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

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Received 13 May 2011; returned 23 June 2011; revised 5 August 2011; accepted 13 August 2011

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
Antibiotic use during the A/H1N1 pandemic

guideline adherence, ranging between 44% and 65%.\textsuperscript{9,10,13–16} With an outlier up to 84%.\textsuperscript{17} Reviewing data from a previous review showed similar compliance, with a median of 45% (range 30%–70%).\textsuperscript{18} Consequently, numerous trials have tried to increase the compliance rate by using a whole array of interventions. Reviews, however, have shown that most interventions deliver only small to moderate improvements.\textsuperscript{19,20} and often fail to consider the cultural, contextual and behavioural determinants of antimicrobial use in different hospitals and countries.\textsuperscript{21} As such, in order to improve intervention efficiency, tailoring to the local situation appears promising.\textsuperscript{14,22} Here we report the impact of low-intensity interventions, based on local observations, on the use of the empirical CAP treatment guidelines in two Belgian hospitals. Concurrently, factors predicting non-compliance were assessed.

\section*{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 diseases (Ziekenhuis Oost-Limburg (ZOL)). It was developed as a two-centre intervention study with an interrupted time-series study design (ClinicalTrials.gov identifier NCT00512772).

\subsection*{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 confirmed diagnosis of pneumonia on admission and confirmed diagnosis of pneumonia on discharge by the attending physician(s), radiological confirmation 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 admission, patients with a recent history (within 30 days before admission) of hospitalization, transfer from another hospital; death within 24 h of admission, (suspected) aspiration pneumonia, immunocompromised patients (active haematological malignancies, asplenia, any dose of systemic glucocorticoids 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 \textit{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 measurements were taken to protect patient privacy. Likewise, the managing physicians were not identified.

\subsection*{Variables}

For each patient, the CURB-65 (confusion – urea nitrogen – respiratory rate – blood pressure – >65 years of age) and pneumonia severity index (PSI) scores were calculated at the time of admission.\textsuperscript{23,24} Patients with both a CURB-65 score >2 and a PSI class equal to 5 were classified as CAP IV,\textsuperscript{23,25} 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.\textsuperscript{26} 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 administration), any recent antibiotic therapy and whether the patient lived in a nursing home or other long-term care facility. Because this study was still on-going 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 treatment 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.wiv-isp.be) provided us with data on the national prevalence of influenza and influenza-like illness.

\section*{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 efficient than more complex ones.\textsuperscript{19,20} First, we actively distributed the hospital 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 influence on guideline knowledge.\textsuperscript{27} Such distribution of educational material is expected to have a modest but consistent effect.\textsuperscript{20} Second, a questionnaire on the use of antibiotic guidelines was distributed between mid-February and the end of April 2009 (Intervention 2).\textsuperscript{28} Although not a real intervention, we wanted to control for this event, as the distribution of this questionnaire 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 consistent effects, but the supplementary promotion with accompanying reminders were found to have moderately good effects.\textsuperscript{29} 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.\textsuperscript{29}

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.

\section*{Outcome measures}

Antibiotic choice for empirical therapy was assessed using a computerized 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 guideline.

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 $\chi^2$ 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 $\chi^2$ 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. Patient characteristics are presented in Table 1.

### 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 $\beta$-lactam allergy. Adherence to the guidelines were shown to be initially constant, without apparent effects from standard guideline distribution or survey. Immediately after re-introduction of the guidelines, adherence dropped sharply; $-28.6\% (P=0.021)$ for therapies on admission and $-33.4\%$

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**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>70 (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>Susception 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 &lt;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>

CAPD, chronic obstructive pulmonary disease. Continuous variables are presented as the median (interquartile range) and other variables are presented as the total number (percentage).
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 (point-biserial = 0.86; P = 0.018) and the frequency of influenza-like illness in the general population nationwide (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% [95% confidence interval (CI) −0.007% to −0.001%]/case of A/H1N1/100000 inhabitants; P = 0.011; R² = 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 (95% CI 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...

