Antibiotic policies in acute English NHS trusts: implementation of ‘Start Smart—Then Focus’ and relationship with Clostridium difficile infection rates

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Objectives: The objective of this study was to establish how antibiotic prescribing policies at National Health Service (NHS) hospitals match the England Department of Health ‘Start Smart—Then Focus’ recommendations and relate to Clostridium difficile infection (CDI) rates.

Methods: Antibiotic pharmacists were surveyed regarding recommendations for empirical treatment of common syndromes (‘Start Smart’) and antimicrobial prescription reviews (‘Focus’) at their hospital trusts. If no response was provided, policy data were sought from trust websites and the MicroGuide app (Horizon Strategic Partners, UK). Empirical treatment recommendations were categorized as broad spectrum (a β-lactam/β-lactamase inhibitor, cephalosporin, quinolone or carbapenem) or narrow spectrum. CDI rates were gathered from the national mandatory surveillance system.

Results: Data were obtained for 105/145 English acute hospital trusts (72%). β-Lactam/β-lactamase inhibitor combinations were recommended extensively. Only for severe community-acquired pneumonia and pyelonephritis were narrow-spectrum agents recommended first line at a substantial number of trusts [42/105 (40%) and 50/105 (48%), respectively]. Policies commonly recommended dual therapy with aminoglycosides and β-lactams for abdominal sepsis [40/93 trusts (43%)] and undifferentiated severe sepsis [54/94 trusts (57%)]. Most policies recommended treating for ≥7 days for most indications. Nearly all policies [100/105 trusts (95%)] recommended antimicrobial prescription reviews, but only 46/96 respondents (48%) reported monitoring compliance. Independent predictors of higher CDI rates were recommending a broad-spectrum regimen for community-acquired pneumonia (P = 0.06) and, counterintuitively, a recommended treatment duration of <48 h for nosocomial pneumonia (P = 0.01).

Conclusions: Hospital antibiotic policies in the NHS ‘Start Smart’ by recommending broad-spectrum antibiotics for empirical therapy, but this may have the unintended potential to increase the use of broad-spectrum antibiotics and risk of CDI unless better mechanisms are in place to improve ‘Focus’.

Keywords: antibiotic policy, antibiotic stewardship, C. difficile

Introduction

Reducing use of broad-spectrum antibiotics is a key component of strategies to counter the emergence of antibiotic resistance.1 Hospital antimicrobial stewardship programmes aim to achieve this through the judicious and proportionate use of antibiotics in hospitals.2 Antimicrobial stewardship interventions that target the choice of drug prescribed (preferentially narrow spectrum), timing of first dose or route of administration are effective in reducing antibiotic resistance and healthcare-acquired infections.3 Conversely, antibiotics selected empirically to treat life-threatening infection need to be reliably active against the likely causative organisms, including antibiotic-resistant strains, since prompt initiation of effective antibiotic treatment in life-threatening infection saves lives.4 There is therefore a conflict of priorities, both for stewardship committees drafting antibiotic policies and for individual prescribers. On one hand there is an
urgent need to reduce broad-spectrum antibiotic use, but on the other it is also important to ensure effective empirical treatment before full diagnostic information to guide antibiotic choices is available.

Antimicrobial prescription review 48–72 h into treatment affords an opportunity to discontinue treatment if infection has been excluded from the differential diagnosis, de-escalate from broad-spectrum empirical therapy to narrower-spectrum targeted therapy according to diagnostic test results (or to escalate if the event of treatment failure) and to revise the prescribed course length in the light of the clinical response. This approach to stewardship in hospitals has been advocated by the Department of Health in England since 2011 in guidance from the Advisory Committee on Antimicrobial Resistance and Healthcare Associated Infection (ARHAI) entitled Antimicrobial Stewardship: ‘Start Smart—Then Focus’.5 The ‘Start Smart—Then Focus’ guidance proposes five prescribing decisions for consideration at antimicrobial prescription review: stop antimicrobials; switch from intravenous to oral therapy; change antimicrobial; continue current prescription; or outpatient parenteral antimicrobial therapy (OPAT).

