Antibiotic prescribing in hospitals: a social and behavioural scientific approach

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Antibiotics have dramatically changed the prognoses of patients with severe infectious diseases over the past 50 years. However, the emergence and dissemination of resistant organisms has endangered the effectiveness of antibiotics. One possible approach to the resistance problem is the appropriate use of antibiotic drugs for preventing and treating infections. This Review describes how the volume and appropriateness of antibiotic use in hospitals vary between countries, hospitals, and physicians. At each specific level—cultural, contextual, and behavioral—we discuss the determinants that influence hospital antibiotic use and the possible improvement strategies to make it more appropriate. Changing hospital antibiotic use is a challenge of formidable complexity. On each level, many determinants play a part, so that the measures or strategies undertaken to improve antibiotic use need to be equally diverse. Although various strategies for improving antibiotic use are available, a programme with activities at all three levels is needed for hospitals. Evaluating these programme activities in a way that provides external validity of the conclusions is crucial.

Introduction

The advent of antibiotics, which are some of the most successful drugs in medicine, dramatically altered the prognoses of patients with bacterial infections. Their power in both therapy and prophylaxis was so convincing that many older antibiotics have never undergone controlled clinical trials. However, the excessive and indiscriminate use of these so-called miracle drugs in both human and veterinary practices has led to the emergence and dissemination of resistant organisms that endanger their efficacy.1 Major problems are encountered for an increasing number of pathogens, including Staphylococcus aureus, Streptococcus pneumoniae, and Clostridium difficile. For the potential, examples of use almost any antimicrobial drug has the potential to induce the onset of C difficile infection. As a consequence, C difficile infection is the leading cause of hospital-acquired infections in most high-income countries, and resistance is an increasing problem.2–4

Resistant pathogens cause infections associated with greater mortality and morbidity.5 Antibiotic resistance has a substantial economic impact because of the need for more expensive second-line drugs and longer hospital stays associated with therapy failure.7 Some studies suggest a relation between resistance rates and the volume of antibiotic use.8–12 In addition, modelling studies show the value of infection-control practices and restricted use of antibiotics to control meticillin-resistant S aureus in hospitals.13,14 Similarly, the quality of both infection-control practices and antibiotic use plays a part in the incidence of C difficile infection.15–17 One way of tackling resistance is to use antibiotics appropriately to prevent and treat infections.

Appropriate antibiotic use in hospitals

Appropriate antibiotic use in hospitals entails finding a middle road between their potent ability to reduce the mortality and morbidity of patients with infectious diseases and their potentially hazardous effects (ie, serious adverse events, drug interactions, and induction of resistant strains). Unnecessary use of antimicrobial agents, and use of the newest, broad-spectrum antibiotics when narrow-spectrum and older agents would suffice can lead to increases in resistance, harm patients, and increase treatment costs.18 Conversely, unjustified therapy with narrow-spectrum agents that ineffectively treats the causative pathogen can also be detrimental to the patient.6

The role of antibiotic stewardship programmes is to strike a balance between the potent ability of antibiotics for individual patients and their potentially hazardous effects. Initiatives to support appropriate antibiotic use are relevant because of its effects on bacterial resistance, clinical outcome, and costs.

By definition, guidelines are documents that include a set of statements about appropriate care. In the field of infectious diseases, guidelines are developed both from a perspective of infection control and management of infectious diseases. These guidelines are developed and disseminated by, for example, the Infectious Diseases Society of America, the US Centers for Disease Control and Prevention, the British Society for Antimicrobial Chemotherapy, and the UK National Institute for Health and Clinical Excellence. Studies have shown that 30–40% of patients do not receive care based on available scientific evidence according to guidelines, and 20–25% of the health care provided is unnecessary.20–22 The findings for antibiotic care are similar, and assessments have found that up to 50% of hospital antibiotic use is inappropriate.23–25 Thus, there is ample room for improvement. But how can we improve it?

