
<td>††</td>
<td>††</td>
<td>††</td>
<td>††</td>
<td>††</td>
<td>††</td>
<td>††</td>
<td>††</td>
</tr>
<tr>
<td>Prift et al 2003††</td>
<td>††</td>
<td>††</td>
<td>††</td>
<td>††</td>
<td>††</td>
<td>††</td>
<td>††</td>
<td>††</td>
<td>††</td>
</tr>
<tr>
<td>Requena et al 2003††</td>
<td>††</td>
<td>††</td>
<td>††</td>
<td>††</td>
<td>††</td>
<td>††</td>
<td>††</td>
<td>††</td>
<td>††</td>
</tr>
<tr>
<td>Garcia Vazquez et al 2003††</td>
<td>††</td>
<td>††</td>
<td>††</td>
<td>††</td>
<td>††</td>
<td>††</td>
<td>††</td>
<td>††</td>
<td>††</td>
</tr>
<tr>
<td>Vink et al 2002††</td>
<td>††</td>
<td>††</td>
<td>††</td>
<td>††</td>
<td>††</td>
<td>††</td>
<td>††</td>
<td>††</td>
<td>††</td>
</tr>
<tr>
<td>Redford et al 2000††</td>
<td>††</td>
<td>††</td>
<td>††</td>
<td>††</td>
<td>††</td>
<td>††</td>
<td>††</td>
<td>††</td>
<td>††</td>
</tr>
<tr>
<td>Heskethen et al 2002††</td>
<td>††</td>
<td>††</td>
<td>††</td>
<td>††</td>
<td>††</td>
<td>††</td>
<td>††</td>
<td>††</td>
<td>††</td>
</tr>
<tr>
<td>Rabynek et al 1985††</td>
<td>††</td>
<td>††</td>
<td>††</td>
<td>††</td>
<td>††</td>
<td>††</td>
<td>††</td>
<td>††</td>
<td>††</td>
</tr>
<tr>
<td>Olofsdot et al 1995††</td>
<td>††</td>
<td>††</td>
<td>††</td>
<td>††</td>
<td>††</td>
<td>††</td>
<td>††</td>
<td>††</td>
<td>††</td>
</tr>
<tr>
<td>Korppi et al 1993††</td>
<td>††</td>
<td>††</td>
<td>††</td>
<td>††</td>
<td>††</td>
<td>††</td>
<td>††</td>
<td>††</td>
<td>††</td>
</tr>
<tr>
<td>Kentula et al 1987††</td>
<td>††</td>
<td>††</td>
<td>††</td>
<td>††</td>
<td>††</td>
<td>††</td>
<td>††</td>
<td>††</td>
<td>††</td>
</tr>
<tr>
<td>McCarthy et al 1978††</td>
<td>††</td>
<td>††</td>
<td>††</td>
<td>††</td>
<td>††</td>
<td>††</td>
<td>††</td>
<td>††</td>
<td>††</td>
</tr>
</tbody>
</table>

Plus, minus or question mark were adjudged if criteria were present, absent, or not mentioned.
*Essential criteria defined by Lijmer et al.23†Fulfilling all Lijmer criteria.
†Filling all Lijmer criteria.

Discussion

C reactive protein testing is neither sufficiently sensitive to rule out nor sufficiently specific to rule in both an infiltrate on chest radiograph and bacterial aetiology of lower respiratory tract infection. The diagnostic value of C reactive protein has been studied to an insufficient degree. Few studies are available, and their methodological quality is generally poor. Therefore, the data refer to a subgroup of epidemiologically, making it impossible to provide an overall diagnostic accuracy. None of the studies met all of Lijmer’s criteria and six of eight studies concerned children, mostly in a secondary care environment. Unfortunately useful quantitative data were lacking in four studies of adults.51 54 56

Methodological considerations

We included all studies with usable quantitative data (sensitivity, specificity, and likelihood ratios) in the statistical analysis, irrespective of the quality assessment. In the sensitivity analysis we compared areas under the curve of the studies that met the Lijmer criteria with those that did not. Although the studies considered for our first research question were of variable methodological quality, the data for the subgroup of adults were robust. For our second research question we were not able to pool and compare the areas under the curve because of statistical heterogeneity. In the future, more methodologically sound diagnostic studies need to be reported to be able to draw conclusions regarding the diagnostic accuracy of C reactive protein in infection of the lower respiratory tract. The recently formulated guidelines for diagnostic studies (STARD, www.consort-statement.org/stardstatement.htm) will probably have an important role in this process.