To understand how National Health Service (NHS) acute care hospitals are implementing ‘Start Smart—Then Focus’ we conducted a survey of antimicrobial pharmacists in English acute trusts. The aims were: (i) to establish what antibiotics are being recommended as empirical treatment (‘Start Smart’) for common life-threatening infections; (ii) to establish what is the potential for antimicrobial prescription reviews (‘Focus’) to minimise unnecessary antibiotic use; (iii) to establish what measures are currently in place to do this; and (iv) to assess whether different antibiotic policy recommendations were associated with hospital-onset Clostridium difficile infection (CDI) rates.

Methods

An invitation to participate in a survey to assess implementation of ‘Start Smart—Then Focus’ at NHS hospitals was posted in July 2013 on a specialist antimicrobial pharmacist online forum hosted by the UK Clinical Pharmacy Association (www.UKCPA.net) and included a hyperlink to a web-based questionnaire (available as Supplementary data at JAC Online). This was followed with a reminder post on the forum in September. A letter inviting participation was also e-mailed on behalf of the Chief Pharmaceutical Officer for England to the chairs of nine regional networks of NHS hospital chief pharmacists in September 2013 for cascade to chief pharmacists and their specialist pharmacists. In the event that no response was obtained by December 2013, the microbiologist responsible for antimicrobial stewardship was identified by telephone, e-mailed and asked to complete the survey.

The NHS Health Research Authority decision tool (available at www.hra.nhs.uk) determined that the study constituted a service evaluation not requiring ethics review.

The survey gathered data describing: first-line policy recommendations for treatment (agent and recommended duration) of severe community-acquired pneumonia, community-acquired upper urinary tract infection (pyelonephritis), hospital-acquired pneumonia, community-acquired abdominal sepsis and severe sepsis with no clear focus; and recommendations for and monitoring of antimicrobial prescription reviews. Respondents were asked to determine, using their most recent monitoring data, how often reviews resulted in each of the five decision options suggested by ‘Start Smart—Then Focus’ using bands of <1%, 1%–10%, 10%–20%, >20%–40%, 40%–60%, 60%–80% and >80%–100%.

Results and discussion

Between July 2013 and March 2014 survey responses were received from 96 acute NHS trusts in England. Data describing antibiotic policies were obtained from nine additional trusts whose policies were available through their web site or on the MicroGuide app (Horizon Strategic Partners, UK). Data were thus available for 105/142 acute English NHS trusts. Of these, 35 were teaching hospitals and 70 acute non-teaching hospitals, 59 were medium-sized (500–1000 beds), 22 small (<500 beds) and 24 large (>1000 beds) hospitals.

Antibiotic policy recommendations

Policy recommendations for first-line treatment of the five key indications are summarized in Figure 1. For all indications these showed enormous reliance on β-lactam/β-lactamase inhibitor combinations. Only for community-acquired pneumonia (40%) and pyelonephritis (48%) were narrow-spectrum agents (benzyl penicillin, amoxicillin, aminoglycosides, doxycycline, trimethoprim) recommended first line at a substantial number of trusts. This very marked reliance on β-lactam/β-lactamase inhibitor combinations and the almost complete absence of quinolone and cephalosporin antibiotics (plausibly driven by a desire to reduce CDI rates) is in keeping with antibiotic usage data reported by hospital pharmacies and is particularly concerning given the need to increase heterogeneity of antibiotic use highlighted in the UK 5 year antimicrobial resistance strategy.

Policies commonly recommended dual therapy. Almost all policies (99/105) recommended addition of a second agent to the backbone treatment for community-acquired pneumonia, either a macrolide (89/99) or doxycycline (8/99), presumably to treat atypical pathogens such as Mycoplasma pneumoniae. Addition of gentamicin was recommended for hospital-acquired pneumonia at 15/105 trusts (14%), for pyelonephritis at 28/105 trusts (27%) (not including 12 trusts where gentamicin monotherapy was recommended for pyelonephritis), for abdominal sepsis at 40/93 (43%) and for severe sepsis at 54/94 (57%) trusts.

