Age- and gender-specific antibacterial prescribing in Norway

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Objectives: To describe the use of antibacterials among outpatients in Norway and to explore patterns of age- and gender-specific use.

Methods: Data were extracted from the Norwegian Prescription Database (NorPD), a complete register of all dispensed prescriptions in Norway, in the period 1 July 2005–30 June 2006. NorPD contains data at an individual level. We extracted patients who had received an antibacterial for systemic use. Results were shown as population prevalences for the total population.

Results: A total of 1.1 million persons had at least one prescription for an antibacterial dispensed. The mean population prevalence of antibacterial use was 24% in total (28% and 19% for women and men, respectively). Population prevalence changed markedly between different age groups and between genders. Children (<5 years) and older elderly people (≥75 years) were high consumers. Females, in general, used more than males. Use by the different subgroups of antibacterials differed between gender and between different age groups. β-Lactamase-sensitive penicillins was the most prevalent antibacterial group in all age groups except for women ≥75 years, for whom penicillins with extended spectrum were the most frequently used. Individuals defined as high users (using more than 60 DDDs/year) represented 3% of the population who were using antibacterials. These patients were older and used co-medication more often than other users of antibacterials.

Conclusions: Over 1 year, a quarter of the total population used antibacterials. Patterns of use and types of drugs used differed markedly between genders and between different age groups.

Keywords: antibiotic use, population prevalence, DDD, prescriptions, antibacterials

Introduction

Population exposure to antibacterial agents is probably a major factor in the development of antibacterial resistance.1–3 The use of antibacterial agents has therefore been frequently studied, although most frequently at an aggregated level. In this way, antibacterial use has been studied and compared in primary care, in hospitals and at the national level.4–9 The use of antibacterials at an individual level has until recently been studied mostly in smaller groups of patients. Therefore, limited knowledge is available on the use of antibacterials within a general population.

The Norwegian Prescription Database (NorPD) covers all individuals living in Norway and enables us to study the use of drugs by discrete individuals. Thus, the aim of this study was to describe the use of antibacterials in primary care in Norway by looking into the pattern of antibacterial use according to both gender and age. Furthermore, the aim was also to identify high users of antibacterials and to analyse differences in age, gender and patterns of antibacterial use between different user groups.

Materials and methods

Data were extracted from the NorPD in the period 1 July 2005–30 June 2006. This period was chosen because we wanted to include one whole winter in the study. The NorPD includes a complete register of all prescriptions dispensed at the 530 Norwegian pharmacies from 1 January 2004.10 Information about gender, age, residence, prescriber, pharmacy and dispensing date is registered at an individual level. NorPD also includes information about the prescribed drug i.e. product name, package size and numbers, Anatomical Therapeutic Chemical (ATC) code, defined daily dose (DDD) and cost.

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Antibacterials are prescription-only drugs, available solely through pharmacies in Norway. We included patients who had received an antibacterial for systemic use, defined as the ATC fifth level, i.e. substance levels in J01 (antibacterials for systemic use). Methenamine (J01XX05), an antiseptic used for prevention of urinary tract infections (UTIs) and extensively prescribed in Norway, was excluded. In addition, we included patients who had received oral vancomycin (A07AA09) and oral and rectal metronidazole (P01AB01) in the study.

We defined antibacterial use as antibacterial prescriptions dispensed at pharmacies. In the NorPD, all antibacterial prescriptions for outpatients in Norway are included, of which 6% were prescriptions without the patients’ national identity number. These prescriptions could be for tourists, newly arrived immigrants or others in need of acute antibacterial prescriptions, who for some reason—although it is compulsory—could not present their national identity number. Analyses showed that the proportion of prescriptions without a national identity number varies in the different age groups and is somewhat higher in the younger age groups. However, for all age groups, these prescriptions represent a small part of the total amount of prescriptions. Since the national identity number is the key link between the prescriptions and the individual patient, these prescriptions were excluded. For the remaining population, we were able to link all dispensed prescriptions for each person over the study period. The ATC index with DDDs 2006 was used.11

We wanted to look into the antibacterial use of the patient group using many courses of antibacterials per year or for a longer period of time. After screening the database for high users, two cut-offs were tested, 60 and 90 DDDs/years, revealing groups of patients with the same antibacterial patterns of use. The cut-off of 60 DDDs was chosen and high users were defined as individuals using more than 60 DDDs over the period of a year. This is a rough estimate of use of antibacterials for >2 months.

