Drug prescribing data used in the assessment of general practitioners’ treatment of asthma and urinary tract infection – Experience from the European Drug Education Project

Per Lagerlov

University of Oslo, Department of Pharmacotherapeutics
Present address: The Drug Information Centre of Southern Norway, The National Hospital, Oslo

ABSTRACT
Describing drug treatment given by general practitioners, and quantifying changes in their prescribing behaviour due to educational intervention, were important parts of the method developed and applied by the European Drug Education Project. Based on the physicians’ prescription data, individual patients were defined as having either asthma or urinary tract infections. Prescribing indicators were established for assessing the quality (acceptable or unacceptable) of the drug treatment. The diagnose definitions and prescribing indicators are discussed in more detail in relation to feeding back individual prescribing data to educational groups of physicians to improve the quality of their drug therapy.

INTRODUCTION
The study design of the European Drug Education Project
In the Drug Education Project (DEP) we used a multinational randomised, controlled trial to examine the effects of group audit on improving general practitioners’ (GPs’) drug therapy.1,4

In Germany, the Netherlands, Norway, the Slovak Republic, and Sweden doctors were recruited to participate in specific continuing medical education groups set up for the DEP. The groups were randomly allocated to focus on either asthma or urinary tract infections (UTIs). The UTI groups were controls for the asthma groups, and vice versa, Figure 1.

The GPs’ prescriptions of anti-asthmatics and relevant antibiotics for UTIs were recorded during a defined time period, before and after an educational intervention made during two educational group meetings. The GPs’ prescriptions were collected from pharmacies (in Germany and the Slovak Republic: from health insurance databases).

Before and after the intervention the GPs received a mailed questionnaire listing a number of different case-vignettes about UTIs and asthma. For each case presented the GPs filled in diagnostic and therapeutic considerations.1,2

The educational intervention comprised two meetings in the educational groups, where the GPs discussed management of either asthma or UTI in relation to international and national guidelines. During the meetings, the GPs received comprehensive and individual feedback on their diagnostic considerations and drug therapy for asthma or UTI, based on the data recorded before the intervention.

Whether this educational intervention influenced the GPs’ diagnostic considerations and prescribing behaviour was subsequently investigated by a second mailed questionnaire and a new study period where the GPs’ prescription data were recorded, Figure 1.4

DEFINING THE PATIENTS
The use of prescribing data requires individual patient age and gender identification, and the doctors must have a unique identification code. In practice prescribing data do not always give all the necessary information. When the patient’s diagnosis is not recorded, a diagnosis has to be allocated to the patient. The drug used, the amount used, the age and gender of the person receiving the drug were therefore used to identify an illness episode or a patient with an illness. The diagnosis or patient group definitions used in the DEP study are described below, table 1.

We defined episodes of uncomplicated UTI as treatments with the drugs methenamine, nalidixic acid, nitrofurantoin, trimethoprim and fluoroquinolones (all countries), pivmecillinam (Norway and Sweden), short-acting sulfonamides and fosfomycin (the Netherlands), and in special cases trimethoprim-sulfamethoxazole (Norway). We then excluded patients younger than 18, older than 75 years (Netherlands and Sweden), or patients younger than 16 years (Norway), and treatments intended for more than two weeks. In
Figure 1. The design of the intervention study as conducted in Norway. The prescribing practices of 199 general practitioners (GPs) were recorded at pharmacies during one year. 32 groups of these GPs were established according to the pharmacies serving their patients. These 32 groups were block randomised to focus either on asthma or urinary tract infection (UTI). During half a year peer review meetings were held at pharmacies or at the GPs' office. At these meetings prescribing feedback and feedback on their response to questions on clinical judgement were discussed in relation to guideline recommendations. Their prescribing practices were then recorded anew. Answers to corresponding questions on asthma and UTI management, mailed to the GPs before and after the meetings, reflected their change in knowledge and attitudes. The asthma and UTI peer review groups represented each other’s intervention and control groups.

Table 1. Patient group definitions used in the Drug Education Project.