Improvement of antibiotic use

Research

Historically, the ability to prescribe antibiotics changed the therapeutic power of physicians in an unprecedented fashion. Although antibiotics have lost much of their glamour due to the increasing antimicrobial resistance of microorganisms, this sense of power probably still underlies antibiotic prescription. Thus, changing
prescribing habits in hospitals can be a challenge. Unfortunately, a rather naive approach to changing professional behaviour is often used to meet this challenge.22 Presenting information on innovations (scientific papers, reviews, guidelines, care bundles, antibiotic booklets, and information about inappropriate care) to medical professionals is assumed to ensure that care will be optimised accordingly. It is also assumed that professionals have the time, motivation, skills, and resources to apply this new knowledge and to change clinical practice. Research into changes of professional behaviour shows varying and often only modest improvement by this approach. Most innovations require further efforts, or so-called implementation strategies.22

Different strategies exist to implement guidelines and other innovations, including educational meetings, feedback, reminders, financial incentives, and revision of professional roles. Many studies have assessed these strategies for improving patients’ care. Reviews, and even reviews of reviews, have summarised them. They conclude that there is no superior strategy or so-called magic bullet that works for all innovations in all circumstances. The challenge lies in building a strategy on the careful assessment of obstacles and on a coherent theoretical base.26–27

Policy

This conclusion from research also appears in several recent international policy reports that have addressed the problem of antibiotic resistance. The European Academies Science Advisory Council underscore the need for commitment to research and development in their policy report on antibacterial resistance in Europe.28 They emphasise that developing novel rapid diagnostics, supporting industry innovation in drug development, and “strengthening the science base” are important.28 The report also states that, “the social sciences need to be more involved in studies concerning antibiotic usage and infection control”, and that, “there is a continuing need for well-designed studies of interventions to try to evaluate what particular factors are influential in practice”.28

Similarly, the European Parliament Scientific and Technological Options Assessment report on antibiotic resistance provides an action plan to contain antibiotic resistance.29 They selected four areas (coordination, standardisation, stimulation, and research) to which the European Union can contribute. One option for containing resistance consists of promoting research aimed at understanding “the cultural, contextual and behavioural aspects of antimicrobial usage, thus generating possibilities for interventions to reduce usage”. What are these aspects of hospital antibiotic use that generate such possibilities?

Determinants of hospital antibiotic use

Various determinants on various levels (ie, cultural, contextual, and behavioural) might influence the prescription of antibiotics and cause antibiotic use to vary in different hospitals. Improvement strategies built on these determinants can make hospital antibiotic use more appropriate. To better understand antibiotic use and its effective improvement, we describe differences of antibiotic use in various countries (cultural level) and hospitals (contextual level), and by professionals (behavioural level). At each specific level, we will discuss the determinants that influence hospital antibiotic use and the possible strategies to make it more appropriate.

Cultural aspects

Cars and colleagues30 obtained data about antibiotic drug sales for 1997 and clearly showed the huge variation in antibiotic use in European countries. Dutch antibiotic use was the lowest in Europe; French use was four times greater (the highest in Europe); Belgian and Italian use were three times greater; and German use was 1·5 times greater. The relative numbers of prescriptions varied, as did the extent to which broad-spectrum and newer
antibiotics were being prescribed. Hospital sales accounted for 7–15% of the total sales. Vander Stichele and colleagues used available data on hospital antibiotic use that was aggregated at the national level (1997–2002) to specifically assess hospital consumption of systemic antibiotics in 15 European countries (figure). The data illustrated substantial cross-national variations in the extent and distribution of exposure to antibiotics in hospital care. In 2002, median national hospital antibiotic consumption in Europe was 2.1 defined daily doses per 1000 inhabitants per day, ranging from 1.3 in Norway and Sweden to 3.9 in Finland and France. Antibiotic consumption in hospital care (as a proportion of total consumption) ranged from 6.4% to 17.8%. There was a strong, positive correlation between the extent of antibiotic use in ambulatory and hospital care (p=0.002), both for overall use and use of five main drug classes (not including macrolides or other drugs; figure). These differences can only partly be explained by differences in the populations of patients studied.

In different countries, people hold different (and often implicit) ideas about health, causes of disease, labelling of illness, coping strategies, and treatment modalities. These ideas shape both the expectations and the behaviour of professionals in a country’s hospitals. Awareness of the role this sociocultural and socioeconomic context has in the pattern of prescribing antibiotics is growing.

