

# Diagnostic value of signs, symptoms and laboratory values in lower respiratory tract infection

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## Summary

**Background:** Lower respiratory tract infections (LRTI) account for the majority of all antibiotics prescribed in the clinical practice, irrespective of the fact that most cases are self-limiting. Using the outcome and microbiology findings as gold standard, we determined sensitivity, specificity, positive and negative predictive values of common used signs and symptoms of bacterial LRTI requiring antibiotic therapy.

**Patients:** 243 consecutive patients with suspected LRTI admitted to a tertiary care hospital.

**Results:** Bacterial LRTI requiring antibiotic therapy and self-limiting LRTI were diagnosed in 32 and 86 patients, respectively. Assessing these two groups, sputum, dyspnea, crackles, fever and leukocytes (WBC) were insensitive and unspecific parameters for the diagnosis of bacterial LRTI requiring antibiotic therapy. Cough was

sensitive (93.8%) but unspecific (5.8%). The sensitivity of infiltrates, C-reactive protein (CRP) >50 mg/L and procalcitonin (PCT) >0.1 ng/mL was 96.9%, 93.8% and 93.8%, respectively. PCT >0.25 ng/mL showed the highest specificity (97.7%), followed by WBC >16 × 10<sup>9</sup>/L (94.2%) and CRP >100 mg/L (91.9%). The sensitivity of WBC >16 × 10<sup>9</sup>/L was low (37.5%).

**Conclusion:** The overall sensitivity and specificity of signs and symptoms for bacterial LRTI requiring antibiotic therapy was poor. Obtaining a chest-X-ray with infiltrates and determining CRP at a cut-off value of 50 mg/L or PCT at a cut-off value of 0.1 ng/mL was required to ascertain the need for antibiotics in LRTI.

**Key words:** laboratory markers; bacterial infection; procalcitonin; LRTI

## Introduction

Lower respiratory tract infections (LRTI), including acute bronchitis, acute exacerbations of chronic bronchitis, asthma exacerbations, and pneumonia, are the leading cause of consultation in primary care medicine. In the out-patient setting, they account for the majority of all antibiotics prescribed, burdening healthcare drug budgets [1, 2]. In most of the adults with LRTI, the illness is self-limiting and its course will not be modified by antibiotic therapy, representing viral or clinically non-relevant bacterial diseases [3–5]. However, failure to initiate antibiotic therapy within four hours in cases of community acquired pneumonia is already associated with an increased mortality [6]. The major problem in the management of the LRTI is the inability to determine the causative micro-organism in the majority of patients [7–9]. Furthermore, the presence of

positive serological or microbiological results does not necessarily prove or refute causality, especially in acute exacerbations of COPD. Thus, the main goal of the initial clinical evaluation is to determine whether the patient presents features suggesting the presence of a bacterial infection that is not self-limiting, ie bacterial pneumonia and severe exacerbations of COPD. Laboratory markers, including serum concentrations of C-reactive protein and leukocyte-counts are commonly used tests for diagnosis and monitoring of different inflammatory processes, despite not being specific markers for bacterial infection [10–12]. More recently, we could show that procalcitonin is reliable marker to guide antimicrobial therapy in LRTI [13]. Considering clearing of symptoms and laboratory abnormalities with and without antibiotics as the main outcome para-

meter, we aimed to determine the accuracy of commonly used clinical and laboratory findings

to diagnose bacterial LRTI, ie LRTI requiring antibiotic therapy.

