Empirical management of community-acquired pneumonia: impact of concurrent A/H1N1 influenza pandemic on guideline implementation

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Background: Guideline-concordant therapies have been proven to be associated with improved health and economic outcomes in the treatment of community-acquired pneumonia (CAP). However, actual use of CAP guidelines remains poor, but using tailored interventions looks promising. Based on local observations, we assessed the impact of low-intensity interventions to improve guideline use.

Methods: Pre- and post-intervention study with segmented regression analysis in a large tertiary care centre [University Hospitals Leuven (UZL)] and a smaller secondary care control hospital [Ziekenhuis Oost-Limburg (ZOL)] from October 2007 through to June 2010 in Belgium.

Results: A total of 477 patients were included in UZL, with 58.5% of the patients treated according to local guidelines. Guideline adherence remained stable, but a decrease (−28.6%; P = 0.021) was observed during guideline re-introduction in October 2009. Further analysis showed a high correlation with the concurrent A/H1N1 influenza pandemic (rpoint-biserial=0.683; P = 0.045) and with suspected influenza infection (odds ratio = 2.70; P = 0.038). In ZOL, 326 patients were enrolled, with 69.3% being treated concordantly. A similar, non-significant decrease in guideline adherence was observed after October 2009.

Conclusions: Our interventions did not lead to a higher proportion of CAP patients receiving guideline-compliant therapy. Instead, a compliance decrease was observed, coinciding with the peak in the A/H1N1 pandemic in the population. Similar observations could be made in ZOL. The widespread attention for this pandemic may have altered the perception of needed antibiotic therapy for pulmonary infections, bypassing our interventions and decreasing actual guideline compliance. Increased vigilance and follow-up is needed when epidemics with similar impact occur in the future.

Keywords: antimicrobial management, antibiotics, CAP

Introduction

Numerous guidelines to optimize the treatment of community-acquired pneumonia (CAP) have been published by several international and national societies while many hospitals have their own, locally adapted versions.3–4 CAP is a common infectious disease with substantial clinical and economic impact: the annual hospital cost is about €5.7 billion in Europe,5 while it averages $8.4–10 billion in North America.6 Important long-term effects on quality of life have also been associated with CAP infections.7,8 It has been proven that guideline-concordant therapies are associated with improved health outcomes and lower expenditures,9 including for more vulnerable elderly patients.10 However, for antibiotic guidelines in general, it is estimated that about 50% of patients are treated discordantly.11,12 For CAP, most studies show a similar order of magnitude of initial

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guideline adherence, ranging between 44% and 65%,
with an outlier up to 84%. Reviewing data from a previous
review showed similar compliance, with a median of 45%
(range 30%–70%). Consequently, numerous trials have tried
to increase the compliance rate by using a whole array of inter-
ventions. Reviews, however, have shown that most interventions
deliver only small to moderate improvements, and often fail
to consider the cultural, contextual and behavioural determin-
ants of antimicrobial use in different hospitals and countries. As
such, in order to improve intervention efficiency, tailoring to
the local situation appears promising. Here we report the
impact of low-intensity interventions, based on local obser-
vations, on the use of the empirical CAP treatment guidelines
in two Belgian hospitals. Concurrently, factors predicting non-
compliance were assessed.

Methods

This study was conducted in two Belgian hospitals: one large (1600 bed),
tertiary care hospital (University Hospitals Leuven (UZL)) and one medium
(800 bed), secondary care hospital with great expertise in pulmonary dis-

cases (Ziekenhuis Oost-Limburg (ZOL)). It was developed as a two-centre
intervention study with an interrupted time-series study design (Clinical-
Trials.gov identifier NCT00512772).

