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Antibacterial Use in Community Practice

Assessing Quantity, Indications and Appropriateness, and Relationship to the Development of Antibacterial Resistance

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Contents

Abstract

Most use of antibacterials occurs in community practice; however, despite the widespread belief of inappropriate use and the resultant increase in antibacterial resistance, little data exist describing antibacterial use in this setting. A MEDLINE search of English-language articles was conducted for epidemiological studies assessing quantity, indication and appropriateness of antibacterial use in community practice.

A 1983 study of international antibacterial use described considerable disparities in quantity of use between countries. Subsequent longitudinal studies from the US, Canada, Australia and the UK described changing patterns of antibacterial use. No increase in the total rate of antibacterial use was reported by any of the 4 countries; however, all countries reported increased use of newer and/or broad-spectrum agents (e.g. fluoroquinolones, amoxicillin-clavulanic acid, cephalosporins and new macrolides] coupled with decreased use of older and/or narrow-spectrum agents [e.g. phenoxymethylpenicillin (penicillin V), erythromycin, ampicillin and tetracycline). Most (approximately three-quarters) use of antibacterials was in the treatment of respiratory tract infections. Prescribing rates for respiratory tract infections of presumed viral aetiology (e.g. the common cold) ranged from 17 to 60% in the UK and US, respectively. Among indications for which antibacterials were indicated, the appropriateness of antibacterial use received little study. Correspondingly, the rates of antibacterial resistance among common respiratory pathogens (*Streptococcus pneumoniae* and *Haemophilus influenzae*) have increased significantly in the past decade, although disparities exist between countries.

Antibacterial use is considered a major factor in the development of antibacterial resistance, although the relationship between community antibacterial use

and resistance has been poorly described. Further study of antibacterial usage patterns and associated resistance patterns is fundamental to the development of methods to reduce unnecessary and inappropriate use, thereby slowing the development of antibacterial resistance in the community.

The cost of antibacterial use worldwide was projected to be $US18 billion for 1990.[1] A vast quantity of literature exists on the comparative benefits, risks and costs associated with these commonly used agents. From randomised controlled trials to practice guidelines to pharmacoeconomic studies to the problem of antibacterial resistance, much has been published on the use of these agents. However, little data exists describing how these agents are actually used in practice.

In institutions, intravenous antibacterials account for a large proportion of the drug budget; in North America this figure is commonly between 20 and 30%.[2-6] Concerns of increasing antibacterial resistance among nosocomial pathogens, coupled with evidence of inappropriate antibacterial use, prompted surveillance and the development of control mechanisms in this setting. At the institutional level, knowledge of patterns of antibacterial resistance and antibacterial utilisation trends is common. This knowledge allowed the development of mechanisms to optimise antibacterial use and impede the development of antibacterial resistance.[7-9]

In the community, courses of therapy are less costly because of the use of oral agents; yet, since most (approximately 70%) antibacterial use occurs in the community setting, this accounts for a significant portion of drug expenditures. Evidence of increasing antibacterial resistance among community-acquired pathogens[10-13] and the widespread belief of unnecessary and inappropriate antibacterial use[3,14-15] have prompted efforts to curtail antibacterial use in this setting. However, before we can hope to optimise antibacterial use in community practice it is imperative to determine current antibacterial usage patterns (including quantity, indication and appropriateness of use) as well as patterns of antibacterial resistance that may be affecting use.

1. Quantifying Antibacterial Use

In 1983, a worldwide study of antibacterial use was commissioned by the Fogarty International Centre of the US National Institutes of Health (NIH).[16] To quantify the extent of antibacterial use by country, information was gathered from many sources: market research companies, ministries of health, pharmaceutical manufacturers and the World Health Organization. The type of data gathered fell into 2 categories: production and trade data or sales data. In developing countries, reliable sales data were not available; thus, production and trade figures were used to estimate antibacterial use. A more reliable measure of actual use is sales data; however, information on sales was only available in the more developed countries.