## Methods

This analysis was based on an intervention trial including 243 patients comparing the routine use of antimicrobial therapy versus procalcitonin-guided antimicrobial treatment for LRTI [13]. In brief, during a 4-month period in 2003, all patients with suspected LRTI, admitted to the medical emergency department of the University Hospital of Basel, Switzerland, were reviewed for inclusion in this study. LRTI was suspected if patients presented with respiratory symptoms as main complains. CAP was defined as the presence of a new infiltrate in the chest-X-ray accompanied by respiratory symptoms (ie cough, dyspnea, fever, abnormal breath sounds on auscultation and leukocytosis or leucopenia with onset before admission to the hospital) according to the ATS guidelines [14]. Chronic obstructive pulmonary disease was defined when patients complained of cough, sputum production or dyspnea in the presence of a post bronchodilator FEV<sub>1</sub> <80% of the predicted value in combination with an FEV<sub>1</sub>/FVC <70%, as proposed by the GOLD guidelines [15]. Acute bronchitis was defined as cough lasting from 2 to 14 days with or without sputum production in the absence of an underlying lung disease and infiltrates on chest-X-ray [16]. The diagnosis of asthma exacerbation was defined by a history of episodic symptoms of airflow obstruction, which is at least partially reversible, as assessed by spirometry [17]. 243 patients were enrolled in the study. On admission, patients were submitted to a panel of diagnostic tests, including blood sampling for white blood counts, C-reactive protein, procalcitonin, blood cultures and a chest-X-ray, according to the standardised study protocol and to the current clinical practice in this institution. Sputum for microbiological cultures according to Murray's criteria was sampled if available [18]. As needed, bronchoalveolar lavage was performed, including culture and/or PCR for *Legionella pneumophila*, *Chlamydia pneumoniae* and *Mycoplasma pneumoniae*. Blood samples were also taken for serological testing

for adenovirus, influenza A, influenza B, parainfluenza virus type 1 to 3, respiratory syncytial virus (RSV), coxsackie B5, cytomegalovirus (CMV), Epstein-Barr virus (EBV), herpes simplex virus type 1 (HSV-1), and varicella zoster virus (VZV) as well as *Mycoplasma pneumoniae*. Virus serology was considered positive if IgM was above established levels, and/or seroconversion of IgG between the acute and convalescence serum samples was detected, and/or very high levels of IgG were documented [19]. All IgM positive samples were re-tested after the removal of IgG and of the rheumatoid factor using IgM sample preparation reagent (Orgenium Laboratories). To eliminate false positivity and possible polyclonal antibody responses to viruses of the herpes group we defined only cases with IgM positivity as true positive in the herpes virus group. Cut-off levels for IgG and IgM in enzyme immunoassay unit (EIU) were: adenovirus (≥100, ≥25); influenza A (≥100, ≥30); influenza B (≥100, ≥45); parainfluenza virus type 1 to 3 (≥100, ≥25); RSV (≥100, ≥30); coxsackie B5 (≥100, ≥25); CMV (≥100, ≥25); EBV (≥100, ≥40); HSV-1 (≥100, ≥25); and VZV (≥100, ≥25) as well as *Mycoplasma pneumoniae* (≥100, ≥50), respectively [19].

These tests were performed on admission and repeated at follow-up foreseen two to three weeks later. In patients presenting an infiltrate in chest-X-ray, search for *Legionella pneumophila* antigen in urine was routinely performed. On a weekly basis, subjects were randomised either to a standard antimicrobial therapy or to a procalcitonin-guided therapy. In both groups, the final decision regarding antibiotic therapy was left at the discretion of the attending physician. However, in the procalcitonin-guided group, attending physicians were advised to follow the antibiotic prescription algorithm based on procalcitonin values. A serum procalcitonin level of ≤0.1 ng/mL was considered to indicate the absence of bacterial infection and the use of antibiotics was discouraged. Values ≥0.25 ng/mL were considered to indicate a possible bacterial infection and antibiotics were encouraged. Except for procalcitonin values, results of all other diagnostic tests (including chest-x-ray, C-reactive protein, white blood counts) were available to the attending physician in both randomised groups.