<table>
<thead>
<tr>
<th>Patient group</th>
<th>Definition</th>
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<tbody>
<tr>
<td>Asthma patients</td>
<td>18–50 year old patient receiving anti-asthmatics a</td>
</tr>
<tr>
<td>UTI b episode (the Netherlands and Sweden)</td>
<td>18–75 year old woman receiving a prescription of anti-infective s</td>
</tr>
<tr>
<td>UTI episode (Norway)</td>
<td>&gt;16 year old patient receiving a prescription of anti-infectives c</td>
</tr>
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</table>

a Anatomical Therapeutic Chemical classification code R03.

b Urinary Tract Infection.

c methenamine, nalidixic acid, nitrofurantoin, trimethoprim and fluoroquinolones (all countries), pivmecillinam (Norway and Sweden), short-acting sulfonamides and fosfomycin (the Netherlands) and in special cases trimethoprim-sulfamethoxazole (Norway).
the Netherlands and Sweden, where this treatment is reimbursed, treatments of men were excluded. Treatments during pregnancy were not excluded, however.

Some of the episodes collected by applying this definition may represent cases of other illnesses, such as respiratory tract infections and more complicated UTIs. The inclusion of these would make the description of the patient treatment less valid and reduce the sensitivity of assessing behaviour change.

When validating the relevance of the drugs applied in defining UTI, by asking the doctors on a questionnaire what they would prescribe in 18 “UTI-paper cases”, 89.8% in the Netherlands, 95.1% in Norway and 97.6% in Sweden chose drugs included in the study.\textsuperscript{2}

In defining asthma patients, all persons receiving anti-asthmatics (ATC class R03) were at first included. Prescriptions to children and to patients with possible chronic obstructive pulmonary disease were avoided by excluding patients younger than 18 and older than 50 years.

When comparing prescribing differences between different countries we must presuppose a relatively uniform patient population in the countries. The proportions of patients having severe asthma, or who smoke, however, may be different in the DEP countries. Nocturnal attacks of breathlessness as an indicator of illness-severity has been shown to correlate well with the uses of oral and inhaled anti-inflammatory agent.\textsuperscript{6} Thus, differences in prescribing practices may be related both to differences in illness severity and differences in doctors’ prescribing habits. We do not have data regarding the patients’ severity of asthma nor their smoking habits. Because the DEP study collected prescriptions from pharmacies located in relatively large geographical regions, such as the south-eastern part of Norway, the northern part of the Netherlands and the middle part of Sweden, any local variations in asthma severity among the included patients will be masked.

When evaluating a patient group definition by using the diagnosis applied to the patients by the doctor as the gold standard, an assessment of this gold standard is important. The process of defining a diagnosis has many subjective elements, and universally accepted diagnostic criteria are lacking.\textsuperscript{6} Because asthma may fluctuate, diagnostic tests for asthma on a random day may be normal. An evaluation of a sample of patients randomly drawn from the above defined prescription data, revealed that a large proportion of patients who received inhaled short acting beta agonists, inhaled steroids or a combination of both drugs, were not identified as asthmatics in their medical records by their general practitioners.\textsuperscript{9} GPs may perhaps be more concerned with what to do with the patients’ symptoms than updating the precise diagnosis. Prescription data may therefore sometimes be a more sensitive indicator of asthma than the diagnoses stated in the medical records.

**RECORDING TREATMENTS**

The doctors’ own recording of prescribed drugs probably best reflects their intended treatments. However, not all doctors use personal computers. Another way is to record dispensed drugs from pharmacies or health insurance databases. This reflects more closely what the patients “intend to eat”. A discrepancy between prescribed and dispensed drugs may exist due to low compliance, or now better described as low concordance between the doctor and the patient.\textsuperscript{10} At the pharmacy, asthmatic patients may ask for the symptomatic and not the prophylactic treatment. This is an argument for recording prescribed and not dispensed drugs. On the other hand, dispensed drugs better reflect the actual treatment received, which therefore corresponds more closely to what the patients actually take.

In improving drug therapy for uncomplicated UTI, one intention of the educational intervention was to influence doctors to prescribe shorter treatment courses. The included drugs therefore had to be available in small packages. If only large packages were available for prescribing, a change in treatment duration could not be assessed. Treatments with trimethoprim-sulfamethoxazole were included when small packages were available.