Quality of included studies

We used the guidelines of the Cochrane method group on systematic reviews of screening and diagnostic tests to assess the quality of the included studies, but we did not assess the quality of the reference standard for each study. The results of a chest radiograph (infiltrate or no infiltrate) and of microbiological work-up (bacterial or viral aetiology) depend on the methods used. For example, the interpretation of chest radiographs is variable between radiologists, the presence of an infiltrate depends on the duration of illness, new microbiological techniques have been developed in recent decades, and the relation between bacterial colonisation and pathogenesis of lower respiratory tract infection cannot always be established.50 56

We investigated the diagnostic accuracy of C reactive protein in detecting bacterial aetiology of lower respiratory tract infection. Studies were highly heterogeneous, both statistically and

First research question: Infiltrate on radiograph

In the first part of the study, where we assessed the diagnostic accuracy of C reactive protein in detecting radiologically defined pneumonia, we found an area under the curve of 0.80 (95% confidence interval 0.75 to 0.85) in adults. The clinical applicability of these results depends largely on the epidemiological characteristics of a population. In general practice, where the prevalence of radiographically evident pneumonia is low, the positive predictive value will be lower and the negative predictive value will be higher than in populations with a higher pretest probability of an infiltrate on chest radiograph. The practical use of the sensitivities and specificities as presented in table B (see online materials) will probably have an important role in this process.
Primary care

Table 2 Characteristics of 17 retrieved studies testing for C reactive protein in infections of the lower respiratory tract, with reference test infiltrate on chest radiograph (first research question) or aetiological microbiological diagnosis (second research question)

<table>
<thead>
<tr>
<th>Author</th>
<th>Sample size</th>
<th>Age in years</th>
<th>Participants and setting</th>
</tr>
</thead>
<tbody>
<tr>
<td>Flanders et al 2004</td>
<td>168</td>
<td>&gt;18</td>
<td>Adults with acute cough at emergency department or acute care ambulatory clinic of the University of California, San Francisco, USA</td>
</tr>
<tr>
<td>Almirall et al 2004</td>
<td>226</td>
<td>&gt;14</td>
<td>Adults with symptoms of infection of the lower respiratory tract and focal signs presenting at primary or secondary care in the Maresme region, Spain</td>
</tr>
<tr>
<td>Hopstaken et al 2003</td>
<td>246</td>
<td>18–89</td>
<td>Adults in the southern part of the Netherlands, who presented to their general practitioner with symptoms and signs of infection of the lower respiratory tract</td>
</tr>
<tr>
<td>Metbye et al 1992</td>
<td>402</td>
<td>&gt;18</td>
<td>Adults with symptoms suggestive of respiratory or throat infection in general practice, Norway</td>
</tr>
<tr>
<td>Babu et al 1989</td>
<td>65</td>
<td>2 months-12</td>
<td>Children with a diagnosis of infection of the lower respiratory tract at Nehru Hospital, India</td>
</tr>
<tr>
<td>Metbye et al 1988</td>
<td>71</td>
<td>&gt;15</td>
<td>Adults who were treated with antibiotics by a general practitioner for a suspected pneumonia, Norway</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Distinction between viral and bacterial aetiology</th>
</tr>
</thead>
<tbody>
<tr>
<td>Almirall et al 2004</td>
</tr>
<tr>
<td>Prat et al 2003</td>
</tr>
<tr>
<td>Requejo et al 2003</td>
</tr>
<tr>
<td>Garcia Vazquez et al 2003</td>
</tr>
<tr>
<td>Virki et al 2002</td>
</tr>
<tr>
<td>Hedlund et al 2000</td>
</tr>
<tr>
<td>Heikkenen et al 2000</td>
</tr>
<tr>
<td>Nohynek et al 1996</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Author</th>
<th>Sample size</th>
<th>Age in years</th>
<th>Participants and setting</th>
</tr>
</thead>
<tbody>
<tr>
<td>Osterdike et al 1995</td>
<td>198</td>
<td>&gt;18</td>
<td>Adults with community acquired pneumonia admitted to Danderyd Hospital, Sweden</td>
</tr>
<tr>
<td>Korppi et al 1993</td>
<td>209</td>
<td>&lt;15</td>
<td>Children treated for infection of the middle respiratory tract* or the lower respiratory tract at Korppi University Hospital, Finland</td>
</tr>
<tr>
<td>Kerttula et al 1987</td>
<td>79</td>
<td>&gt;15</td>
<td>Adults admitted for suspected community acquired pneumonia to Aurora Hospital, Helsinki, Finland</td>
</tr>
<tr>
<td>McCarthy et al 1978</td>
<td>156</td>
<td>1 month-16</td>
<td>Children with radiologic pulmonary infiltrate at paediatric emergency room, Yale-New Haven Hospital, USA</td>
</tr>
</tbody>
</table>

*Term not specified by the authors of the original study.

Limitations of the model

We applied a statistical model for diagnostic reviews, based on that of Midgette et al.30 31 The methods using a summary receiver operating characteristic curve deal with the problem of different cut-off points in studies and is useful in providing an overall diagnostic accuracy by means of the area under the curve. However, it does not directly provide an exclusive estimate of optimal sensitivity and specificity. The question of which C reactive protein value can be used to obtain optimal sensitivity and specificity can unfortunately not be answered.