According to microbiology results and outcome (resolution of complains and laboratory abnormalities without antimicrobial therapy), patients were classified in three groups: (1) bacterial infection requiring antibiotic therapy (proven bacterial growth in blood cultures or sputum cultures [in the absence of COPD]); (2) self-limiting infection (resolution of complains and laboratory abnormalities without antimicrobial therapy, irrespective of microbiological studies) and (3) possible bacterial infection (all other cases).

Thereafter, sensitivity, specificity, predictive positive value, negative predictive value for different clinical parameters (cough, sputum, discoloured sputum, dyspnea, crackles, fever), laboratory parameters (leukocyte counts, c-reactive protein, procalcitonin), and the presence of an infiltrate on the chest-x-ray were calculated

### Blood sampling and assays

EDTA samples were collected and C-reactive protein levels were measured on a Hitachi Instrument 917 (Roche Diagnostics, Rotkreuz Switzerland, using reagents by

**Table 1**

Baseline characteristics of 243 patients with lower respiratory tract infection

Age mean (SD), years	64 (19)
Men (%)	128 (53%)
Current smokers (%)	62 (26%)
Antibiotic pre-treatment (%)	49 (20%)
<i>Coexisting illnesses</i>	
Coronary artery disease	59 (24%)
Congestive heart failure	18 (7%)
Peripheral vascular disease	19 (8%)
Cerebrovascular disease	9 (4%)
Renal insufficiency	40 (17%)
Liver dysfunction	12 (5%)
Diabetes mellitus	32 (13%)
<i>Final diagnosis</i>	
Community acquired pneumonia	87 (36%)
Acute exacerbation of COPD	60 (25%)
Acute bronchitis	59 (24%)
Acute exacerbation of asthma	13 (5%)
other	24 (10%)

\* COPD denotes chronic obstructive pulmonary disease.

Wako Chemicals GmbH, Neuss, Germany). Procalcitonin was measured by a newly developed sensitive immunofluorescent immunoassay (Kryptor<sup>®</sup> PCT, Brahms Diagnostica, Berlin, Germany) with an improved functional sensitivity of 0.06 ng/ml, ie 3- to 5-fold above normal mean values [20]. *Legionella pneumophila* antigen in urine was detected using Legionela now Binax Real-time-PCR using a light cyclor was performed for bacterial detection in the BAL. Virus serology was performed using

a commercially available, sensitive enzyme immunoassay (EIA) for IgG and IgM (Orgenium, Turku, Finland).

**Statistical analysis**

Given the observational character of the present study, we only report descriptive statistics [21]. Quantitative variables are summarized by means and standard deviations, and the Spearman rank correlation coefficient was used to describe associations between quantitative variables.

**Results**

The mean age of the 243 patients was 64 years (range 17 to 96) and 52% were male. Final diagnoses were community acquired pneumonia in 87, acute exacerbations of COPD in 60, acute bronchitis in 59, acute exacerbation of asthma in 13, and other diagnoses in 24. A total of 8 patients died and 13 were lost to follow-up.

Bacterial LRTI requiring antibiotic therapy infection was diagnosed in 32 and self-limiting LRTI in 86 patients (see figure 1). Microorganisms were cultured from the blood stream in 16 cases (11 *Streptococcus pneumoniae*, 3 *Escherichia coli*, *Pseudomonas* spp. and *Klebsiella* spp. 1 case each) and in sputum and/or bronchoalveolare lavage in 23 cases (10 *Streptococcus pneumoniae*, 3 *Pseudomonas* spp., 3 *Moraxella catarrhalis*, 2 *Klebsiella* spp., 2 *Enterobacteriaceae*, 2 *H influenzae*, *Streptococcus milleri*, coagulase negative *Staphylococcus*, *Enterococcus*, and *Mycoplasma pneumoniae* 1 case each). In 3 cases, 2 different organisms grew in sputum. In 7 cases, bacterial growth was observed both in the blood culture and in sputum/or bronchoalveolare lavage.