The rationale for addition of an aminoglycoside to backbone β-lactam therapy may be to ensure activity against resistant organisms, especially where the backbone agent is less reliably active against them (e.g. benzyl penicillin, amoxicillin or co-amoxiclav). Interestingly, 29/55 policies recommending piperacillin/tazobactam for treatment of severe sepsis recommended combination with an aminoglycoside. This is in keeping with Surviving Sepsis guidelines and is recommended by Public Health Wales, but a recent Cochrane review concluded that β-lactam/aminoglycoside combination therapy does not provide an advantage over β-lactams alone in this situation and is associated with an increased risk of renal toxicity.

At the great majority of trusts, antibiotic policies also made recommendations for duration of first-line treatment (Figure 2). For community-acquired pneumonia, nosocomial pneumonia, pyelonephritis and community-acquired abdominal sepsis the commonest recommendation was to treat for ≥7 days. Given the fact that the majority of policies recommended broad-spectrum
β-lactam/β-lactamase inhibitor combinations for empirical treatment, minimizing unnecessary use of these agents thus depends on antibiotic prescription reviews being effective in stopping treatment where a non-infective diagnosis is made or switching agent as microbiology culture and susceptibility data become available. It is noteworthy, though, that the majority of community and

**Figure 1.** First-line antibiotic or antibiotic class recommendations for treatment of five key indications at 105 acute English NHS trusts. Where policies recommended combination treatment (e.g. co-amoxiclav with a macrolide for community-acquired pneumonia) only the backbone agent is included. *Recommendation for an aminoglycoside as the only agent active against aerobic bacteria. This figure appears in colour in the online version of JAC and in black and white in the print version of JAC.

**Figure 2.** Recommendations for duration of first-line antibiotic treatment of five key indications at 105 acute English NHS trusts. This figure appears in colour in the online version of JAC and in black and white in the print version of JAC.
hospital-acquired pneumonia cases are not microbiologically confirmed in routine clinical practice and thus susceptibility data are usually not available to guide switching to an agent with a narrower spectrum. However, across the different indications, 18%–28% of policies recommended only giving first-line treatment for 24–48 h, presumably to encourage review at this time. Although nearly all trust policies (95%) recommend antibiotic prescription reviews, only just under half the survey responses [46/96 (48%)] reported monitoring of compliance with this recommendation. Interestingly, given the statutory requirement for trusts to be able to evidence good practice in this area, 19/96 trusts (20%) reported both no monitoring and no plans to audit antibiotic prescribing reviews.11 Furthermore, only 33/96 survey responses supplied any data from monitoring of reviews and of these only 15 supplied data about how often reviews resulted in any change in treatment (intravenous to oral switch, change or agent, stopping treatment or OPAT). Only 2/15 respondents (13%) stated that >60% of reviews at their trust resulted in a change of treatment while 8/15 (53%) stated that >60% of reviews resulted in no change of treatment while only 15 supplied data about how often reviews resulted in any change in treatment (intravenous to oral switch, change or agent, stopping treatment or OPAT). Only 2/15 respondents (13%) stated that >60% of reviews at their trust resulted in a change of treatment while 8/15 (53%) stated that >60% of reviews resulted in no change of treatment. Although these numbers are too small to draw reliable conclusions it is likely that the trusts from which monitoring data were supplied are those with the best developed antimicrobial stewardship services. It therefore seems unlikely from our data that treatments prescribed empirically for common infections in secondary care are being substantially modified by antibiotic prescription reviews as currently undertaken in the NHS. This is in keeping with a report from the National Audit Office in 2009 which estimated that a third of acute hospitals in England did not have robust systems to ensure antibiotic prescription reviews.12

**CDI rates**

We sought to establish how antibiotic policy recommendations at trusts relate to incidence rates of CDI (Table 1). On univariate analysis, CDI rates tended to be lower at hospitals where monitoring of antibiotic-prescribing reviews was undertaken. This may be a marker of organizational effectiveness more generally rather than directly related to better implementation of reviews. Trusts with policies avoiding use of broad-spectrum antibiotics for community-acquired pneumonia had lower CDI rates than trusts recommending narrow-spectrum agents. Counterintuitively, CDI rates were markedly higher at trusts that stipulated <48 h as a duration of empirical therapy for community-acquired pneumonia, hospital-acquired pneumonia and pyelonephritis. In a multivariate analysis based on backward elimination (exit $P>0.1$) on all factors with $P<0.3$ in the univariate analysis and using only complete cases ($n=101$), use of broad-spectrum antibiotics for