Antibacterial usage in 8 countries is shown in figure 1, reported as defined daily dosage (DDD) per 1000 persons per day (DDD/1000/day). The DDD is a technical unit of measurement defined by the World Health Organization as the usual adult

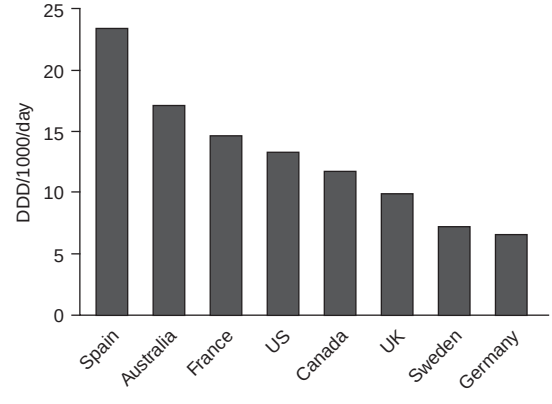

Fig. 1. Retail sales of antibacterials from 8 countries in 1983 in DDD/1000/day (reproduced from Col & O'Connor,[16] with permission). **DDD/1000/day** = defined daily dosage per 1000 persons per day.

daily dosage for the major indication for a specific agent. In 1983, Spain and Australia were the highest users of antibacterials at 23.5 and 17.1 DDD/1000/day, respectively, whereas Sweden and Germany were relatively conservative users of antibacterials with values of 7.0 and 6.4 respectively (fig. 1). Canada and the US were moderate users of antibacterials, at 11.6 and 13.2 DDD/1000/day respectively. Although all the countries shown used more broad-spectrum agents [e.g. cephalosporins, tetracyclines, aminopenicillins and cotrimoxazole (trimethoprim-sulfamethoxazole)] than narrow-spectrum agents [e.g. benzylpenicillin (penicillin G) and erythromycin], the extent to which they favoured broad-spectrum agents varied considerably. Germany, although the lowest overall user of antibacterials, had the highest ratio of broad-spectrum to narrow-spectrum agents. Conversely, Sweden, also a country with relatively small overall antibacterial use, had the lowest ratio of broad-spectrum to narrow-spectrum use. The ratio of broad-spectrum to narrow-spectrum agents in Canada and the US was intermediate.

Wyatt et al.[17] analysed community use of oral antibacterials in Northern Ireland from 1983 to 1987. Data were gathered from the Central Services Agency in Northern Ireland which records the number of doses of each drug dispensed by pharmacist or physician. The annual number of prescriptions dispensed did not change appreciably over the 5 years, remaining fairly constant at approximately 2 million. Broad-spectrum penicillins (amoxicillin and ampicillin), cotrimoxazole, phenoxymethylpenicillin (penicillin V) and erythromycin accounted for 70% of antibacterial use as measured by the number of 'dosing units' dispensed per year. A 'dosing unit' was defined as a single recommended adult dose for an agent. Since total antibacterial use remained static, changes in antibacterial use reflect changing preferences for some agents over others, possibly because of the improved pharmacokinetic or safety profile of alternative agents. For example, ampicillin use decreased, possibly in favour of amoxicillin, while cotrimoxazole use decreased, possibly in favour of trimethoprim alone whose use increased almost 140% over 5 years. Similarly, oxytetracycline use decreased by approximately 20% whereas minocycline and doxycycline use increased by approximately 80 and 130%, respectively. In fact, there was a significant trend toward increased use of all the newer or broad-spectrum agents, such as amoxicillin-clavulanic acid, tetracyclines and various cephalosporins. The use of many of these agents doubled over the 5-year study.