In the group with self-limiting LRTI, virus serology was positive in 84% (63/75) of patients. Parainfluenza virus type 3 (n = 19), influenza B (20) and adenovirus (12) were the most frequent viral infections. Similarly, in the group with bacterial LRTI requiring antibiotic therapy, a positive virus serology was noted in 82% (23/28) of cases. Serological evidence of acute *Mycoplasma pneumoniae* infection

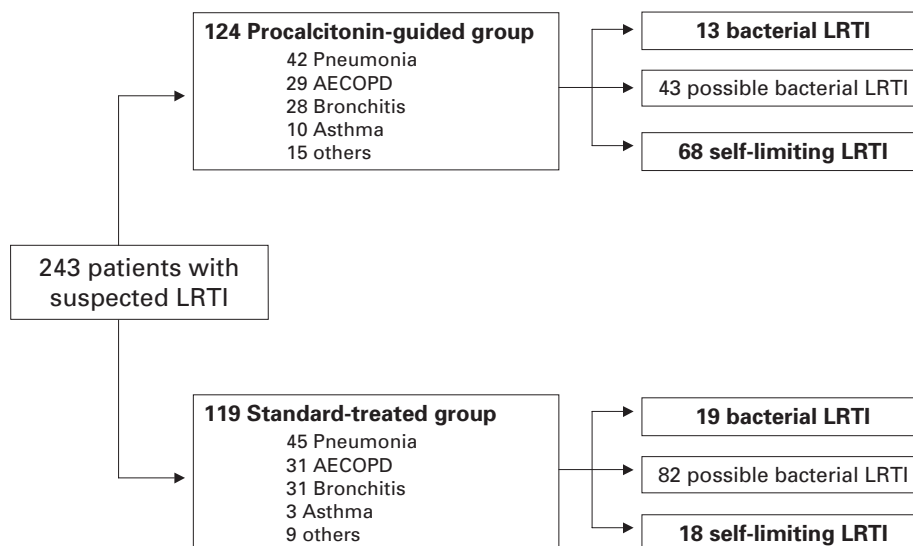
was found in 3 cases classified as self-limiting LRTI, and this microorganism was cultured in the bronchoalveolar lavage from one patient with bacterial LRTI. *Legionella pneumophila* and *Chlamydia pneumoniae* have not been detected in the bronchoalveolar lavage fluid of those who underwent bronchoscopy. No patient had a positive *Legionella pneumophila* urine test. In 125 cases bacterial infection could be neither proven nor reliably excluded.

Clinical and laboratory parameters in the three diagnostic groups are shown in table 2. Crackles and infiltrates were more common in patients presenting bacterial LRTI requiring antibiotic therapy. Accordingly, body temperature, leukocyte counts and C-reactive protein levels were higher in these patients.

The diagnostic value of signs, symptoms and laboratory values for detecting bacterial LRTI requiring antibiotic therapy is presented in table 3. Comparing patients with bacterial LRTI requiring antibiotic therapy (n = 32) and patients with self-limiting LRTI (n = 86), sputum, dyspnea, crackles, fever and moderately elevated leukocyte counts (>12 × 10<sup>9</sup>/L) presented poor sensitivity and specificity. Cough was one of the inclusion criteria in this study, and therefore, very sensitive and not specific. Markedly elevated leukocyte counts (>16 × 10<sup>9</sup>/L) were specific but not sensitive. Infiltrates on chest-x-ray showed a very good sensitivity, acceptable specificity and good negative predictive value. C-reactive protein was a very sensi-

**Figure 1**

Trial profile. AB denotes antibiotics, AECOPD acute exacerbation of COPD.



**Table 2**

Clinical and laboratory parameters in the group of patients with bacterial lower respiratory tract infection (LRTI) requiring antibiotic therapy (bacterial LRTI), possible bacterial LRTI and self-limiting LRTI. Values are percentages (absolute numbers) or medians (interquartile range).