Patient population

We prospectively enrolled patients from 16 October 2007 until 1 July 2010
(UZL) and from 1 December 2007 until 1 June 2010 (ZOL). Eligible patients
met the following criteria: adult (>18 years old) patients, suspected or con-
formed diagnosis of pneumonia on admission and confirmed diagnosis of
pneumonia on discharge by the attending physician(s), radiological confir-
mation of a new pulmonary infiltrate, admitted through the emergency
department (ED), and with at least two of the following symptoms: fever
(>38.5°C) or hypothermia (<36°C), chills, excessive sweating, new cough
or changed sputa in the case of chronic cough, dyspnoea, abnormal lung
auscultation. Exclusion criteria were failure to obtain informed consent,
other major non-pulmonary infections, pneumonia not present on admis-
sion, patients with a recent history (within 30 days before admission) of
hospitalization, transfer from another hospital; death within 24 h of admis-
sion, (suspected) aspiration pneumonia, immunocompromised patients
(active haematological malignancies, asplenia, any dose of systemic glu-
socorticoids or other immunomodulating drugs, cytotoxic treatment
within the last 3 months, HIV infection), pregnancy, patients with cystic
fibrosis, admission for social reasons and patients in a palliative setting.
Patients with a known history of methicillin-resistant Staphylococcus
aureus (MRSA) or other multidrug-resistant (MDR) organisms were also
excluded. Patients were identified in the ED by P.-J. C. (in the case of UZL)
or H. L. (in the case of ZOL) through chart review, admission papers and
additional daily rounds in the ED. In accordance with the advice of both
Ethics Committees and national legislation, informed consent was
obtained for all patients before definitive inclusion and measures were
taken to protect patient privacy. Likewise, the managing physicians were
not identified.

Variables

For each patient, the CURB-65 (confusion–urea nitrogen–respiratory
rate–blood pressure–age 65 years of age) and pneumonia severity index
(PSI) scores were calculated at the time of admission. Patients with
both a CURB-65 score >2 and a PSI class equal to 5 were classified as
CAP IV, while other hospitalized CAP patients were defined as CAP
III. We have specifically chosen this criterion for CAP IV because using
this definition showed the highest correspondence with actual clinical
practice (Table S1, available as Supplementary data at JAC Online) and
because both scores should in fact be considered together. Empirical
therapies were assessed on two separate moments: on first dose, and
between 24 and 48 h after presentation. This latter timepoint was
chosen because therapy that is initiated by residents is frequently
adjusted after consultation with their supervisors, which usually takes
place within 24 h. Other included variables were additional co-morbidities
(diabetes, history of obstructive/restrictive lung pathology, dementia),
allergies (any documented adverse reaction related to antibiotic admin-
istration), any recent antibiotic therapy and whether the patient lived in a
nursing home or other long-term care facility. Because this study was still
ongoing during the 2009 A/H1N1 influenza pandemic, additional entries
were made for ‘suspected A/H1N1’ (patient tested for A/H1N1 infection
and/or A/H1N1 explicitly stated in differential diagnosis). During the
entire study, including the pandemic, there were no changes in the treat-
ment protocols. All data were extracted using the nursing and medical
files and the electronic patient management systems, and entered into
an electronic database (MS Access for Windows). The Belgian Scientific
Institute of Public Health (http://influenza.uiv-isp.be) provided us with
data on the national prevalence of influenza and influenza-like illness.

Interventions

The approach of our study was mainly observational and the interventions
used were of low complexity and intensity. This was due to limited
resources, to avoid interference with the normal hospital structures and
to maintain optimal cooperation with both hospitals. Also, previous
reviews stated that minor interventions may be equally or even more effi-
cient than more complex ones. First, we actively distributed the hospi-
tal antimicrobial guidelines at the start of their residency, starting early
August 2008 (Intervention 1). We used this active distribution because
in a previous study we found that most physicians failed to collect the
booklet at the secretarial office and this was felt to have an important influ-
ence on guideline knowledge. Such distribution of educational material is
expected to have a modest but consistent effect. Second, a questionnaire
on the use of antibiotic guidelines was distributed between mid-February
and the end of April 2009 (Intervention 2). Although not a real interven-
tion, we wanted to control for this event, as the distribution of this question-
aire and the heightened attention towards antibiotic guidelines might
lead to improved compliance. Unfortunately, the actual results of this
specific study were not available on time to be used in intervention
design. Third, an already planned update of the guideline booklet (no
changes to the CAP guidelines were made), including a bookmark reminder
on intravenous–oral switch and antibiotic streamlining was sent directly to
every physician in UZL. Use of the new booklet was also actively promoted
in mailings and on the intranet starting in mid-October 2009 (Intervention
3). Again, this distribution of written guidelines could deliver small but con-
sistent effects, but the supplementary promotion with accompanying
reminders were found to have moderately good effects. Finally, interim
analysis results (up to June 2009) were distributed among and discussed
between the research team and the major involved disciplines (general
internal medicine, including ED physicians, geriatrics and pulmonology)
during 1 h interactive team meetings where attendance was highly
expected (January–February 2010; Intervention 4). Individual feedback
was not available. The effects of such feedback are thought to be modest.
In ZOL, only the second (September–November 2009) and fourth
(September 2009) intervention were executed. No active redistribution
of the guideline booklet or promotion of the guidelines took place.