Sociocultural factors

Deschepper and Vander Stichele studied antibiotic use in 14 European countries and its relation to various cultural characteristics described in Hofstede’s model of cultural dimensions. Hofstede describes major differences between countries with regard to concepts such as “uncertainty avoidance” (ie, unwillingness to accept uncertainty and risks) and “power distance” (ie, willingness to accept that power is unevenly distributed). Great power distance exists in a hierarchical society, but much less in an egalitarian society. Interestingly, Deschepper and Vander Stichele found that more antibiotic use is associated with more uncertainty avoidance (correlation r=0.70). Thus, in societies that tend to avoid uncertainty, antibiotics have a defensive function: the prescriber and the patient aim for certainty. They also found that hierarchical societies use more antibiotics, whereas more egalitarian societies use less (r=0.83). Antibiotics apparently provide the health-care professional with therapeutic power that will be used particularly in hierarchical societies. More recently, Deschepper and colleagues concluded that the culture-specific way that people deal with authority is important in explaining cross-national differences in antibiotic use, and that uncertainty avoidance also plays a part.

Kooiker and van der Wijst’s study of therapeutic drug use in Europe confirms that egalitarian societies (Netherlands, UK, and Scandinavia) consume fewer antibiotics than hierarchical societies (France, Italy, Spain, Portugal, and Greece). They conclude, as Deschepper and Vander Stichele suggest, that these differences in use coincide with differences in religion, whereby the traditionally and predominantly Protestant countries tend to consume fewer antibiotics than predominantly Catholic countries. This is perhaps not surprising, because attitude to disease and treatment are closely linked to religious background. The Protestant predilection for austerity and simplicity probably has a role: no fuss, so no medication, if it is not necessary. Protestantism is about discussion of the Scripture (resulting in the many schisms in the church), whereas Catholicism is more about rituals. Protestant professionals might choose to discuss the appropriateness of a medication with their colleagues or patients more often than do their Catholic colleagues. The Protestant church is more egalitarian, whereas the Catholic church is more hierarchical. Power distance in religion and power distance in society might be related; the value a society attaches to equality might be reflected in church organisation or vice versa. Research on the influence of religion has yet to show whether these latter presumptions are true.

Socioeconomic factors

Socioeconomic factors are also likely to influence antibiotic use. For example, the way in which health care is funded or reimbursed affects antibiotic prescription in a country’s hospitals. Harbarth and colleagues found that fewer generic drugs and more new drugs are used in France (pharmacies received more reimbursement for expensive drugs such as broad-spectrum antibiotics) than in Germany. Similarly, a Belgian study showed the effectiveness of only reimbursing evidence-based prophylaxis, which profoundly affected the pattern of prophylactic antibiotic use in surgery. Before 1997, Belgian doctors often prescribed long courses of sophisticated antibiotics for surgical prophylaxis; however, the reimbursement changes in 1997 led to rapid implementation of optimised antibiotic prophylaxis.

Furthermore, pharmaceutical industries sometimes aggressively try to influence doctors’ prescribing habits, which affects hospital antibiotic use. Although many doctors claim that they do not feel influenced, research has reached other conclusions. Harbarth and colleagues describe how low drug prices in France motivated the pharmaceutical industry to compensate with extremely offensive marketing. After the first national public campaigns on the danger of emerging resistance by antibiotic overconsumption in Belgium, a pharmaceutical company used the message of increasing resistance to market their new broad-spectrum fluoroquinolone for community-acquired respiratory-tract infections (I C Gyssens, Radboud University Nijmegen Medical Centre, Nijmegen, Netherlands, personal communication).

Improvement strategies

Because of the various sociocultural and socioeconomic determinants of antibiotic use in hospitals in different
Panel: Examples of potentially effective strategies to improve antibiotic use in hospitals

**Improvement strategies at the cultural level**
- Intensify international cooperation with regard to antibiotic use and antimicrobial resistance
- Develop international guidelines for appropriate antibiotic use
- Develop international programmes to implement these guidelines
- Regularly assess antibiotic use and antibiotic resistance problems in countries and give these outcomes to both politicians and professionals in each country

**Improvement strategies at the organisational level**
- **Antibiotic policies**
  - Provide an antibiotic formulary
  - Provide an antibiotic order form
  - Provide an antibiotic order form including restriction requiring prior authorisation of prescriptions by infectious disease physicians, microbiologists, pharmacists
  - Provide automatic stop orders
  - Install an infection prevention committee
  - Provide written antibiotic guidelines
  - Provide an antibiotic booklet
- **Strategies to improve coordination, collaboration, communication, teamwork, and care logistics**
  - Introduce pharmacists to review orders and to contact physicians to reinforce appropriate use
  - Introduce ward rounds to stimulate collaboration between doctor and pharmacist or microbiologist
  - Introduce telephone advice for doctors to discuss prescriptions with the pharmacist or microbiologist
  - Introduce flow sheets regarding the coordination of care
  - Improve the logistics of care, for example, to reduce the time between requesting laboratory diagnostics and prescribing antibiotics