	<b>Bacterial LRTI n = 32</b>	<b>Possible bacterial LRTI n = 125</b>	<b>Self-limiting LRTI n = 86</b>
Cough (%)	31 (97%)	109 (87%)	83 (97%)
Sputum production (%)	24 (75%)	82 (66%)	60 (70%)
Discoloured sputum (%)	14 (44%)	56 (45%)	34 (40%)
Dyspnea (%)	22 (69%)	73 (58%)	66 (77%)
Crackles (%)	23 (72%)	42 (34%)	22 (26%)
Chest-X-ray Infiltrate (%)	32 (100%)	71 (57%)	12 (14%)
SaO <sub>2</sub> <90% (%)	6 (19%)	19 (15%)	9 (10%)
Fever (>38 °C) (%)	19 (59%)	51 (41%)	24 (28%)
WBC ×10 <sup>9</sup> /L (IQR)	14.4 (10.5–23.0)	11.1 (8.1–15.9)	9.22 (6.2–12.2)
CRP mg/L (IQR)	239 (160–260)	58 (22–134)	24 (4–51)
PCT ng/mL (IQR)	1.97 (0.39–6.22)	0.14 (0.07–0.65)	0.07 (0.04–0.10)

\* IQR denotes interquartile range.

**Table 3**

Usefulness of clinical and laboratory parameters to identify bacterial LRTI requiring antibiotic therapy. Three different analyses are shown (x, y, z) x excludes patients with possible bacterial infection (n = 118), y includes patients with possible bacterial infection classed as bacterial LRTI (n = 243) and z includes patients with possible bacterial infection classed as self-limiting LRTI (n = 243).

	<b>Sensitivity % x (y, z)</b>	<b>Specificity % x (y, z)</b>	<b>PPV % x (y, z)</b>	<b>NPV % x (y, z)</b>
Cough	<b>94</b> (93, 94)	<b>6</b> (6, 7)	<b>27</b> (64, 13)	<b>71</b> (31, 88)
Sputum production	<b>75</b> (71, 71)	<b>34</b> (33, 31)	<b>29</b> (66, 14)	<b>76</b> (38, 88)
Discoloured sputum	<b>44</b> (45, 41)	<b>62</b> (61, 57)	<b>29</b> (67, 13)	<b>74</b> (38, 93)
Dyspnea	<b>66</b> (63, 69)	<b>27</b> (26, 33)	<b>25</b> (61, 14)	<b>68</b> (28, 88)
Crackles	<b>69</b> (43, 72)	<b>74</b> (76, 69)	<b>51</b> (76, 26)	<b>87</b> (42, 94)
Infiltrate	<b>97</b> (54, 100)	<b>86</b> (87, 70)	<b>73</b> (88, 34)	<b>99</b> (51, 100)
SaO <sub>2</sub> <90%	<b>19</b> (17, 18)	<b>91</b> (91, 87)	<b>43</b> (77, 18)	<b>75</b> (38, 88)
<i>Temperature</i>				
>38 °C	<b>59</b> (48, 65)	<b>72</b> (71, 62)	<b>44</b> (75, 21)	<b>84</b> (44, 92)
>39 °C	<b>25</b> (20, 32)	<b>88</b> (88, 85)	<b>100</b> (75, 25)	<b>78</b> (38, 89)
<i>Leukocyte count</i>				
>12 × 10 <sup>9</sup> /L	<b>69</b> (49, 66)	<b>74</b> (74, 63)	<b>48</b> (78, 21)	86 (45, 92)
>16 × 10 <sup>9</sup> /L	<b>38</b> (28, 38)	<b>94</b> (95, 83)	<b>71</b> (92, 26)	80 (42, 90)
<i>C-reactive protein</i>				
>50 mg/L	<b>94</b> (61, 97)	<b>72</b> (73, 59)	<b>56</b> (81, 26)	<b>97</b> (51, 99)
>100 mg/L	<b>84</b> (44, 84)	<b>92</b> (94, 78)	<b>80</b> (93, 37)	<b>94</b> (48, 97)
<i>Procalcitonin</i>				
>0.1 ng/mL	<b>94</b> (67, 94)	<b>72</b> (71, 53)	<b>55</b> (81, 23)	<b>97</b> (54, 98)
>0.25 ng/mL	<b>84</b> (50, 84)	<b>98</b> (98, 75)	<b>93</b> (98, 34)	<b>94</b> (52, 96)