Outcome measures

Antibiotic choice for empirical therapy was assessed using a computer-
ized algorithm based on the local guidelines and accounting for CAP
classification (Table S2, available as Supplementary data at JAC Online), recent use of antibiotics with therapy duration >3 days, allergies and a history of chronic pulmonary disease. Primary outcomes were the overall proportion of patients treated according to the local CAP guidelines.

As a proxy measure for the overall use of the local antibiotic guidelines in UZL, an electronic counter was installed on the intranet/internet web site version. This provided weekly data on the number of hits on the guidelines’ main access page from 1 October 2007 through to 1 August 2010. For technical reasons, a similar tracker was not possible in ZOL. For both guideline compliance and web site use, no results were available for individual physicians.

The effect of the interventions on therapy compliance and the use of the intranet/internet version of the local guidelines was analysed using segmented regression analysis. A 2 month period was chosen, counting forwards and backwards from 15 October 2009 (re-introduction of the new guidelines), which allowed sufficient valid data points covering at least 30 patients. In ZOL, due to insufficient data, a more parsimonious analysis was done using the χ² test.

To assess predicting factors for guideline non-compliance, a backward logistic regression was used. Possible predictors were selected from the admission variables, severity scores, period and time of admission using a χ² test for dichotomous variables and point biserial correlations for continuous variables with P<0.10 as the inclusion criterion. All statistical analysis and assessment of guideline use were done using SPSS 16.0 for Windows. A P value <0.05 was considered significant for all other tests.

The web site data were analysed using an ARMAX intervention model using gretl 1.9.1 for Windows. A more detailed description of the analysis and parameter estimation is provided as Supplementary data (available at JAC Online).

Results

Patient characteristics

Of the 3327 patients with symptoms of respiratory tract infection that were screened in UZL, 2725 patients did not fulfill all inclusion criteria of CAP, 16 patients had a known history of MDR organisms, 11 patients died before informed consent could be obtained, 33 patients refused to participate in the study and 60 patients left the hospital before formal inclusion. Five patients had incomplete files and were also excluded from analysis. In total, 477 eligible patients gave their consent in UZL. In ZOL, 2012 patients were initially followed, of which 1533 patients did not fulfill all inclusion criteria, 4 patients were known with MDR microorganisms, 28 patients refused and no informed consent could be obtained for 110 patients. Eleven intensive care unit (ICU) patients could not be included due to local interference with other studies. In the end, 326 patients were included in ZOL. Patient characteristics are presented in Table 1.

For both hospitals, groups are comparable between the different evaluation periods. Only in the last period in ZOL were there fewer CAP IV patients, due to local interference with other concurrent studies in the ICU.

Intervention evaluation in UZL

For the whole period of the study, 58.5% of the patients were treated in line with CAP guidelines at the first dose. Twenty-four to 48 h after admission, this increased slightly to 60.6%. The major causes of deviation are represented in Table S3 (available as Supplementary data at JAC Online). Seventy-nine percent of deviations are related to CAP III patients, with the most common subtypes being the use of macrolides without specific risk factors for atypical pathogens and inappropriate use of intravenous quinolones, which are normally restricted to cases with β-lactam allergy. Adherence to the guidelines were shown to be initially constant, without apparent effects from re-introduction of the guidelines, adherence dropped sharply; −28.6% (P=0.021) for therapies on admission and −33.4%...