In 1993, as part of a study of market penetration of new drugs in the UK, McGavok et al.[18] published usage data for cefuroxime axetil and ciprofloxacin in Northern Ireland. The Central Services Agency was once again used as the data source to quantify usage trends for these broad-spectrum agents shortly after their introduction. Antibacterial usage was not reported as a rate but simply the number of DDD for the years 1988 to 1991. Ciprofloxacin use increased 205% (from 6157 DDD in 1988 to 18 782 DDD in 1991). Cefuroxime use increased 210% (from 2792 DDD in 1988 to 8647 DDD in 1991).

McManus et al.[19] studied antibacterial use in community practice in Australia between 1990 and 1995, using several data sources. The database of the Drug Utilisation Subcommittee (which contained information on all government subsidised prescriptions in addition to an estimate of nonsubsidised prescriptions) was used to quantify antibacterial use. Total oral antibacterial use remained stable between 1990 (24.7 DDD/1000/day) and 1995 (24.8 DDD/1000/day). Most commonly used agents in 1995, measured in DDD/1000/day were amoxicillin (5.6), doxycycline (4.5), amoxicillin-clavulanic acid (2.9) and erythromycin (2.2). Over the study period, the use of newer or broad-spectrum agents (e.g. amoxicillin-clavulanic acid, cefaclor or roxithromycin) increased, while the use of older or narrow-spectrum agents (erythromycin, cotrimoxazole and amoxicillin) decreased.

Trends in oral antibacterial prescribing among office-based physicians in the US were studied by McCaig and Hughes.[20] Data were compiled from National Ambulatory Medical Care Surveys (NAMCS) for the years 1980, 1985, 1989 and 1992. NAMCS are conducted by the National Center for

Health Statistics, Centers for Disease Control and Prevention, and are based on a national probability sample. A select sample of US physicians were asked to supply specific data on a sample of patient visits and as such the data reflect antibacterials prescribed rather than dispensed.

Prescribing rates are reported as number of prescriptions per 1000 persons annually (Rx/1000/year). During the 13-year span, the estimated number of antibacterial prescriptions increased from 86 million in 1980 to 110 million in 1992; however, no increase in the prescribing rate was reported overall or when patients were subdivided by age, race or gender. The highest rates of antibacterial use were seen in children less than 15 years of age. Prescribing trends were tracked in terms of antibacterial class rather than individual agents in most cases. Broad-spectrum penicillins (amoxicillin and ampicillin combined) were the most commonly used agents in all years studied and their use as a class increased over the 13-year span. However, amoxicillin use increased from 50 Rx/1000/year in 1980 to 175 Rx/1000/year in 1992, while ampicillin use decreased from 55 Rx/1000/year in 1980 to 10 Rx/1000/year in 1992. Cephalosporin use increased from 30 Rx/1000/year in 1980 to 90 Rx/1000/year in 1992, becoming the second most commonly prescribed agents. Meanwhile, the usage of narrow-spectrum penicillins decreased from 75 Rx/1000/year in 1980 to 25 Rx/1000/year in 1992. No significant changes in prescribing rates were observed for cotrimoxazole, macrolides or tetracyclines; approximate usage in 1992 was 25, 75 and 40 Rx/1000/year respectively.

The lack of recent Canadian data on antibacterial use in community practice prompted us to undertake study in this area.[21] We quantified antibacterial use and usage trends in Manitoba, a province in central Canada, between 1995 and 1997 using data from the Manitoba Health Drug Programs Information Network (DPIN). The DPIN, instituted in 1994, is a pharmaceutical claims database which records details of over 90% of prescriptions dispensed in Manitoba community pharmacies. In Manitoba, restrictions are in place to curtail use of broad-spectrum second-line agents (e.g. fluoroquinolones, second/third generation cephalosporins and amoxicillin-clavulanic acid). During the first quarter of 1997, antibacterials were dispensed at a rate of 894 Rx/1000/year. Amoxicillin was the most used antibacterial, accounting for 35.9% of prescriptions, followed by: cotrimoxazole (12.5%), erythromycin (11.7%) and phenoxymethylpenicillin (6.4%). There was no increase in total antibacterial use over the 3-year study period. However, use of older or narrow-spectrum agents declined (phenoxymethylpenicillin –12.6%, tetracycline –7.9% and erythromycin –19.4%), while use of newer or broad-spectrum agents increased (fluoroquinolones +40.6%, second/third-generation cephalosporins +28.1%, clarithromycin/azithromycin +34.1% and minocycline/doxycycline +29.2%) [fig. 2]. The use of restricted second-line agents as a percentage of all agents increased from 13.9 to 17% over the study period ($p < 0.02$).