\* PPV = positive predictive value, NPV = negative predictive value

tive parameter with excellent negative predictive values at a cut-off value of 50 mg/L.

Patients with possible bacterial infection were classified first as bacterial LRTI (table 3 and 4, y) and then as self-limiting LRTI (Table 3 and 4, z) for further analyses. As expected, accuracy measures, particularly positive and negative predictive values, were affected depending on whether the group of possible bacterial infection was assumed to be bacterial LRTI or self-limiting LRTI. Sensitivity and specificity of cough, sputum production, discoloured sputum, dyspnea, crackles, fever (>38 °C and >39 °C), and moderately elevated leukocyte counts (>12 × 10<sup>9</sup>/L) did not change significantly, irrespective of group assumptions. However, accuracy measures for infiltrates, markedly elevated leukocyte (>16 × 10<sup>9</sup>/L) counts, C-reactive protein and procalcitonin varied considerably depending on group definitions.

The usefulness of procalcitonin to detect bacterial LRTI requiring antibiotic therapy is additionally reported in table 4. Since potentially biased, as used to guide antibiotic therapy in half of the cases, data is presented for both the standard and procalcitonin-guided group separately. Procalcitonin presented a high sensitivity and specificity at the cut-off value of 0.1 ng/mL and 0.25 ng/mL, respectively. Both positive and negative predictive values of procalcitonin at a cut-off value of 0.25 ng/mL reached over 93%. The positive predictive value of procalcitonin at a cut-off value of 0.1 ng/mL in the procalcitonin-guided group was 40% compared to 73% in the standard-group, reflecting the antibiotic prescription algorithm based on procalcitonin values. There was a moderate correlation between C-reactive protein and procalcitonin levels (R<sup>2</sup> = 0.46).

**Table 4**

Usefulness of procalcitonin to identify bacterial LRTI requiring antibiotic therapy. Three different analyses are shown (x, y, z). x excludes patients with possible bacterial infection, y includes patients with possible bacterial infection classed as bacterial LRTI, and z includes patients with possible bacterial infection classed as self-limiting LRTI.

	All patients n = 118 (243, 243)		Procalcitonin guided-group n = 81 (124, 124)		Standard treated-group n = 37 (119, 119)	
	0.1 ng/mL	0.25 ng/mL	0.1 ng/mL	0.25 ng/mL	0.1 ng/mL	0.25 ng/mL
sensitivity	94 (67, 94)	84 (50, 84)	92 (78, 92)	77 (66, 83)	95 (60, 95)	90 (41, 85)
specificity	72 (71, 53)	98 (98, 75)	75 (73, 54)	99 (99, 74)	61 (65, 52)	94 (95, 76)
PPV **	55 (81, 23)	93 (98, 34)	40 (71, 18)	91 (97, 26)	73 (89, 29)	94 (98, 42)
NPV ***	97 (54, 98)	94 (52, 96)	98 (79, 98)	96 (76, 98)	93 (25, 98)	86 (25, 96)