**Improvement strategies at the individual level**
- Distribute educational materials (eg, guidelines)
- Provide group education including conferences, seminars, and skills training programmes
- Provide small group education
- Stimulate local consensus processes
- Use local opinion leaders
- Provide individual instruction at the physician’s office (outreach visits or academic detailing)
- Provide feedback (provision of summary of clinical performance, based on, for example, medical records)
- Provide reminders (prompts to perform specific actions), including decision support by computer

Countries, several strategies for improvement at this level might be suggested (panel). The differences between countries make it essential to intensify international cooperation regarding antibiotic use and antimicrobial resistance. Developing international guidelines for appropriate antibiotic use and international programmes to implement these guidelines (eg, including internationally-agreed stewardship programmes) is one possibility. Regular assessment of antibiotic use and antibiotic resistance problems is also important in countries, and the outcomes of such assessments should be disseminated to both politicians and professionals in each country. This would provide insight into antibiotic use and its variation, and emphasise the urgency of reducing these differences.

**Contextual aspects**
The way in which individual hospitals organise patients’ care also influences their antibiotic prescribing. Schouten and colleagues show wide variation between hospitals in nine aspects, or quality indicators, of appropriate antibiotic use at eight medium-sized Dutch hospitals (table). Dedier and colleagues describe similar results in their study of antibiotic use in 38 US university hospitals. The proportion of patients receiving antibiotics within 8 h of hospital admission was 53·8–100% across the 38 hospitals, and the proportion with a blood culture before antibiotic administration was 9·5–100%. Various other studies describe quantitative and/or qualitative differences in antibiotic use between hospitals. Gilbert and colleagues showed significant variation in prescribing practices for 18 of 20 parenteral agents prescribed for inpatients across four treatment sites; the overall median cost of antimicrobial therapy also varied significantly between sites (p<0·0001). Shalit and colleagues showed significant variation in prescribing practices for 18 of 20 parenteral agents prescribed for inpatients across four treatment sites; the overall median cost of antimicrobial therapy also varied significantly between sites (p<0·0001).

**Organisational policies**
Many hospital antibiotic policies might influence antibiotic use in a specific organisation. In their Cochrane review, Davey and colleagues included 66 studies of strategies to improve antibiotic prescribing practices for hospital inpatients. Of these studies, 27 used organisational restrictive strategies, such as selective reporting of laboratory susceptibilities, formulary restriction, requirement for prior authorisation of prescriptions (by infectious disease physicians, microbiologists, pharmacists, etc), therapeutic substitutions, and automatic stop orders. They also included three studies of structural organisational strategies, such as changing from paper to computerised records and the introduction or organisation of quality-monitoring mechanisms. They concluded that most of these strategies effectively improved prescribing and decreased the numbers of infections and deaths, illness, and length of hospital stays. However, they also noted the varying effectiveness of the studies and the little existing evidence of external validity, with only five studies evaluating strategies in ten or more hospitals. This last point is underscored by a study of the quality of strategies for improving hospital antibiotic prescription: most evaluations use fundamentally flawed methods.
Effective organisational policies are available. These policies are even summarised in guidelines related to antimicrobial stewardship. However, the degree to which these various policies are used differs greatly between hospitals. Our study in 64 Dutch hospitals showed that almost all hospitals had an infection prevention committee, had written antibiotic guidelines, and used an antibiotic formulary. About half the hospitals restricted the use of certain antibiotics by requiring the authorisation of a medical microbiologist or a pharmacist (55%); six hospitals (10%) used automatic stop orders, and two (3%) used an antibiotic order form. Several US studies also show variation in use of control measures.

All 47 hospitals participating in the Intensive Care Antimicrobial Resistance Epidemiology study had programmes for improving antimicrobial use, but the practices reported varied substantially. All hospitals used a formulary, 70% had clinical practice guidelines available, 60% used stop orders, and 40% had restriction policies. A survey on the implementation of the Infectious Diseases Society of America and Society for Healthcare Epidemiology of America guidelines for developing an institutional programme to enhance antimicrobial stewardship showed that, a year after publication of the guidelines, most hospitals were using many stewardship functions, but fewer than half had an antimicrobial stewardship programme in place. Data from the UK and Italy also show varying practices and room for improvement.