Table 1. Patient characteristics

<table>
<thead>
<tr>
<th>Variables</th>
<th>UZL, N=477</th>
<th>ZOL, N=326</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female</td>
<td>228 (47.8)</td>
<td>115 (35.3)</td>
</tr>
<tr>
<td>Age, years</td>
<td>71.6 (55.3–80.6)</td>
<td>67.6 (53.8–77.4)</td>
</tr>
<tr>
<td>PSI score</td>
<td>90 (67–120)</td>
<td>84 (55–103)</td>
</tr>
<tr>
<td>CURB-65 score</td>
<td>2.0 (1.0–2.0)</td>
<td>1.0 (0.0–2.0)</td>
</tr>
<tr>
<td>CAP IV according to PSI</td>
<td>72 (15.1)</td>
<td>30 (9.2)</td>
</tr>
<tr>
<td>CAP IV according to CURB-65</td>
<td>95 (19.9)</td>
<td>31 (9.5)</td>
</tr>
<tr>
<td>CAP IV according to both scores</td>
<td>46 (9.6)</td>
<td>16 (4.9)</td>
</tr>
<tr>
<td>Neoplastic disease present</td>
<td>20 (4.2)</td>
<td>12 (3.7)</td>
</tr>
<tr>
<td>History of liver failure</td>
<td>6 (1.3)</td>
<td>4 (1.2)</td>
</tr>
<tr>
<td>History of congestive heart failure</td>
<td>114 (23.9)</td>
<td>78 (23.9)</td>
</tr>
<tr>
<td>History of cerebrovascular disease</td>
<td>54 (11.3)</td>
<td>17 (5.2)</td>
</tr>
<tr>
<td>History of renal failure</td>
<td>87 (18.2)</td>
<td>30 (9.2)</td>
</tr>
<tr>
<td>History of COPD or other chronic pulmonary disease</td>
<td>137 (28.7)</td>
<td>119 (36.5)</td>
</tr>
<tr>
<td>Diabetes type I/II</td>
<td>84 (17.6)</td>
<td>49 (15.0)</td>
</tr>
<tr>
<td>Dementia or other mental illness</td>
<td>33 (6.9)</td>
<td>13 (4.0)</td>
</tr>
<tr>
<td>Confusion/Altered mental status on admission</td>
<td>70 (14.7)</td>
<td>28 (8.6)</td>
</tr>
<tr>
<td>Pleural effusion</td>
<td>136 (28.5)</td>
<td>60 (18.4)</td>
</tr>
<tr>
<td>Admitted during weekends</td>
<td>107 (22.4)</td>
<td>71 (21.8)</td>
</tr>
<tr>
<td>Admitted during night shifts</td>
<td>87 (18.2)</td>
<td>68 (20.9)</td>
</tr>
<tr>
<td>Suspicion of A/H1N1 infection</td>
<td>27 (5.7)</td>
<td>19 (5.8)</td>
</tr>
<tr>
<td>Known allergy to one or more antibiotics</td>
<td>39 (8.2)</td>
<td>40 (12.3)</td>
</tr>
<tr>
<td>Antibiotic therapy before admission</td>
<td>151 (31.7)</td>
<td>64 (19.6)</td>
</tr>
<tr>
<td>Resident in a nursing home/long-term care facility</td>
<td>35 (7.3)</td>
<td>10 (3.1)</td>
</tr>
<tr>
<td>Mortality during hospitalization</td>
<td>9 (1.9)</td>
<td>8 (2.5)</td>
</tr>
<tr>
<td>Mortality within 30 days after discharge</td>
<td>5 (1.0)</td>
<td>7 (2.1)</td>
</tr>
<tr>
<td>Admission to intensive care ≤48 h after admission</td>
<td>65 (13.6)</td>
<td>21 (6.4)</td>
</tr>
<tr>
<td>Length of stay</td>
<td>8.0 (5.2–13.9)</td>
<td>7.0 (4.9–10.0)</td>
</tr>
<tr>
<td>Guideline compliant therapy on first dose</td>
<td>279 (58.5)</td>
<td>226 (69.3)</td>
</tr>
<tr>
<td>Guideline compliant therapy 24–48 h after admission</td>
<td>289 (60.6)</td>
<td>193 (59.2)</td>
</tr>
</tbody>
</table>