In summary, several countries have published population-based studies of antibacterial use in community practice. These studies, performed over varying time periods between 1980 and 1997, employed a variety of data collection methods and measurement systems. The US, Canada, Australia and Northern Ireland all reported no increase in the rate of total antibacterial consumption. All countries reported increasing use of newer or broad-spectrum agents (e.g. fluoroquinolones, second/third generation cephalosporins and new macrolides) with declining use of older or narrow-spectrum agents (e.g. phenoxymethylpenicillin, erythromycin, cotrimoxazole and tetracycline).

2. Indications for Antibacterial Use

Few studies are available describing antibacterial use by indication. Available population-based studies which describe antibacterial use by indication use physician surveys as the data collection mechanism. McCaig and Hughes[20] reported the 5 leading diagnoses for which antibacterials were prescribed in community practice in the US in 1992. Five diagnoses accounted for 76% of total antibacterial prescriptions. They were otitis media

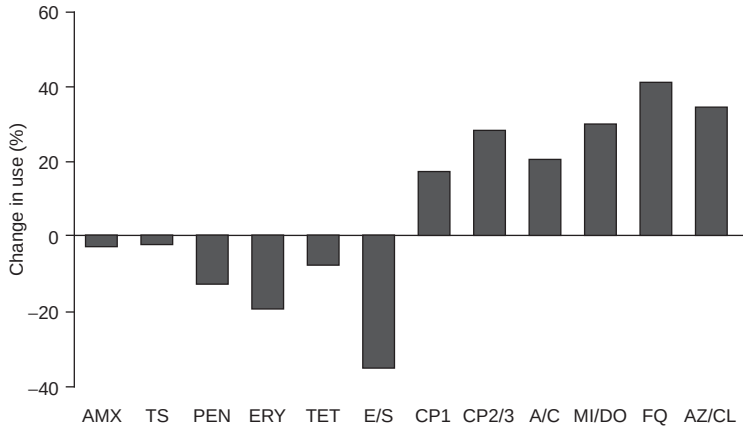

Fig. 2. Change in oral antibacterial use in Manitoba, Canada, 1995 to 1997. **A/C** = amoxicillin-clavulanic acid; **AMX** = amoxicillin; **AZ/CL** = azithromycin/clarithromycin; **CP1** = cephalexin; **CP2/3** = cefaclor/cefuroxime axetil/cefprozil/cefixime; **ERY** = erythromycin; **E/S** = erythromycin-sulfisoxazole; **FQ** = ciprofloxacin/ofloxacin/norfloxacin; **MI/DO** = minocycline/doxycycline; **PEN** = benzylpenicillin/phenoxymethylpenicillin (penicillins G/V); **TET** = tetracycline; **TS** = cotrimoxazole (trimethoprim-sulfamethoxazole).

(21%), upper respiratory tract infection (16%), bronchitis (15%), pharyngitis (12%) and sinusitis (12%). The leading diagnoses for the prescribing of particular antibacterials included: amoxicillin (otitis media), cephalosporins (otitis media), penicillin (pharyngitis), erythromycin (bronchitis) and cotrimoxazole (otitis media).