<table>
<thead>
<tr>
<th>Variable</th>
<th>Mean CDI rate/100000 bed days (n)</th>
<th>Mean difference (95% CI)</th>
<th>$P$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trust type ($n=103$)$^a$</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>non-teaching</td>
<td>38.6 (68)</td>
<td>teaching</td>
<td>+1.4 (−4.5, +7.3)</td>
</tr>
<tr>
<td>Trust size ($n=103$)$^b$</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>small</td>
<td>38.1 (22)</td>
<td>medium</td>
<td>39.9 (58)</td>
</tr>
<tr>
<td>Monitor 48 h reviews? ($n=93$)$^c$</td>
<td>yes</td>
<td>36.1 (45)</td>
<td>no</td>
</tr>
<tr>
<td>Recommended antibiotic regimen ($n=103$)$^c$</td>
<td>narrow spectrum</td>
<td>35.6 (40)</td>
<td>broad spectrum</td>
</tr>
<tr>
<td>Community-acquired pneumonia</td>
<td>37.6 (9)</td>
<td>39.2 (94)</td>
<td>+1.6 (−8.3, +11.5)</td>
</tr>
<tr>
<td>hospital-acquired pneumonia</td>
<td>36.9 (51)</td>
<td>41.3 (52)</td>
<td>+4.4 (−1.2, +9.9)</td>
</tr>
<tr>
<td>pyelonephritis</td>
<td>39.4 (24)</td>
<td>37.5 (67)</td>
<td>−2.0 (−8.2, +4.3)</td>
</tr>
<tr>
<td>undifferentiated severe sepsis</td>
<td>42.9 (14)</td>
<td>37.3 (78)</td>
<td>−5.6 (−13.3, +2.1)</td>
</tr>
<tr>
<td>Recommended antibiotic duration ($n=103$)$^c$</td>
<td>&lt;48 h</td>
<td>44.1 (28)</td>
<td>&gt;48 h</td>
</tr>
<tr>
<td>Community-acquired pneumonia</td>
<td>47.2 (20)</td>
<td>37.3 (67)</td>
<td>35.6 (14)</td>
</tr>
<tr>
<td>nosocomial pneumonia</td>
<td>45.4 (18)</td>
<td>37.6 (65)</td>
<td>37.9 (18)</td>
</tr>
<tr>
<td>pyelonephritis</td>
<td>40.3 (21)</td>
<td>36.5 (44)</td>
<td>38.8 (33)</td>
</tr>
<tr>
<td>community-acquired abdominal sepsis</td>
<td>38.3 (24)</td>
<td>40.2 (21)</td>
<td>37.7 (54)</td>
</tr>
</tbody>
</table>

*a* C. difficile rate data were not available for two trusts; one survey was returned anonymously and one trust was broken up during the financial year.

*b* 95/96 survey responses answered this question and C. difficile rate data were not available for two trusts.

*c* Not all trusts provided data on specific regimens and durations.
Table 2. Multivariate predictors of CDI rate (cases per 100 000 bed days)

<table>
<thead>
<tr>
<th>Variable</th>
<th>Mean difference (95% CI)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Recommended antibiotic regimen:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>community-acquired pneumonia:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>broad spectrum versus narrow spectrum</td>
<td>+5.3 (−0.3, +10.9)</td>
<td>0.06</td>
</tr>
<tr>
<td>Recommended antibiotic duration:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>nosocomial pneumonia:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt;48 versus &lt;48 h treatment recommended</td>
<td>−9.1 (−16.0, −2.1)</td>
<td>0.01</td>
</tr>
<tr>
<td>no duration versus &lt;48 h treatment recommended</td>
<td>−10.3 (−19.9, −0.8)</td>
<td>0.03</td>
</tr>
</tbody>
</table>

Independent predictors of CDI rate (cases per 100 000 bed days) were identified using backward elimination (exit P > 0.1) on all factors with P < 0.3 in Table 1 using complete cases (n=101) and including all levels of categorical factors. P > 0.15 for all other factors in Table 1 after adjusting for those shown above.

Community-acquired pneumonia and recommendation of <48 h treatment for nosocomial pneumonia were independent predictors of higher CDI rates (Table 2).