\*\* PPV = positive predictive value, \*\*\* NPV = negative predictive value

## Discussion

The prescription of antibiotic therapy in LRTI is often guided by clinical signs and symptoms, despite limited scientific evidence. Based on our data, the majority of routinely used clinical parameters had an insufficient diagnostic accuracy to identify patients with bacterial infection, ie patients in whom antimicrobial treatment for LRTI was required. In contrast, the presence of infiltrates in the chest-X-ray as well as C-reactive protein and procalcitonin levels at well defined cut-offs provided a more adequate discrimination between patients with and without bacterial LRTI requiring antibiotic therapy. Procalcitonin levels below 0.1 ng/mL excluded bacterial LRTI requiring antibiotic therapy, while levels higher than 0.25 ng/mL indicated the need for antibiotics. Similarly, a cut-off value of 50 mg/L for C-reactive protein seemed equally safe to withhold antibiotics whereas a cut-off value of 100 mg/L denoted bacterial LRTI.

In contrast to former studies, we have defined the gold standard for bacterial infection according to both 1) the response to therapy and 2) microbiology results. The choice to include outcome in the definition of the gold standard allowed us to predict antibiotic-responsive illness, rather than bacterial infection. This approach may have underestimated the presence of bacterial infection, as a large proportion of bacterial respiratory tract infections will have a favourable outcome even in the absence of antibiotic therapy. This is supported by large amounts of historical data from the preantibiotic era. Hence, in nonpneumonic LRTI, particularly COPD exacerbations – in contrast to community acquired pneumonia – the key question appears to be whether the host can successfully deal with the severity of the illness, rather than simply whether bacteria can be cultured or not. Correspondingly, in this study, positive sputum bacteriology did not preclude recovery without antibiotics in acute COPD exacerbations, assuming procalcitonin levels were below 0.25 ng/mL.

The goal of this study was to characterise the usefulness of signs and symptoms in helping the clinician to decide whether antibiotics are deemed mandatory or not, rather than to predict microbiologic findings. Thus, we refrained from performing a bronchoscopic evaluation in all patients. Yet,

even if all invasive diagnostic steps were taken, aetiological pathogens may still remain undiscovered in the majority of the cases [22, 23]. Conversely, more than one pathogenic organism might be responsible for the infection in any given patient, ie a combination of bacteria and viruses [24, 25]. In our patients, viral serology results were positive in more than 80% of the cases, both in patients with and without bacterial infection. Accordingly, a positive viral serology was found in 35% to 75% of immunocompetent adults hospitalised with LRTI in previous studies [26, 27]. Therefore, serological documentation of acute viral infection does not exclude concomitant relevant bacterial infection. Correspondingly, most of our patients with positive blood cultures also demonstrated serologic evidence of an acute viral infection.

Paralleling the topic of LRTI, which *per se* has an inherent weakness – the lack of a reliable gold standard for relevant bacterial infection – our study has some limitations. As neither bacteriology – due to its low sensitivity – nor a single clinical parameter can be used as gold standard to diagnose relevant bacterial LRTI, the only evidence based approach to define which patients require antibiotics is the outcome. Therefore, a randomised trial analysing the outcome with and without antibiotics would be needed. While theoretically ideal, a study that randomly withholds delivery of antibiotic treatment for potential lethal bacterial infection would present substantial ethical challenges.

Taking into account that cases in whom bacterial infection was neither confirmed nor ruled out may potentially bias the measures of accuracy of diagnostic parameters, results were presented both excluding and including this “undefined” diagnostic group. As showed in tables 3 and 4, accuracy measures of most parameters varied according to the assumption made in regard to the “possible bacterial LRTI” group. Still, cases of “possible bacterial infection” are not a new finding: most former studies classifying patients with LRTI in bacterial or viral describe this largely used entity [22, 28]. Therefore, whereas clinical signs were clearly insufficient to diagnose the presence of bacterial LRTI requiring antibiotic therapy, the ultimate diagnostic accuracy of WBC, C-reactive protein and procalcitonin is difficult to define.

Another problem concerns a potential bias of the diagnostic accuracy of procalcitonin due to the design of the study, which used procalcitonin-guidance in one of the two arms. However, sensitivity and specificity at defined cut-offs were similar between both randomised groups, suggesting that a specific group-related bias was not relevant.