Indications for antibacterial use in Australia were studied by McManus et al.,[19] using data from the Therapeutics Resource and Education Network for Doctors (TREND). The TREND database includes information on prescribed treatment from a survey of general practitioners in urban and rural New South Wales. In 1995, the most commonly prescribed agents for otitis media included cefaclor (35.5%), amoxicillin (21%) and amoxicillin-clavulanic acid (20.5%). For bronchitis, treatment included amoxicillin (18.1%), roxithromycin (16.5%) and cefaclor (15.2%). Antibacterials prescribed for upper respiratory tract infections included amoxicillin (29.5%), cefaclor (10.2%) and amoxicillin-clavulanic acid (9.4%). Antibacterials most commonly prescribed for sinusitis included doxycycline (20.7%), amoxicillin-clavulanic acid (18.1%) and cefaclor (15.1%).

Thus, most antibacterial use in community practice is for the treatment of respiratory tract infections. In Australia, broad-spectrum agents (e.g. cefaclor and amoxicillin-clavulanic acid) were commonly employed in the treatment of these infections.

3. Appropriateness of Use

Addressing the appropriateness of use within a country or region is perhaps the most difficult aspect of assessing antibacterial use; this is probably why few such studies exist. Antibacterial use may be best termed unnecessary where no antibacterial is indicated, and inappropriate where an antibacterial is indicated but an incorrect agent is selected. What constitutes unnecessary use may be open to debate. Although it is generally agreed that the use of antibacterials for the common cold is unnecessary, the necessity of antibacterials for otitis media and bronchitis may be controversial.[22-24]

Several recent studies exist which describe the unnecessary use of antibacterials. In a study of Kentucky (US) Medicaid claims from 1993 to 1994, Mainous et al.[25] described antibacterial usage trends in patients diagnosed with the common cold (ICD-9-CM 460.0). 60% of patients thus diagnosed filled prescriptions for antibacterials. Antibacterials used included amoxicillin (54%), second/third-generation cephalosporins (14%) and erythromycin (11%). Gonzales et al.[26] described the treatment of colds, upper respiratory tract infections and

bronchitis in adults in the US. Data from the 1992 NAMCS were used to determine prescribing rates for these indications considered to be of viral aetiology, for which antibacterial therapy would be unnecessary. Antibacterial prescribing rates for colds (ICD-9-CM 460), upper respiratory tract infections (ICD-9-CM 465) and bronchitis (ICD-9-CM 466,490) were 51, 52 and 66% respectively. Similar rates of antibacterial prescribing for these indications in children were reported by Nyquist et al.[27] In Australia, McManus et al.[19] reported antibacterial prescription rates for new cases of upper respiratory tract infections/pharyngitis (ICD codes not provided) of 57 and 73% in urban and rural areas respectively.

A study of the management of upper respiratory tract infections in Dutch family practice provides an interesting contrast.[28] Data from the National Study of Illness and Procedures of the Netherlands Institute of Primary Healthcare between 1987 and 1988 were used to determine rates of antibacterial prescribing. Antibacterial prescribing rates for first contacts for acute otitis media, acute upper respiratory tract infection and acute tonsillitis (ICD codes not provided) were 27, 17 and 74% respectively. Similar results were reported from a study by Froom et al.,[29] in which 31.2% of patients diagnosed with acute otitis media in The Netherlands received antibacterials, compared with 98.2 and 97.9% in Australia and the US respectively. Thus the unnecessary use of antibacterials in the treatment of infections of largely viral aetiology is common, although international differences in prescribing practices exist.

The authors are unaware of any recent studies that examine the extent of inappropriate antibacterial use within a population. This is likely, in no small part, because of the difficulty in defining inappropriate use. Inappropriate antibacterial treatment may be defined as: (i) selection of an agent inactive against the most likely causative organisms; (ii) use of a broad-spectrum agent when an equally effective narrow-spectrum agent is available; (iii) inappropriately long or short duration of treatment; and (iv) treatment which deviates from accepted practice or published treatment guidelines. A recent study by Gleason et al.[30] highlights the problems associated with using published guidelines as a measure of appropriate use. These investigators compared outcomes in community-acquired pneumonia in patients treated, or not treated, in accordance with American Thoracic Society (ATS) guidelines. This multicentre, observational, prospective, cohort study in the US and Canada, involving 864 patients, reported that 82.4% of patients over age 60 years with 1 or more comorbid conditions were not treated in accordance with ATS guidelines. ATS guidelines recommend treatment with a second-generation cephalosporin, cotrimoxazole or amoxicillin-clavulanic acid for this patient population. There were no differences in therapeutic outcome between those treated, or not treated, in accordance with the guidelines. However, adherence to these guidelines resulted in a 10-fold increase in cost of treatment as well as an increased potential for development of antibacterial resistance to these newer or broad-spectrum agents.