Previous studies have demonstrated that introducing restrictive antibiotic policies can result in reduced CDI rates at an individual hospital and across healthcare systems. We believe our data are the first indicating that differences in CDI rate between hospitals could, at least in part, be accounted for by variation in antibiotic policy. Our finding that CDI rates relate most closely to policies for treatment of pneumonia is in keeping with the most recent point prevalence survey data, which showed that treatment of respiratory infection is responsible for 30.9% of antimicrobial use in acute hospitals. Other indications are responsible for proportionately much less antibiotic use (sepsis 14% and urinary infection 13.7%).

Our finding that recommending <48 h of empirical treatment for nosocomial pneumonia is associated with higher CDI rates is counterintuitive; however, we have not measured the actual duration of empirical treatment and it may be that policy writers recommend short durations of empirical therapy as a means of stimulating clinicians to review their prescriptions at 24–48 h and do not therefore implement strategies such as stewardship ward rounds to ensure empirical treatment is actually modified at this time. An important limitation of our study is that we have conducted an ecological analysis using trust-level rather than patient-level data. When electronic prescribing is used more widely, it may be possible to explore the relationship between prescribing and rate of CDI directly. Furthermore, we have only gathered limited data about each trust and thus it is possible that the associations observed between policies recommending narrow-spectrum agents and low CDI rates are not causal, but accounted for by wider organizational factors. It is also important to note that trust-level outcome data for the major syndromes of infection were not available and consequently we could not assess whether there may be adverse patient consequences of recommending narrow-spectrum antibiotic regimens for empirical treatment.

Barriers to implementation of antimicrobial prescription reviews

Lastly, pharmacists were asked their views as to barriers to achieving 100% compliance with a policy to review all patients prescribed antimicrobials at 24–48 h post-prescription. Among 93 pharmacists who answered this question, very important barriers were considered to be the generally poor documentation of prescribing decisions (84%), fear of treatment failure (58%), reluctance to change the previous doctor’s prescribing decision (53%), which supports the concept of prescribing etiquette as a barrier to antibiotic prescription reviews proposed by Chirani et al. Interestingly, few pharmacists perceived lack of reliable diagnostic tests to confirm the presence or absence of infection (18%), lack of infection specialist support (24%) or lack of confidence in susceptibility/completeness of culture and susceptibility results (5%) to be a very important barrier.

Study limitations

Our study has significant limitations. First, it is likely that the trusts that participated in this survey are more engaged in antimicrobial stewardship activity than the 40 (28% of acute trusts in England) that did not. Second, trust antibiotic policies are regularly updated and may have changed during the financial year for which we have used CDI rates in our analysis. Furthermore, trusts with high CDI rates may be expected to have introduced policies with greater use of narrow-spectrum agents. Although we cannot account for this, it is likely that this would diminish, rather than magnify, the relationship we have observed between the recommendation of broad-spectrum antibiotics and CDI rate. There is also the possibility that trust antibiotic policies do not reflect actual use within the organizations; the correlation of policies with antibiotic consumption data needs to be explored.

Conclusions

In conclusion, there is huge reliance on β-lactam/β-lactamase inhibitor combinations for the empirical treatment of the common syndromes of infection presenting to secondary care. Trusts with policies that recommend broad-spectrum antibiotic treatment for community-acquired pneumonia have higher CDI rates than trusts that recommend narrow-spectrum agents first line. Most trusts recommend prolonged courses of treatment and thus antimicrobial prescription reviews, as recommended by ‘Start Smart—Then Focus’, are a critical tool to minimize unnecessary antibiotic use. Although most trusts recommend antimicrobial prescription reviews, monitoring is variable and we found little evidence that reviews are limiting the use of broad-spectrum antibiotics effectively. Starting ‘Smart’ therefore may have the unintended potential to increase the use of broad-spectrum antibiotics and risk of CDI, unless better mechanisms are in place to improve ‘Focus’. Further research on optimizing ‘Focus’, addressing the barriers identified in our survey, is therefore urgently needed.
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Disclaimer
The views expressed are those of the authors and not necessarily those of the NHS, the NIHR, the Department of Health or Public Health England.

Supplementary data
The questionnaire is available as Supplementary data at JAC Online (http://jac.oxfordjournals.org/).

References