COPD, chronic obstructive pulmonary disease.
for therapies given 24–48 h after admission, with a quick recovery afterwards [Figure 1, Table 2 and Figure S1 (available as Supplementary data at JAC Online)]. Logistic regression showed that a preceding course of antibiotics, CAP IV and a suspected H1N1 infection were associated with lower adherence to the empirical guidelines (Table 3).

While the proportion of patients with preceding antibiotic course or with CAP IV was rather constant over time, the introduction of the new guidelines coincided strongly with the presence of patients with suspected H1N1 infection ($r_{\text{point-biserial}} = 0.86; P = 0.018$) and the frequency of influenza-like illness in the general population nationwide ($r_{\text{point-biserial}} = 0.683; P = 0.045$) during the 2009–10 influenza season. Influenza prevalence was also a significant predictor in a regression model for therapies 24–48 h after admission ($-0.004 \% \pm 0.001 \%$/case of A/H1N1/100000 inhabitants; $P = 0.011$; $R^2 = 0.512$). A/H1N1 suspicion was not correlated with PSI and CURB-65 scores or with the CAP classifications. Immediately after guideline re-introduction, CAP III patients treated with third-generation cephalosporin-based regimens were more common [odds ratio $= 3.71$ ($1.06–12.94$); $P = 0.052$ (one-sided Fisher's exact test)]. Similarly, but non-significantly, there was a lower prevalence of patients treated with oral moxifloxacin.

### Intervention evaluation in ZOL

Applying the stringent CAP IV classification, 69.3% of the patients in ZOL were treated according to local guidelines. Twenty-four to 48 h after admission, this fell to 59.2%. The types of deviation are comparable to UZL, with a lower amount of unnecessary coverage against atypical pathogens, but also very low use of macrolides when risk factors are present (Table S3). Comparing the period before and after the main intervention in UZL...
showed a somewhat lower compliance, especially for the therapies 24–48 h after admission (Table 4). However, this did not reach statistical significance. Also, a comparison of the types of deviation revealed no extra information. Logistic regression showed similar results as in UZL, with preceding antibiotic therapy and high severity scores again having the highest impact (Table 3). Suspected A/H1N1 infection did not significantly predict non-compliance in this hospital.

Use of online electronic guidelines (UZL only)

Initially, page view count was relatively stable, at an estimated 296 views/week, but rose by 4.9 views/week on average after standard distribution of the guideline booklet ($P = 0.037$) (Figure 2). From February 2009 until the guideline re-introduction, the number of views decreased again, with an average of 6.5 views/week ($P = 0.011$). With the active re-introduction of the new guidelines, the number of views rose immediately, with 244 views ($P < 0.0001$), with a sharp decrease in the weeks afterwards ($-18.6$ views/week; $P = 0.004$). In January 2010, the number of views recovered again to previous levels (Figure 2). Based on a likelihood ratio test, the direct effects of Interventions 1 and 2 were negligible ($\chi^2 = 0.936; P = 0.626$), allowing for a reduced model (Table S4, available as Supplementary data at JAC Online).

No correlations were found between page view counts and the proportion of compliant therapies.

Discussion

The initial aim of this study was to see whether the use of antibiotic guidelines in the hospital could be improved using low-intensity and low-cost interventions. Therefore, specific interventions were identified and their impact on empirical antibiotic CAP treatment was evaluated using a standardized algorithm. Simultaneously, antibiotic management of CAP was assessed in another hospital where no specific interventions were introduced. Next to the actual compliance with the guidelines, overall guideline use was assessed using an electronic counter.