Thus, the appropriateness of antibacterial use has been poorly studied. There appears to be sufficient evidence of unnecessary use in viral infections (e.g. the common cold) but little information is available regarding the appropriateness of antibacterial use in other indications. Guidelines for treatment of common community-acquired infections are available but are often not followed. This may be, in part, because of the lack of evidence supporting improved clinical outcomes through use of current practice guidelines.

4. Antibacterial Resistance in Community Practice

The problem of antibacterial resistance has existed since shortly after antibacterials came into widespread use. Presently, antibacterial resistance is a growing problem for many reasons, but partly because of the lack of development of new agents which affect novel bacterial targets. With respiratory tract infections accounting for most community antibacterial use, increasing antibacterial resistance among respiratory pathogens assumes

great importance. *Streptococcus pneumoniae*, a major respiratory pathogen, has become increasingly resistant to penicillin in the last decade.[10-12] Recent studies in Canada, the US and Spain report penicillin resistance rates among *S. pneumoniae* of 11.7, 23.6 and 40%, respectively.[10-12] Penicillin-resistant strains were more likely to be isolated from children and were also more likely to exhibit cross-resistance to macrolides, cephalosporins, tetracyclines and cotrimoxazole than were penicillin-sensitive strains.[10-11] Rates of penicillin resistance varied considerably between centres in both Canada and the US.[10-11]

Similarly, *Haemophilus influenzae* has become increasingly resistant to aminopenicillins (e.g. amoxicillin) through production of TEM or ROB β-lactamases. A recent study of antibacterial resistance in Europe and the US reported β-lactamase production by *H. influenzae* in the UK, US and Spain as 9.7, 27.4 and 32.2% respectively.[13]

Antibacterial use is thought to be a major factor in the development of antibacterial resistance, although the exact relationship remains unclear.[31] The association between antibacterial use and antibacterial resistance patterns has been well studied in the hospital setting,[32-36] but little study has been conducted at the community level. One such recent study, performed in Finland,[37] examined the temporal relationship between antibacterial use and resistance in the community setting. Increased rates of erythromycin resistance among group A streptococci from 5% in 1988 to 13% in 1990 had followed steady increases in macrolide use throughout the 1980s. National recommendations were issued in 1991 to decrease the use of macrolide antibacterials. Macrolide use decreased from 2.4 DDD/1000/day in 1991 to 1.3 to 1.7 DDD/1000/day in 1992 to 1995. Erythromycin resistance among group A streptococci continued to increase to a high of 19.0% in 1993, followed by steady yearly decreases to a low of 8.6% in 1996.

Following an examination of antibacterial use and resistance patterns in Europe and the US, Baquero[38] indicated that cephalosporin use appeared to be an important factor in the selection of low level resistant pneumococci. These data provide evidence of the role of community antibacterial use in the development of antibacterial resistance and further illustrate the possibility of controlling antibacterial resistance through prudent antibacterial use.

5. Discussion and Conclusions

The 1983 study by the NIH reported large international disparities in antibacterial usage.[16] Spain and Australia were described as high users of antibacterials, whereas usage in Germany and Sweden was much less; Canada and the US were relatively moderate users. It is tempting to speculate on the results from this study and identify countries such as Spain and Australia as overusers of antibacterials, while designating Germany and Sweden as responsible antibacterial users. However, it is important to note that geography, population demographics, economic conditions, nutritional status and access to healthcare can all affect morbidity patterns and hence antibacterial usage patterns.[16] The quality of antibacterial prescribing in any country cannot be determined by these international comparisons. Each country must determine the appropriateness of its antibacterial use and work within its constraints to optimise antibacterial use.