Multiprofessional care-delivery system

Factors other than patient-care organisational policies probably also influence antibiotic use. Different hospital disciplines are usually involved in antibiotic prescription (eg, clinicians, nurses, pharmacists, microbiologists). Several factors related to this multiprofessional care-delivery system of antibiotics are probably important (eg, care coordination, professionals’ collaboration and communication, teamwork, and care logistics). Unfortunately, research in this area is scarce. With regard to teamwork, Davey and colleagues selected several improvement strategies that included pharmacists to review orders and to contact physicians to reinforce appropriate use. These were effective, although the organisational restrictive strategies seemed to have a larger effect. A recent review on team effectiveness reported that teams with enhanced clinical expertise provide better care: patients who receive care from a team of carers might benefit from more “eyes and ears”, from the insights of different bodies of knowledge and from a wider range of skills. This is important, given that Schouten and colleagues qualitative study reports that clinicians do not accept the interference of clinical pharmacists and, to a lesser extent, medical microbiologists in clinical antibiotic management.”

Turnbull and colleagues analysed system factors that interfered with the appropriate administration of surgical antimicrobial prophylaxis. A positive factor for an effective first dose was the writing and giving of the order in the operating room; same-day surgery was a negative factor.

Obstacles

Qualitative data from several studies emphasise the importance of the hospital’s social and institutional context. Our group qualitatively studied the obstacles to appropriate antibiotic treatment for community-acquired pneumonia (CAP). We used in-depth interviews and focus-group sessions (with clinicians, medical microbiologists, pharmacists, and nurses) to discuss key recommendations for antibiotic use. We also used a validated framework to standardise obstacle reporting. This model suggests that physicians within hospitals fail to use antibiotics appropriately in the presence of an internal obstacle that has a cognitive (knowledge) or affective (attitude) component, or in the presence of an external obstacle (organisational, social, political, or economical) that restricts the professionals’ ability. Each recommendation elicited its own pattern of obstacles.

External organisational obstacles influenced the timeliness of antibiotic administration: “substantial delays in delivering laboratory results to the emergency department”, “antibiotics not present on the ward”, “intravenous drip not started”, “antibiotics not directly available”, “lack of time”, and “ward nurses prioritising non-medical issues during hospital admission, leaving prescribed medication to the end of the round or postponing administration until regular medication rounds”. Social influence or pressure (eg, “out of courtesy to colleagues, no criticism of the chosen antibiotic regimen is made at end-of-shift meetings”, “one tends to postpone a decision about antibiotic change until the supervisor’s ward round”, and the ward culture to “never change a winning team”) influenced the prescribing of guideline-adherent empirical therapy, streamlining, and switching.

### Table: Performance levels of quality indicators for antibiotic treatment of community-acquired pneumonia

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<tr>
<th>Indicator</th>
<th>Median adherence (range)*</th>
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<tr>
<td>Timely initiation of antibiotic therapy (within 4 h after presentation)</td>
<td>68% (36–87%)</td>
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<tr>
<td>Prescription of empirical antibiotic regimen according to national guidelines</td>
<td>45% (5–59%)</td>
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<tr>
<td>Adaptation of dosage and dose interval of antibiotics to renal function</td>
<td>77% (40–100%)</td>
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<tr>
<td>Switching from intravenous to oral therapy according to existing criteria and when clinical stability is present</td>
<td>81% (35–93%)</td>
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<tr>
<td>Change of broad-spectrum empirical therapy to pathogen-directed therapy (streamlining therapy)</td>
<td>80% (50–100%)</td>
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<tr>
<td>Stopping antibiotic therapy after 3 consecutive days of defervescence</td>
<td>11% (2–32%)</td>
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<tr>
<td>Two sets of blood samples are taken for culture</td>
<td>57% (48–67%)</td>
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<tr>
<td>Sputum samples are taken for gram staining and culture</td>
<td>54% (20–62%)</td>
</tr>
<tr>
<td>Urine antigens are tested against Legionella spp on clinical suspicion</td>
<td>84% (67–100%)</td>
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*Data from eight hospitals.
Similarly, important obstacles to the use of a general, hospital-wide antimicrobial treatment guideline were the use of different guidelines by different wards, and the fact that residents are not independent decision-makers because specialists from the various wards supervised their prescribing decisions. A resident clearly described the social influence on the various wards: “...and when you move to another department, you learn the supervising specialist’s prescribing preferences within a week”. What if this specialist’s preference is not appropriate? Barlow and colleagues report that environmental factors hinder adherence to a CAP management pathway. Work intensity was an obstacle, with intensity compounded by organisational issues such as lack of beds, an inadequate triage system, lack of porters to take patients to the radiography department, lack of a system to review radiographs, and the effect of the shift system. Similarly, lack of senior support affected adherence: communication and teamwork were poor, and approachable senior support for inexperienced junior staff was lacking. van Kasteren names several organisational constraints that influence the timing of administration of the first dose of prophylaxis: time of arrival at the surgical suite, time spent in the holding area, the need of a test dose before a full dose, administrating antibiotic as an infusion instead of a bolus injection, and a written order for prophylaxis instead of having to wait for instructions. The way these factors influenced the timing differed by surgical specialty. Gyssens and colleagues also looked at the timing of surgical prophylaxis, and described the operating department differences in the ways that the anaesthetist was informed about the need for administration of antibiotics.