COPD, chronic obstructive pulmonary disease.

**Table 3.** Logistic regression predictors for guideline adherence

<table>
<thead>
<tr>
<th>Hospital</th>
<th>Predictor</th>
<th>Odds ratio (95% CI)</th>
<th>$P$ value</th>
<th>Nagelkerke $R^2$</th>
</tr>
</thead>
<tbody>
<tr>
<td>UZL ($N=437$)</td>
<td>no suspicion of A/H1N1 influenza infection</td>
<td>3.35 (1.320–8.521)</td>
<td>0.011</td>
<td>0.222</td>
</tr>
<tr>
<td>UZL ($N=437$)</td>
<td>no recent antibiotics</td>
<td>2.50 (1.593–3.909)</td>
<td>$&lt;0.0001$</td>
<td></td>
</tr>
<tr>
<td>UZL ($N=437$)</td>
<td>no CAP IV</td>
<td>6.64 (2.655–16.580)</td>
<td>$&lt;0.0001$</td>
<td></td>
</tr>
<tr>
<td>UZL ($N=437$)</td>
<td>respiratory rate/min</td>
<td>0.96 (0.925–0.994)</td>
<td>0.023</td>
<td></td>
</tr>
<tr>
<td>UZL ($N=437$)</td>
<td>oxygen saturation on admission</td>
<td>1.05 (1.006–1.088)</td>
<td>0.024</td>
<td></td>
</tr>
<tr>
<td>UZL ($N=437$)</td>
<td>systolic blood pressure on admission</td>
<td>1.01 (1.002–1.018)</td>
<td>0.010</td>
<td></td>
</tr>
<tr>
<td>ZOL ($N=235$)</td>
<td>no suspicion of A/H1N1 influenza infection</td>
<td>1.19 (0.419–3.386)</td>
<td>0.743</td>
<td>0.165</td>
</tr>
<tr>
<td>ZOL ($N=235$)</td>
<td>no recent antibiotic use</td>
<td>2.54 (1.212–5.335)</td>
<td>0.014</td>
<td></td>
</tr>
<tr>
<td>ZOL ($N=235$)</td>
<td>no CAP IV</td>
<td>9.05 (1.844–44.380)</td>
<td>0.007</td>
<td></td>
</tr>
<tr>
<td>ZOL ($N=235$)</td>
<td>no history of COPD or other chronic pulmonary problem</td>
<td>0.43 (0.231–0.817)</td>
<td>0.010</td>
<td></td>
</tr>
<tr>
<td>ZOL ($N=235$)</td>
<td>oxygen saturation on presentation</td>
<td>1.05 (1.002–1.091)</td>
<td>0.042</td>
<td></td>
</tr>
</tbody>
</table>

Odds ratio $>1$, positive association with the outcome variable.

**Table 4.** Overview of guideline compliant therapies in ZOL

<table>
<thead>
<tr>
<th>Time of assessment</th>
<th>Baseline$^a$</th>
<th>Standard distribution guidelines$^b$</th>
<th>New guidelines$^c$</th>
<th>$P$ value$^d$</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>151</td>
<td>111</td>
<td>64</td>
<td>0.388</td>
<td>326</td>
</tr>
<tr>
<td>Guideline adherent therapy on admission</td>
<td>99 (65.6)</td>
<td>81 (73.0)</td>
<td>46 (71.9)</td>
<td>0.388</td>
<td>226 (69.3)</td>
</tr>
<tr>
<td>Guideline adherent therapy 24–48 h after admission</td>
<td>85 (56.3)</td>
<td>75 (67.6)</td>
<td>33 (51.6)</td>
<td>0.071</td>
<td>193 (58.2)</td>
</tr>
</tbody>
</table>

Data are presented as n (%).


$^d$Pearson’s $\chi^2$. 