Table 2. Segmented regression analysis for therapy adherence 24–48 h after admission (UZL only)

<table>
<thead>
<tr>
<th>Factor</th>
<th>Unstandardized B (95% CI)</th>
<th>P value</th>
<th>R²</th>
</tr>
</thead>
<tbody>
<tr>
<td>(Constant)</td>
<td>75.76 (50.89–100.63)</td>
<td>&lt;0.0001</td>
<td>0.883 (P = 0.002)</td>
</tr>
<tr>
<td>Autocorrelation factor</td>
<td>−0.43 (−0.77 to −0.10)</td>
<td>0.017</td>
<td></td>
</tr>
<tr>
<td>Trend before Intervention 1</td>
<td>1.25 (−2.62–5.11)</td>
<td>0.478</td>
<td></td>
</tr>
<tr>
<td>Intervention 1</td>
<td>−0.08 (−10.33–10.18)</td>
<td>0.987</td>
<td></td>
</tr>
<tr>
<td>Time after 1</td>
<td>1.16 (−3.10–5.41)</td>
<td>0.549</td>
<td></td>
</tr>
<tr>
<td>Intervention 3</td>
<td>−33.40 (−45.42 to −21.38)</td>
<td>&lt;0.0001</td>
<td></td>
</tr>
<tr>
<td>Time after 3</td>
<td>5.50 (1.23–9.78)</td>
<td>0.018</td>
<td></td>
</tr>
</tbody>
</table>

Intervention 1, active distribution of antibiotic guidelines; Intervention 3, re-introduction of updated guidelines.
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 (χ² = 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. Guideline compliance in UZL is comparable to other studies, with a compliance rate of 60% after 24 h in UZL, but in some time periods attaining ~70%. In ZOL this was even higher when looking at the first antibiotics administered. More importantly, however, re-introduction of the local guidelines was associated with a temporary but considerable drop in compliant therapies in UZL, which was unexpected. There are only a few possible causes for this phenomenon.

A first possibility is a direct negative effect from this intervention. This is unlikely because of the overall positive results, although mostly small, of reminders and educational material.
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, short-lived effects of this epidemic on physicians and antibiotic management should be considered. 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. 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. 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.

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
for this using appropriate time periods that would cover enough patients to provide a reliable measure. Another problem is the difference between the two hospitals in patient population and setting owing to quick transfer of geriatric patients and a local policy prohibiting inclusion of ICU patients enrolled in other clinical studies in ZOL. Therefore, a full comparison between both hospitals would be inherently inaccurate and is not included. Results are only compared for a better understanding of separate trends and to assess the presence of more general phenomena. In an ideal situation, however, more hospitals should be included and efforts should be made to obtain more homogeneous patient populations. We used a very strict criterion for CAP IV combining two severity scores. This provided the most accurate prediction of clinical practice during the study period. One could suggest that using ICU admission as a severity criterion would be more pragmatic. Still, when applying this definition, the same trends remain, especially the lower adherence in the period 15 October–14 December 2009 (data not shown), while actual ICU admission may be less clear on admission and may depend on subjective and non-clinical factors. This indicates that using our methods allows for the detection of important deviations from the treatment guidelines. For both guideline compliance and web site data, the interrupted time-series design and the lack of a same-site control cannot fully exclude the presence of other unregistered but contemporaneous events, delayed effects from preceding interventions or that the interventions actually prevented a steeper or continuing decline in prescribing quality. Also, the number of web site visitors shows a large variability, making predictions less reliable. Finally, using CAP as model pathology to monitor overall guideline use, we were unable to see the effect of the guidelines’ re-introduction on the management of other diagnoses.

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 decline 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.

Acknowledgements

We wish to acknowledge all the patients who cooperated with this study. We would also like to thank the respective boards and antibiotic management committees of UZL and ZOL for their support for this study. We are heavily indebted to the patient administration and nursing staffs of the EDs of UZL and ZOL and the Belgian Scientific Institute of Public Health for providing us with the necessary data.

Funding

This study was supported by an unconditional grant from the Flemish Society of Hospital Pharmacists (VZA), Belgium.

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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