Improvement strategies
Various contextual determinants of antibiotic use in hospitals play their part in appropriate antibiotic use. These include both the chosen antibiotic policies and multiprofessional care-delivery systems for antibiotics in hospitals. The effectiveness of various antibiotic policies (eg, formularies and stop orders) has been confirmed (panel). Given the large variation in the application of organisational antibiotic policies in hospitals, the challenge lies in improving the application of these strategies. Hospitals should be encouraged to apply antibiotic policies. The effectiveness of improving various aspects of multiprofessional care-delivery systems for antibiotics should be explored to find new ways of improving antibiotic use in hospitals. Interventions should be developed and tested to improve the coordination of care, professionals’ collaboration and communication, teamwork, and the logistics of care (panel).

Behavioural aspects
The third level of determinants of hospital antibiotic use is that of individual professionals. Differences in antibiotic use between professionals (within the same hospital or at different hospitals) have not been described. In general, large gaps exist between the care recommended in guidelines and the care provided in daily practice, with variation between and within organisations. Several studies have quantitatively shown how professional background or clinical experience can influence antibiotic use or antibiotic-practice beliefs. Many characteristics of individual professionals might influence the decision to prescribe antibiotics, which creates differences. However, most studies describing these factors are based on qualitative research.

Knowledge
A physician’s knowledge might influence antibiotic use; a lack of familiarity with or awareness of available evidence or consensus on appropriate antibiotic use might negatively affect individual prescribing behaviour. Physicians might not know enough about infectious diseases, the potential causative microorganisms, their susceptibility to antimicrobial agents, or antimicrobial drugs. Avorn and Solomon report that, in teaching hospitals, junior staff (interns and residents) frequently make prescribing decisions, even though hospital inpatients are becoming more acutely ill and their cases increasingly complex. The first priority then becomes “the prevention of disaster” within the next 24 h, a goal often thought to be best met by broad-spectrum antibiotics or “a cacophony of narrow-spectrum agents used in combination.” This situation might encourage excessive antibiotic use.

Barlow and colleagues describe education (recognised as inadequate with regard to antimicrobial therapy), experience, and confidence as factors that influence adherence to a CAP management pathway. The difficulty of diagnosing CAP also influences adherence. Given these problems, many clinicians tend to prefer the route of certainty. Many years ago, Kunin and colleagues called antibiotics “drugs of fear”, which seems to be confirmed by the qualitative study of obstacles to appropriate antibiotic treatment for CAP. When interviewing professionals about determinants of the choice of the empirical regimen, Schouten and colleagues reported that, “everyone feels safe with a broad-spectrum antibiotic: colleagues will not criticise you for this choice”, and that, “we are afraid of missing things, afraid to take risks with our patients, no matter what the guideline recommends”.