Discussion

The initial aim of this study was to see whether the use of antibiotic guidelines in the hospital could be improved using low-intensity and low-cost interventions. Therefore, specific interventions were identified and their impact on empirical antibiotic CAP treatment was evaluated using a standardized algorithm. Simultaneously, antibiotic management of CAP was assessed in another hospital where no specific interventions were introduced. Next to the actual compliance with the guidelines, overall guideline use was assessed using an electronic counter.

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in two large reviews.\textsuperscript{19,20} Because there were no substantial differences between the old and new CAP guidelines, confusion with subsequent use can be excluded as a second possibility. A third reason may be the A/H1N1 influenza pandemic coinciding with this intervention and with a potential influence on CAP management. When comparing the observed compliance trend with the number of nationally registered influenza cases, there is a remarkable correlation. Also, the logistic regression shows that A/H1N1 suspicion is enough to negatively influence guideline use, while actual confirmed cases remained rare in our populations (only one case in UZL). One may argue that during this period there was a shift towards patients with greater disease severity and longer time to clinical stability needing more complex therapies and necessitating deviations from available guidelines. However, this cannot fully explain the lower guideline compliance. While disease severity and time to clinical stability remained elevated during the next period, guideline compliance returned to normal. Similarly, when looking at the other hospital, ZOL, there was also a decrease in guideline use, with no intervention made, while the number of CAP IV patients was lower. With worldwide attention, initial severity overestimation and more aggressive antibiotic treatment,\textsuperscript{33} short-lived effects of this epidemic on physicians and antibiotic management should be considered.\textsuperscript{34,35} Unfortunately, little comparable data are available on the effects of epidemics on medical care. However, prior research revealed that habits can play a significant role in antibiotic guideline use.\textsuperscript{28} It can be argued that a major event such as an pandemic has the potential to alter perceptions and, as such, has a greater influence on guideline use and habits.\textsuperscript{36} Although treatment guidelines remained unchanged, this period around the peak of the pandemic was surely marked by increased concern over possible shortages in staff and facilities for both hospitals, possibly influencing prescribing decisions. If similar conditions occur in the future, we recommend an increased follow-up towards appropriate antimicrobial prescriptions.

Apparently the interventions that were used had marked effects on guideline consulting. However, except for the period after guideline re-introduction, such changes in guideline consulting were not followed by changes in clinical behaviour; neither has the number of visitors had a significant influence on the percentage of compliant therapies. On the other hand, our study design is not adequate to detect small differences. Still, this observation should warn other researchers that more guideline consulting does not automatically result in improved use. The rapid decrease in visits to the web site after the re-introduction is most likely a rebound effect due to the sharp initial rise, but may also be related to removal of the direct link on the intranet home page, which was part of the guideline re-introduction, stressing the beneficial effect of reminders. However, no detailed data are available to confirm this. Whether the survey had a negative effect on guideline consultation is unclear, but this is more probably due to normal habituation after standard guideline distribution, being comparable to other types of interventions.\textsuperscript{19,20}

**Limitations**

The fact that a substantial proportion of potential patients could not be included is a limitation of our study. However, apart from patients that actively refused to give their consent, unincluded patients were either hospitalized for a very short period as a safety measure, or were elderly people with dementia or other mental health problems. While the first group has an important bias towards very low disease severity, the second group has a high risk of multiple pathologies or silent aspiration combined with a very long-term hospitalization. As such, the importance of these patients needs to be put into perspective. Still, due to recommendations of the Ethics Committees and legal issues, we have no means to retrieve the necessary data on these patients and fully confirm this. Also, the uneven distribution of patients in time may cause important bias. We tried to correct
Conclusions

While our interventions to improve antibiotic guideline use were successful in increasing the use of the online version, they did not lead to a higher proportion of CAP patients receiving guideline-compliant therapy. In contrast, an important but temporal decrease in compliance was observed in UZL, which is linked with high probability to the peak in the concurrent A/H1N1 pandemic. For future epidemics with a potential to influence antibiotic management, increased vigilance and follow-up are needed.

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Transparency declarations

None to declare.

Supplementary data

Tables S1 to S4, Figure S1 and a description of the web site analysis are available as Supplementary data at JAC Online (http://jac.oxfordjournals.org/).

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