Statistical analysis

The data were analysed using SPSS 13.0 for Windows, with descriptive statistics shown as population prevalence for the Norwegian population at 1 January 2006 (4.6 million) and mean values. Only P values <0.05 were regarded as statistically significant.

Results

Sales of antibacterials for systemic use constituted 26 million DDDs for the period studied. Of these, 14% were delivered to institutions (hospitals and nursing homes); so 86% of antibacterials had been prescribed in primary care. Only 3% were sold directly to prescribers. In the period studied, antibacterials represented 6% of all medicines dispensed on prescription in Norway.

A total of 1.1 million individuals had at least one prescription of an antibacterial dispensed. Figure 1 shows age- and gender-specific 1 year population prevalence for the use of antibacterials. The mean population prevalence of antibacterial use for all age groups was 24% in total: 28% for women and 19% for men.

Patterns of use

Patterns of use differed between genders and between different age groups (Table 1). We found the highest prevalence for both genders among those aged <75 to be the antibacterial subgroup of β-lactamase-sensitive penicillins (J01CE). Macrolides (J01F) was the second most prevalent group used in those aged <55. In elderly women (≥75 years), penicillins with extended spectrum (J01CA), followed by trimethoprim and sulphonamides (J01E), were the antibacterials most frequently used—by 12% and 9% of the females, respectively. In elderly men (≥75 years), the most frequently used groups were β-lactamase-sensitive penicillins and penicillins with extended spectrum, both being groups used by 8% of the men. There was an age-related trend of decreasing prevalence of use of antibacterials from β-lactamase-sensitive penicillins and macrolides for females, whereas the trend for the penicillins with extended spectrum, tetracyclines (J01A), trimethoprim and sulphonamides and quinolones (J01M)

![Figure 1](https://academic.oup.com/jac/article-abstract/59/5/971/728090/figure1)
<table>
<thead>
<tr>
<th></th>
<th>0–4 years</th>
<th>5–14 years</th>
<th>15–34 years</th>
<th>35–54 years</th>
<th>55–74 years</th>
<th>≥75 years</th>
<th>All age groups pp</th>
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<td><strong>Females</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<td>0</td>
<td>0</td>
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<td>10</td>
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<td>25</td>
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<td>13</td>
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<td>6</td>
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<td>14</td>
</tr>
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<td>1</td>
<td>7</td>
<td>9</td>
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<td>10</td>
</tr>
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<td>0</td>
<td>15</td>
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<td>146</td>
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<td></td>
<td></td>
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<td>0.1</td>
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<td>9</td>
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<td>14</td>
<td>79</td>
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<td>7</td>
<td>3</td>
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<td>17</td>
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<tr>
<td>J01D cephalosporins</td>
<td>7</td>
<td>1</td>
<td>3</td>
<td>1</td>
<td>8</td>
<td>2</td>
<td>11</td>
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<tr>
<td>J01E sulphonamides and trimethoprim</td>
<td>16</td>
<td>3</td>
<td>4</td>
<td>3</td>
<td>19</td>
<td>7</td>
<td>49</td>
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<tr>
<td>J01F macrolides</td>
<td>112</td>
<td>35</td>
<td>45</td>
<td>32</td>
<td>52</td>
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<tr>
<td>J01G aminoglycosides</td>
<td>0.1</td>
<td>0</td>
<td>0.13</td>
<td>2</td>
<td>0.02</td>
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<tr>
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<td>0.3</td>
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<td>0.06</td>
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<td>0</td>
<td>0.4</td>
<td>0</td>
<td>1</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>P01AB01 metronidazole oral and rectal</td>
<td>0.5</td>
<td>0</td>
<td>0.5</td>
<td>0</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>All antibacterials</td>
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<td>100</td>
<td>125</td>
<td>100</td>
<td>223</td>
<td>100</td>
<td>268</td>
</tr>
</tbody>
</table>

Antibacterials included are antibacterials for systemic use (ATC code J01), vancomycin (A07AA09) and metronidazole (P01AB01). Methenamine (J01XX05) is excluded.

pp, population prevalence.
showed an increase with age. For males, the trends were similar except for β-lactamase-sensitive penicillins.