Harbarth and Samore also see diagnostic uncertainty as a key driver of drug use and misuse. Fear of being sued for not prescribing an antibiotic, or prescribing the wrong antibiotic, is more common in the USA than in Europe. De Souza and colleagues concluded that prescription decisions seem to be based primarily on instructions passed down through a hierarchical system and subsequently on personal experience. Formal education, rationale for use, existing guidelines, and concerns about emerging resistance seem to have
minor influence. Other investigators record that most clinicians presume that the patient’s immediate risk outweighs the long-term disadvantages of the liberal use of antibiotics.13,38,58

**Attitudes**

Physicians’ attitudes might influence antibiotic use. Disagreement with guidelines in general (eg, “challenge to autonomy”, “too much cookbook”, or “too rigid”) or with the specific recommendations, lack of outcome expectancy (“performance will not lead to desired outcome”), lack of self-efficacy expectations, and lack of motivation might all lead to inappropriate antibiotic use.60 Both Schouten and colleagues61 and Barlow and co-workers62 emphasise the importance of these influencing factors. Some examples of statements given as follows: “I have been treating patients with this non-guideline-adequate antibiotic since medical school and it is always successful” (lack of motivation); “microbiologists (who drew up the antibiotic guidelines) have a fundamentally different view from clinicians” (disagreement with guideline); or “we can do a lot for myocardial infarction, and minutes mean muscle, to coin a phrase; but with pneumonia, it’s just pneumonia” (CAP has a lower priority status than other clinical presentations).63 Majumdar and colleagues64 in-depth interviews with physicians indicate that perceived characteristics of a critical pathway (limited applicability, lack of flexibility to accommodate atypical clinical presentations, and perception of insufficient evidence to support recommendations), and the physician’s need for local adaptation, influence adherence to that pathway.

**Improvement strategies**

Many professional-oriented strategies are available to influence individual antibiotic use. Various strategies to improve the knowledge and attitudes of professionals have been used and tested. They include distributing educational materials, educational meetings or conferences, local consensus processes, educational outreach visits, and use of local opinion leaders, reminders, audit, and feedback (panel). The Cochrane Effective Practice and Organisation of Care Group has provided a classification of strategies.65 Avorn and Solomon66 concluded that traditional education is ineffective in improving antibiotic use. Professional-oriented strategies that did work included computer-based algorithms that prompted professionals to prescribe antibiotics appropriately. These studies often combined different professional-oriented strategies. As described above, these persuasive strategies were effective. However, restrictive strategies seemed to have a larger effect.

**Conclusions**

Improving appropriate antibiotic use in hospitals is crucial for the containment of resistance. A focus on novel drug development is also imperative, particularly because the average time from inception to market is more than 13 years.

In this Review, we have not discussed patients’ views with regard to antibiotic prescribing. Research in general practice has provided insight into the major influence of patients’ knowledge and behaviour about antibiotic use in the community. Knowledge of the difference between viral and bacterial infections, knowledge of the resistance problem, the way in which people label illness, the coping strategies they adopt, specific notions on the effectiveness of antibiotics, expectations in terms of being given a prescription, and compliance with regard to the medication are all patient-related factors that affect appropriate antibiotic use in general practice care. However, information about this fourth level for hospital care is lacking.

We have also not discussed antibiotic use in hospitals in low-income countries. Our comprehensive but not exhaustive search strategy resulted in papers that were mainly from North America and Europe. Therefore, our review does not specifically provide information on variation, determinants of variation, and methods to improve antibiotic use in low-income countries.

The need to improve antibiotic prescribing in hospitals worldwide is urgent. Changing hospital antibiotic use is a challenge of formidable complexity. Many determinants—cultural, contextual, and behavioural—affect antibiotic use in hospitals. Our current knowledge of the relative effect of each determinant is still limited. The great diversity of the determinants dictates that measures or strategies to improve antibiotic use need to be equally diverse.

**Search strategy and selection criteria**

We searched Medline for English-language articles on the determinants of variation in hospital antibiotic use in the period January, 1990, to March 11, 2009, inclusive. We combined keywords (non-MeSH) on variation (variation*; determinant*; factor*; difference*; barrier*; cultural; organisational; organizational; individual; all in Title) with antibiotic use (antibiotic*; antibacterial*; antimicrobial*; all in Title). We also reviewed the reference lists of the included papers. This resulted in 34 papers discussing variation of antibiotic use, of which 20 explicitly described determinants of variation.
Fortunately, many strategies are available. We need, however, more insight into the best strategies to tackle the determining factors. Although programmes with activities at all three levels seem potentially the most successful, a proper analysis of relevant determinants should be at the heart of an effective improvement programme. Furthermore, an evaluation of the improvement activities in which the conclusions are externally validated is crucial.

References