Bronchodilators and anti-inflammatory drugs received by the patients reflect the treatment of immediate symptoms and prophylactic treatment, respectively. A description of this treatment should not only include their relative use, but also the total amount given to the patient. The ratio of amount of inhaled steroids to amount of inhaled beta agonists does not reflect the severity of the asthmatic illness. A high and a low consumer may have similar relative use of these drugs. The ratios between the amounts of these drugs have not been found to relate to the severity of asthma as reflected by hospital admission rates.\textsuperscript{14} A measurement also including the total amount of drugs received by the patients, has visualised the relationship between the asthmatic conditions described and hospital admission rates.\textsuperscript{14}

The unit Defined Daily Dose (DDD)\textsuperscript{5} is defined as the assumed average maintenance dose per day for a drug used on its main indication in adults. This corresponds well for single treatments of UTI, however, we employed a prescribed daily dose of trimethoprim of 0.75 DDD, because this coincided better with the most commonly prescribed dose. In the case of asthma, however, combined treatment is often applied, and thus the DDD cannot be interpreted literally as the recommended daily dose. Another unit often applied when describing treatment of asthma is the number of inhalations per day. However, the metered doses delivered by aerosols or powder inhalators differ greatly. A given frequency of use may therefore represent wide variations in inhaled amount of a drug. Furthermore,
the drugs show dose dependent effects, both in immediate symptoms relief and in the duration of the bronchodilating effect. The frequency of use was thus judged unsuit when describing treatment based on prescribing data.  

The number of tablets or metered doses in a package and the length of the recording period may influence the validity of the calculated mean daily dose received by the patients. Only in the Netherlands is it common practice to break the packages to tailor the dispensed amount to the prescribed time period. If the package size is large, intended for longer duration of treatment than the recording period, the estimated mean daily dose may be too high compared to the intended treatment. To give an example, one Bricanyl Turbohaler, with 200 doses of terbutaline powder, dispensed during a six-month recording period, as applied in Sweden, represents just above one inhalation per day. If it is dispensed during a twelve-month recording period, as applied in Norway, the average daily dose will be just above half an inhalation per day. The calculated proportion of patients who, on average, used inhaled bronchodilators daily without inhaled steroids was twice as high in Sweden as in Norway. This difference is most probably explained by the fact that to be defined as a high consumer in Sweden, the patients need only to receive one Turbohaler, while a patient in Norway must be dispensed two Turbohalers during the recording period. The recorded differences in prescribing habits are therefore most probably related to different duration of the prescription-recording period, and not to differences in practice.

ASSESSING TREATMENT QUALITY

Guideline recommendations are designed to help doctors to make appropriate treatment decisions for individual patients. They may also be used as yardsticks for judging the quality of treatment given to patients within different countries. But when guidelines are applied to judge treatment quality based on prescribing data, a translation from the context at the doctor’s office to the treatment mirrored by prescribing data is needed. A prescribing indicator may be defined as a measurable element of prescribing performance for which there is evidence or consensus that it can be used to assess quality, and hence a change in the quality, of drug prescribing.

To measure the outcome-effect of an educational intervention, recommending short-term treatments of UTI, a change in the mean duration of treatment may be estimated. A statistically significant reduction in treatment duration of, for instance one day, may then be detected. Whether this has any clinical importance may be disputed. Another way of judging the treatment is to classify the courses as “acceptable” or “unacceptable” when they lasted 3 days or less, or 7 days or more, respectively, according to guideline recommendations. Then an increased proportion of “acceptable” and a reduced proportion of “unacceptable” treatments may have clinical significance.

The stepwise introduction of anti-inflammatory drugs, according to the extent of symptoms, was used to make key-messages for the treatment of asthma, to be applied in the educational intervention. Based on these key-messages indicators were developed, reflecting the proportions of asthma patients treated “acceptably” or “unacceptably”. The use of inhaled anti-inflammatory drugs was defined as “acceptable” treatment. The use of inhaled bronchodilators in doses enabling daily use without using inhaled anti-inflammatory drugs was defined as “unacceptable” treatments. The prescribing indicators used in the DEP study are presented in more detail in table 2.