Despite efforts to develop diagnostic rules as guidance for antimicrobial treatment [25, 28–32], neither a single nor a combination of clinical findings seems to reliably predict radiological pneumonia. Physical examination alone has a sensitivity of 50% to 70% and specificity of 60% to 75% [33]. Physicians judgement has a negative and positive predictive value of 50% to 60% [34]. In our study, C-reactive protein at the cut-off value of 50 mg/L had a sensitivity and specificity to predict radiological pneumonia of 78.9% and 71.4%, respectively. Assuming the cut-off value of 100 mg/L, sensitivity and specificity reached 64.2% and 91.2%. Figures for procalcitonin were similar: sensitivity and specificity were 77.9% and 63.9% at the cut-off value of 0.1 ng/mL compared to 65.3% and 87.8% at the cut-off value of 0.25 ng/mL (data not shown). In contrast, sensitivity of markedly elevated leukocyte counts ( $>16 \times 10^9/L$ ) was only 25.3%.

A new infiltrate on chest-X-ray is often considered the gold standard for the diagnosis of CAP. However, the rate of pulmonary infiltrates in these patients was higher if a CT-scan was used [35]. Moreover, only 40% of radiographs were requested by the practitioners at the first presentation of the patient with LRTI [36]. Conversely, many self-limited pathogens and other conditions, eg tumours, lung congestion due to heart failure, can cause radiographic abnormalities in the setting

of LRTI [13]. Consequently, the presence of an infiltrate on a chest-X-ray should not be considered true microbial (= bacterial) pneumonia. In ambulatory medicine most of these patients should probably receive antibiotics. This may explain the differences of the diagnostic accuracy between radiological defined pneumonia and bacterial infection. Thereby, in the presence of radiological abnormalities, procalcitonin levels  $<0.1$  ng/mL and C-reactive protein levels  $<50$  mg/L suggested a differential diagnosis other than bacterial pneumonia, as reported in 10% of cases with suspected LRTI [13].

The need to promptly identify and treat patients with CAP in order to decrease mortality and length of hospital stay has been recently shown [37]. CAP is defined as the presence of a new infiltrate in the chest-X-ray accompanied by respiratory symptoms (ie cough, dyspnea, fever, abnormal breath sounds on auscultation) and leukocytosis or leucopenia [14]. The results of our study suggest that in order to both increase diagnostic accuracy for bacterial lower respiratory tract infection and avoid unnecessary antibiotic therapy in patients with self-limited infiltrates, it might be advisable to include either C-reactive protein or procalcitonin in the initial work-up.

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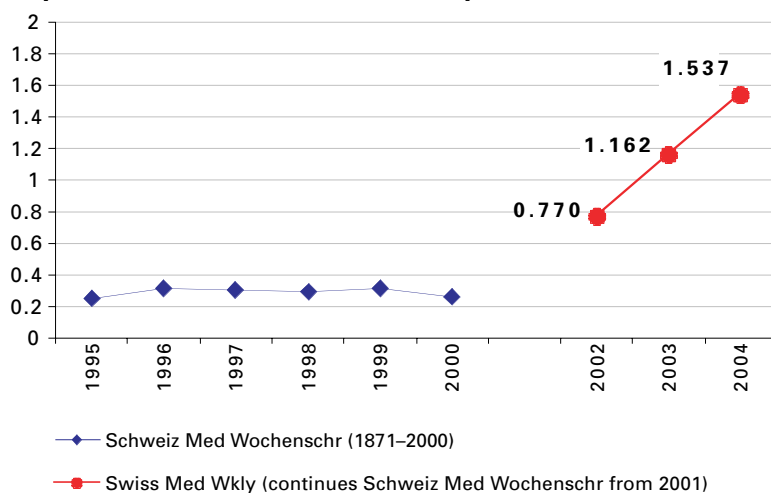
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