Subsequent to the NIH study, several countries have performed population-based studies to quantify their antibacterial use and assess longitudinal changes in antibacterial selection. In all cases, concerns of antibacterial misuse and increasing antibacterial resistance were cited as reasons for the studies. Four developed countries for whom data was available (the US, Canada, Australia and Northern Ireland), reported no increase in the overall rate of antibacterial use.[17,19-21] However, all 4 countries exhibited a trend toward the use of newer and/or broad-spectrum agents (newer tetracyclines, cephalosporins, fluoroquinolones and amoxicillin-clavulanic acid) while the use of older and/or narrow spectrum agents (phenoxymethylpenicillin, ampicillin, nitrofurantoin and cotrimoxazole) declined or remained unchanged. The reasons for changes in antibacterial selection are unknown but may be interpreted. All 4 countries reported changes

within antibacterial classes that appeared to be increased preferences for agents with similar spectrum of activity but improved pharmacokinetic and/or safety profile. Examples of this trend include:

- increased use of amoxicillin coupled with a decreased use of ampicillin
- increased use of minocycline and doxycycline coupled with a decrease in the use of oxytetracycline or tetracycline
- increased use of trimethoprim coupled with a decrease in the use of cotrimoxazole.

These changes reflect reasonable therapeutic choices (i.e. improved pharmacokinetics and/or safety) and are unlikely to affect antibacterial resistance trends, although their use may have economic implications. Reasons for changes between antibacterial classes may be more complex. Increasing resistance to older agents, industry advertising or promotion, and a trend toward deinstitutionalised care necessitating treatment with oral broad-spectrum agents may all play a part. The extent to which these or other explanations accounted for changed prescribing patterns was not determined.

Varying time periods, data collection systems and units of measurement make it difficult to compare trends in antibacterial usage between these 4 countries. The use of the NAMCS in the US generated data based on prescriptions dispensed, with no knowledge of whether the prescriptions were actually filled. Conversely, use of pharmacy claims databases in Australia, Northern Ireland and Canada measured prescriptions dispensed, thus avoiding the possible errors and biases inherent in surveys of samples of physicians. In addition, choice of units of measurement may affect study conclusions. For example, use of DDD/1000/day is sensitive to changes in prescribed dosage. A trend toward the use of higher dosages of amoxicillin and cephalexin was observed in an earlier Australian study,[39] possibly in response to increasing antibacterial resistance among *S. pneumoniae*. Use of the DDD/1000/day in this study made a significant contribution to the conclusion of increased use of these agents, and to a lesser extent, increased rates of antibacterial use in general, between 1987 and 1989. Thus, the evidence provided by McManus et al.[19] suggesting increased total rates of antibacterial use between 1985 to 1994 by Canada, the US and other countries, (based on sales to retail and hospital markets translated into DDD/1000/day) may reflect increased daily dosages rather than increased numbers of prescriptions.

Limited data exist describing indications for, and appropriateness of, antibacterial use in community practice. McCaig and Hughes[20] reported that most antibacterial use was in the treatment of respiratory tract infections, many of which are of largely viral aetiology. McManus et al.[19] quantified antibacterial use by indication and observed respiratory tract infections were commonly treated with new or broad-spectrum antibacterials (e.g. amoxicillin-clavulanic acid, cefaclor and roxithromycin). The unnecessary use of antibacterials in viral infections has been well documented.[19,25-28] Unnecessary use is widely believed to be a result of real or perceived patient demand coupled with physician time constraints and the belief that patients will simply seek out antibacterials elsewhere.[40] Perception, by physicians and patients, of antibacterials as innocuous together with diagnostic uncertainty may both also be factors. In addition, Kunin[41] has written extensively regarding the powerful influence of pharmaceutical companies on the use of antibacterials. The extent of unnecessary use varied widely between countries, but is deserving of improved control measures globally. Use of antibacterials in the treatment of viral infections confers no benefit, but unnecessarily exerts pressure for the selection of antibacterial-resistant organisms and increases healthcare costs. These healthcare costs may be considerable when costs of medication, increased morbidity and mortality related to adverse drug reactions and antibacterial resistance are considered.[42]