The process of transforming guidelines into yardsticks defining “acceptable” or “unacceptable” treatments may be utilised in postgraduate vocational education of doctors. In Norway we categorised the asthma regimens into specific combined mean daily dosage intervals of inhaled short acting beta agonists and inhaled steroids, based on data on what the patients had received. With the application of guideline recommendations to these categories, the treatment quality could subsequently be judged by all educational groups of doctors that were included. Their combined judgement was then used as the yardstick. In this case the participating doctors felt an ownership to the quality assessment, and they also ensured its relevance to their practice. Figure 2 shows the matrix of the 16 combined mean dosage interval boxes, as developed in the Norwegian part of the DEP study. Superimposed on the matrix, the doctors’ judgements of the treatment quality for the patients within each mean dosage interval box are shown.

The validity of the criteria “acceptable” and “unacceptable” treatments, as defined by these indicators, relies on the indicators’ correspondence with guidelines and rational clinical practice. The guidelines consider patients treated with inhaled anti-inflammatory drugs as acceptably treated. They do not always make detailed reservations as to dose or the relative use of symptomatic drugs for these patients. The treatment quality for patients on inhaled steroids was not uniformly judged as “acceptable” by the participating Norwegian general practitioners in the asthma-intervention groups. They also classified some treatments of patients using inhaled steroids as “unacceptable” or “difficult to judge”, figure 2. Thus, the proportion of asthma patients receiving inhaled anti-inflammatory drugs is a less useful indicator of “acceptably” treated patients than the indicator developed in collaboration with the participating general practitioners in Norway.

The ability of outcome measurements to detect a change in prescribing behaviour is affected by the frequency of doctor-patient contacts and the amount of
Table 2. Definitions of prescribing indicators used in the Drug Education Project.

<table>
<thead>
<tr>
<th>Indicators</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acceptable asthma treatment</td>
<td>Patient receiving inhaled steroids</td>
</tr>
<tr>
<td>Unacceptable asthma treatment</td>
<td>Patient receiving inhaled short acting bronchodilators in an average daily dose of &gt; 1/4 DDD without receiving inhaled steroids</td>
</tr>
<tr>
<td>Unacceptable asthma treatment</td>
<td>Patient receiving inhaled steroids in an average daily dose of &lt; 1/2 DDD and inhaled short acting bronchodilators in an average daily dose of &gt; 1/2 DDD</td>
</tr>
<tr>
<td>Acceptable treatment of UTI</td>
<td>First line drug according to national guidelines, short treatment duration (3 days or less)</td>
</tr>
<tr>
<td>Unacceptable treatment of UTI</td>
<td>Second line drug according to national guidelines, long treatment duration</td>
</tr>
</tbody>
</table>

*Defined Daily Dose. b Urinary Tract Infection*

**Figure 2.** The matrix of combined mean daily dosage-intervals of inhaled short acting beta agonist and inhaled steroids. The doctors’ judgement on treatment quality of patients within each dosage-interval box is superimposed on the matrix. The doctors judged patients in the medium grey dosage-interval boxes to be “acceptably” treated. Patients “unacceptably” treated were located in the dark grey dosage-interval boxes. The treatments of patients in the light grey boxes were difficult to judge. The patients in the blank box were infrequently labelled as asthmatics in their medical records. The 12 dosage-interval boxes to the right imply treatments with anti-inflammatory drugs, but these treatments are not always judged as “acceptable” since they include boxes of all kinds of grey-shade.

The proportion of asthma patients receiving inhaled steroids from their doctors in the five countries before the intervention, varied almost twofold: 31% in Germany, 39% in the Slovak Republic, 45% in Sweden, 46% in Norway and 58% in the Netherlands. In the Netherlands, but not in Norway, the Slovak Republic or Sweden, the educational intervention significantly increased the proportion of asthma patients receiving inhaled steroids. In Norway, the use of the prescribing indicator for acceptable treatment of asthma, developed in collaboration with the participating GPs, showed a significant improvement in the prescribing behaviour.

**CONCLUSION**

The quality of the drug treatments that doctors give their patients, can be described using guideline recommendations as a yardstick. The doctors themselves
may elaborate the yardsticks, in peer review groups, in the context of their practice.

The DEP study has demonstrated that extensive prescribing feedback with discussions in peer review groups improved the quality of drug treatment given by doctors. In the new area of information-technology, individual prescribing data may be used in educational groups of doctors to enable them to improve the treatment they give their patients.

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