In general, between the ages of 5 and 75 years, the population prevalence of use for females was higher than for males for most antibacterial subgroups. For children aged <5, the situation was the opposite, except for trimethoprim and sulphonamides. For the oldest individuals (≥75 years), we found a higher male prevalence for tetracyclines, penicillins with extended spectrum and quinolones, whereas the prevalence for women was highest for penicillins with extended spectrum and trimethoprim and sulphonamides. The largest difference between the genders was in the use of trimethoprim and sulphonamides. In this group, females used 4, 10 and 5 times more than males in the age groups of 5–14, 15–34 and 35–54 years, respectively.

In the total population, β-lactamase-sensitive penicillins was the most common drug group, followed by macrolides, penicillins with extended spectrum and tetracyclines with population prevalence of 93, 66, 50 and 37 patients per 1000 inhabitants, respectively. By using the DDDs, the pattern looked somewhat different, with the β-lactamase-sensitive penicillins being the most common—3.4 DDDs/1000 inhabitant per day—followed by tetracyclines, penicillins with extended spectrum and macrolides: 2.6, 1.9 and 1.8 DDDs/1000 inhabitants per day, respectively.

**High users**

Individuals defined as high users represented 3% of the population using antibacterials (Table 2). High use was more frequent among adolescents and older elderly people (≥75 years) than among the middle-aged individuals. Few high users were found among small children (Figure 2). Gender differences were not pronounced, except in adolescents, where the prevalence of high users was highest in males. As a group, individuals using more than 60 DDDs/year were characterized by being significantly older and having more co-medications than those using less than 60 DDDs/year (Table 2).

Therapy patterns also differed (Figure 3). Tetracyclines were used by 48% of the high users, followed by trimethoprim and sulphonamides (12%) and penicillins with extended spectrum (10%).

**Discussion**

A quarter of all people living in Norway consumed antibacterials for systemic use during a 1 year period. Whether the population prevalence reflects appropriate prescribing of antimicrobials is difficult to evaluate until similar data are available from other countries and information on diagnoses has been incorporated into the NorPD database.

Most individuals used antibacterials for a short period of time, as only 3% constituted the high users. In addition to having increased risk of antibacterial resistance, the high users were older and used more other drugs, which imply an increased risk of drug–drug interactions. This group of patients should therefore be of interest to specialists in microbiology, infectious diseases and pharmacology/pharmacotherapy.

Surveillance of antibiotic prescription has been performed using costs, weight in grams, DDDs or number of prescriptions as units of measurement. Studies reporting prevalence rates have been performed on patients visiting GPs or through the use of sickness fund databases. In these studies, patients are the denominator. Therefore, the prevalence rates of the general population have been just estimates. Moreover, until now we have not been able to follow drug use in discrete individuals—that is, continuously over time and place—within the general population. Data retrieved from the NorPD are unique in the sense that they cover a country’s total population (i.e. including the healthy part of the population). The database therefore enables us to achieve a better understanding of drug use in all age groups and by both genders.

The large differences between the genders raise the question of appropriateness of antibiotic prescribing by indicating a possible over-prescription to females or an under-prescription to males. Some gender differences may be explained by women having more symptomatic infections of the genital and urinary tract system than men, as shown in our data on the increased use of trimethoprim and sulphonamides and metronidazole in women. Another explanation could be the under-use of primary healthcare services by men, which has been reported in other studies. The gender distribution of the high users shows less prominent differences between the genders. Furthermore, the finding of young men as high users—in fact as prevalent as

**Table 2. Characteristics of patients included in the NorPD, i.e. patients being prescribed at least one prescription in the period**