The extent of inappropriate use is largely unknown. Lack of study in this area may be a result of a lack of consensus regarding what constitutes appropriate use. At the most basic level, the appropriate agent is one that cures the patient with as few untoward effects as possible at minimal cost. This requires knowledge of:

- likely aetiological agents
- antibacterial efficacy
- resistance patterns
- patient-specific variables
- the costs of treatment and of treatment failure.

Practice guidelines are an attempt to incorporate all these variables to arrive at optimum treatment. However, as Gleason et al.[30] reported, actual practice patterns do not often conform to guidelines. Nationally produced treatment guidelines, often a consensus of expert opinion, by their nature do not reflect local patterns of resistance which vary widely between centres. These treatment guidelines may be dismissed by physicians as not reflective of their patient population. Thus it is necessary to define and encourage appropriate antibacterial use by utilising local outcome–specific data. Although inappropriate use in general is undesirable, of foremost concern is the inappropriate use of new broad-spectrum agents because of the possibility of promoting antibacterial resistance to these valuable agents.

Antibacterial resistance among the common respiratory pathogens *S. pneumoniae* and *H. influenzae* has increased over the last decade; rates of resistance vary significantly between and within countries.[10-13] The role of community antibacterial use in the development of antibacterial resistance has been poorly studied. The recent Finnish study of macrolide use and erythromycin resistance among group A streptococci provides evidence of a causal link.[37] Also encouraging is the possibility of decreasing antibacterial resistance through decreased antibacterial use. However, many questions remain to be answered. To what extent does increased use lead to increased resistance? How does an increase in the prevalence of antibacterial-resistant strains affect treatment outcome? What proportion of the increase in new broad-spectrum agents is warranted by antibacterial resistance to older narrow-spectrum agents? To what extent can we expect to decrease or retard antibacterial resistance through decreased antibacterial use?

Optimising antibacterial use will include reducing unnecessary and inappropriate use, thus minimising the development of antibacterial-resistant strains. Further study is required to achieve this goal.

Administrative databases offer a unique opportunity for large, economical, cohort studies to identify current practice patterns and associated treatment outcomes. Continuing surveillance of resistance patterns among community-acquired pathogens in conjunction with antibacterial usage patterns may provide further evidence of the relationship between antibacterial use and resistance. Communication of aggregate data regarding practice patterns and treatment outcomes, in conjunction with antibacterial resistance patterns, enables physicians to better understand the impact of their clinical decisions. Results from such studies may provide a definitive answer to the question: 'What constitutes appropriate treatment?' and may be used to refine national treatment guidelines into ones which reflect local variables. It has been previously demonstrated that provision of such data in educational programmes with appropriate leadership may have substantial effects on practice patterns, obviating the need for externally imposed interventions. Administrative data remain a cost-effective means to evaluate effectiveness of such programmes.

The process of surveillance, analysis, intervention and evaluation is an iterative one. Rapidly changing patterns of resistance may require modifications of treatment recommendations to minimise poor clinical outcome. Ideally, antibacterial resistance among all pathogens to all agents will be kept to the lowest possible levels. This may be accomplished through the elimination of unnecessary use and the reduction of inappropriate use of broad-spectrum agents, which may hasten the development of antibacterial resistance to a dwindling supply of new agents. A continuous process of surveillance, analysis, intervention and evaluation will be required to attain this goal.

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