Conclusion

The methodological quality of the diagnostic studies is generally poor. The current evidence does not consistently and sufficiently support a wide introduction of C reactive protein as a rapid test to guide antibiotics prescription.

We thank Jordi Almirall, Intensive Care Unit, Hospital de Mataró, Barcelona, Spain; Rogier M Hopstaken, Department of General Practice, Maastricht University, Netherlands; Hase Melbye, Institute of Community Medicine, University of Tromsø, Norway; and Cristina Prat, Serviè de Microbiologia, Hospital Universitari Germans Trias I Pujol, Badalona, Spain for making additional data available for this review. This systematic review was conducted according to the checklist and flow diagram of the QUOROM Statement (www.consort-statement.org/evidence.html#quorom).

Contributors: VvdM collected data, performed the analysis and wrote the manuscript. AKN performed the analysis and revised the paper. PJvdB extensively revised the paper. WJJA conceived the study and extensively revised the paper. VvdM and WJJA are guarantors.

Funding: None.

Competing interests: None declared.

Ethical approval: Not required.

Measurements of C reactive protein are presented in ascending order.

Requejo et al 2003 (CRP:+/-)42
Virkki et al 2002 (CRP:120)36
Prat et al 2003 (CRP:100)41
Kerttula et al 1987 (CRP:80)49
Nohynek et al 1995 (CRP:40)46
Heiskanen et al 2000 (CRP:60)45
Virkki et al 2002 (CRP:80)36
Heiskanen et al 2000 (CRP:40)45
Virkki et al 2002 (CRP:60)45
Korppi et al 1993 (CRP:20)48
Nohynek et al 1995 (CRP:20)46
Prat et al 2003 (CRP:20)41
Melbye et al 1992 (CRP:50)40
Hopstaken et al 2003 (CRP:100)37
Almirall et al 2004 (CRP:100)34
Flanders et al 2004 (CRP:40)17
Babu et al 1989 (CRP:35)38
Melbye et al 1992 (CRP:20)42
Babu et al 1989 (CRP:20)42
Melbye et al 1988 (CRP:11)43
Hoptstaken et al 2004 (CRP:20)37
Flanders et al 2004 (CRP:11)37
Meltby et al 1988 (CRP:11)43
Meltby et al 1988 (CRP:11)43
Flanders et al 2004 (CRP:40)17
Meltby et al 1992 (CRP:50)40
Prat et al 2003 (CRP:11)17
Heiskanen et al 2000 (CRP:20)46
Nohynek et al 1995 (CRP:20)46
Korppi et al 1993 (CRP:40)46
Virkki et al 2002 (CRP:40)35
Prat et al 2003 (CRP:60)41
Heiskanen et al 2000 (CRP:60)46
Virkki et al 2002 (CRP:60)41
Nohynek et al 1995 (CRP:11)46
Korppi et al 1993 (CRP:11)46
Kerthula et al 1987 (CRP:11)46
Almirall et al 2004 (CRP:100)34
Prat et al 2003 (CRP:100)41
Almirall et al 2004 (CRP:120)41
Virkki et al 2002 (CRP:20)42
Reguej et al 2003 (CRP:+/-)42

Fig 2 Sensitivity-specificity plot (with 95% confidence intervals) of C reactive protein in relation to detection of an infiltrate (top) or bacterial aetiology (bottom). Measurements of C reactive protein are presented in ascending order.

Primary care

Primary care

Fig 3

What is already known on this topic

Irrational prescription of antibiotics for respiratory tract infections is partly caused by diagnostic uncertainty about the presence of an infiltrate and about bacterial aetiology.

Tests for C-reactive protein are increasingly used to guide antibiotic prescribing for infections of the lower respiratory tract.

Some recently published studies report useful diagnostic accuracy of C-reactive protein in infections of the lower respiratory tract.

What this study adds

C-reactive protein testing is neither sufficiently sensitive to rule out nor specific enough to rule in an infiltrate on chest radiograph and bacterial aetiology of infections of the lower respiratory tract.

The use of tests for C-reactive protein to guide antibiotic prescription in lower respiratory tract infection is not consistently supported by the present evidence.

What this study adds

C-reactive protein testing is neither sufficiently sensitive to rule out nor specific enough to rule in an infiltrate on chest radiograph and bacterial aetiology of infections of the lower respiratory tract.

The use of tests for C-reactive protein to guide antibiotic prescription in lower respiratory tract infection is not consistently supported by the present evidence.

What this study adds

C-reactive protein testing is neither sufficiently sensitive to rule out nor specific enough to rule in an infiltrate on chest radiograph and bacterial aetiology of infections of the lower respiratory tract.

The use of tests for C-reactive protein to guide antibiotic prescription in lower respiratory tract infection is not consistently supported by the present evidence.