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Individuals in the population not using antibacterials</th>
<th>All individuals using antibacterials</th>
<th>Individuals using &gt;60 DDDS antibacterials/year</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n = 1 855 038 (male); 1 687 439 (female)</td>
<td>n = 446 943 (male); 650 799 (female)</td>
<td>n = 15 878 (male); 21 430 (female)</td>
</tr>
<tr>
<td>Age in years (mean)</td>
<td>male: 37; female: 39</td>
<td>male: 41; female: 43</td>
<td>male: 50; female: 53</td>
</tr>
<tr>
<td>Gender (% of male/female population)</td>
<td>male: 81; female: 72</td>
<td>male: 19; female: 28</td>
<td>male: 0.7; female: 0.9</td>
</tr>
<tr>
<td>Number of ATC codes purchased in the period (excluding antibacterials)</td>
<td>male: 1.7; female: 2.3</td>
<td>male: 3.6; female: 4.5</td>
<td>male: 6.7; female: 8.4</td>
</tr>
</tbody>
</table>

Data are shown for individuals not using antibacterials, all individuals using antibacterials and individuals using more than 60 DDDs of antibacterials. Antibacterials for systemic use include ATC group J01, vancomycin (A07AA09) and metronidazole (P01AB01). Methenamine (J01XX05) is excluded.
those aged >70—is interesting. The explanation could be antibacterial treatment for severe acne in this age group.\textsuperscript{20}

Differences in patterns of use with regard to age could be explained by different types of infections in different age groups. The high use of broad-spectrum antibacterials in the elderly (\(\geq 75\) years) is not unexpected because the immune response lessens with age. Prevalence of UTIs increases with age and the telling increase in the age-related use of trimethoprim and sulphonamides, pivmecillinam and quinolones by both genders is most probably a result of this. It should be mentioned that, in Norway, fluoroquinolones are not recommended for the treatment of respiratory tract infections among outpatients; so the high prevalence of quinolones in the elderly is most likely to be the result of complicated UTIs.\textsuperscript{21}

As the NorPD does not hold information about diagnoses, we were not able to analyse correlations between diagnoses and antibacterial use nor evaluate the appropriateness of prescribing. However, it was encouraging that \(\beta\)-lactamase-sensitive

\begin{figure}
\centering
\includegraphics[width=\textwidth]{figure2.png}
\caption{Age- and gender-specific population prevalence of patients using more than 60 DDDs of antibacterials in the Norwegian population in the period 1 July 2005–31 June 2006. Antibacterials for systemic use include ATC group J01, vancomycin (A07AA09) and metronidazole (P01AB01). Methenamine (J01XX05) is excluded.}
\end{figure}

\begin{figure}
\centering
\includegraphics[width=\textwidth]{figure3.png}
\caption{Distribution of antibacterial subgroups for high users of antibacterials (i.e. using more than 60 DDDs/year) and all users of antibacterials in the Norwegian population 1 July 2005–31 June 2006. Antibacterials for systemic use include ATC group J01, vancomycin (A07AA09) and metronidazole (P01AB01). Methenamine (J01XX05) is excluded.}
\end{figure}
penicillins (J01CE) were most frequently used in all age groups in males and almost all age groups in females. This is exceptional in Europe and is possible because we have a low prevalence of resistant pathogens in Norway. \(^\text{22,23}\) It also reflects prescribers being loyal to national antibacterial guidelines. \(^\text{21}\)

It is of interest to identify patients being exposed to a high amount of antibacterials, and this study enabled us to distinguish high users. The cut-off of 60 DDDs was chosen after testing the database for different cut-offs. Our aim was to include patients with frequent or refractory infections and those using antibacterials continuously for a long period of time. We did not want to include those using one or two short courses of antibacterials or those in need of an additional course due to therapeutic failure. A patient using 60 DDDs per year implies that he/she probably has used high doses of antibacterials, many antibacterials concomitantly or used antibacterials for >2 months per year. The high users might create more problems with antibacterial resistance. The fact that these patients in our study were also high users of tetracyclines, an antibacterial group regarded as driving resistance, emphasizes the need for increased multidisciplinary focus on this group of patients.

In the future, our current data will be included in the annual national surveillance of antibacterial use. Through this surveillance system, we will quickly be able to track changes in usage trends and in therapy traditions.

Acknowledgements

We are all employed at the Norwegian Institute of Public Health. Otherwise, the study was carried out without financial support.

Transparency declarations

None to declare.

References


