Methods to analyse medicine utilization and expenditure to support pharmaceutical policy implementation
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INTRODUCTION

Many low- and middle-income countries are transitioning their health care systems to enable universal health care coverage. In most instances, the coverage includes support for access to medicines, recognizing that this needs to be at a cost both the individual and the community can afford. Central to health systems providing access to medicines is the need for a formulary that stipulates which medicines are covered under universal health care and under what circumstances they are covered. The World Health Organization (WHO) is supporting efforts to ensure health technology assessment underpins the decision-making process for including medicines on the formulary.

An additional requirement to support universal access to medicines is the analysis of the utilization of and expenditure on medicines. Analysis of medicines utilization can inform whether overall expenditure on medicines is within budget, whether particular medicines are responsible for budget over-spend or under-spend, or whether medicine use aligns with the expected and desired treatment rates. Analysis of medicine utilization can also support decision-making and be used to predict the likely effect on the budget of a potential new listing in a reimbursement list or formulary. The analyses can be used to review the effect of including medicines on the formulary, to determine if medicines are being used in accordance with their listed use, or to determine the effect of policy or regulatory changes. The analyses can also inform whether medicine use varies by region or age group.

This manual includes an overview of the governance structures and human resources required to support routine analysis of medicine utilization and expenditure. The data sources and methods that can be used to undertake the analyses are described, and examples of analyses are given. The final section of the manual includes a list of guidance documents for research on medicine utilization research, and web addresses of agencies that routinely publish reports of medicine utilization and expenditure to inform pharmaceutical policy.
SECTION 1: OVERVIEW

GOVERNANCE

A routine mechanism is required to enable ongoing analysis of medicine utilization and expenditure. This is best served by establishing a dedicated unit for analysis of medicine use within the agency responsible for the programme that supports access to medicines. The size of the unit will depend on the workload, however, the minimum requirement would include a person with knowledge of medicines who can contribute to the context and clinical issues required for analyses and a person with analytical skills who can make use of the data to create the output. For the analytical methods described in this manual, basic analytical skills are required.

Consideration should also be given to establishing an expert advisory committee to support the medicine utilization unit. The functions of the committee could include: providing advice on data collection, determining the analyses to be undertaken, and assisting with the interpretation and dissemination of the results of the analyses. Members of the committee could include individuals with expert knowledge of the data sources, expertise in medicine or pharmacy and expertise in research on medicine utilization, as well as representatives of the groups that will use the analyses, for example government agencies. Where there is a separate committee or unit responsible for formulary listings, representation from the formulary committee is an advantage. The expert committee should meet at regular intervals, for example every three months, to oversee the analyses. The terms of reference and a standing agenda should be developed to assist the committee with its business processes. Processes for dealing with conflicts of interest should be established. An example of terms of reference and a standing agenda are included in Appendix 1.

A mechanism to enable formal feedback and advice from the unit analysing medicine utilization and expenditure to the agency responsible for the programme supporting access to pharmaceuticals is required so that actions can be taken in response to the findings, where warranted. Types of actions could include the need to change listings or restrictions, the need for educational programmes, or the need to adopt additional or alternative policy options so that the overall goals and objectives of the programme supporting access to pharmaceuticals can be met. An overview of the suggested process is shown in Fig. 1.

DATA SOURCES

A number of different types of data can be used in analyses of medicine utilization and expenditure. In this manual, the data sources are divided into aggregated data and patient-level data. Aggregated data sets are those where the data are compiled as a summary statistic. For example, the number of units of stock of a medicine purchased each month or each year. Aggregated data do not include information on the provision of medicines to an individual person. Patient-level data are those where information on individual patients is available.

The type of data available in each country will depend on the source of the data. Data may need to be sourced from multiple organizations. Examples of data sources include importation records, sales and purchasing records, and health practitioner prescribing or dispensing records. Organizations that hold these data include customs offices for importation data, manufacturers or wholesalers, health care organizations, other medicines outlets (e.g. pharmacies), health practitioners, government agencies or health insurance agencies. Possible data sources and the type of data usually available are summarized in Table 1 and described in more detail in Section 2 of this manual.
Within Section 2, the main advantages and limitations of the data types are described; however, there will also be country-specific limitations of data sets that should be recognized. Limitations may include missing data, incomplete capture of data or incomplete capture of populations. Different data sources may produce variable results (1); this is usually because of differences in the way the data are collected or differences in the population from which the data are collected or in the medicines included in the data collection. These differences need to be considered when interpreting results from different data sources.

Data can be sourced as cross-sectional data or longitudinal data. Cross-sectional data are data that capture information on medicine utilization or expenditure at a single period of time. Longitudinal data are data collected over multiple time points.

In general, it is best to consider setting up mechanisms to enable longitudinal data collection so that changes in medicine use and expenditure over time can be analysed. When collecting longitudinal data, it is important to record changes that occur in the data collection over time. For example, where wholesaler data are collected, information on specific products can disappear if the wholesaler no longer stocks the product. Where only partial data are available or only a sample of the data is available, it is helpful to ascertain the representativeness of the data so that inferences can be made from the analyses.

Because data from different data sources may be recorded differently—for example, some may be recorded by generic name, some by brand name, some by text entry which creates opportunities for misspelling—it is better if data are coded with a
Table 1 | Potential data sources and data types for analyses of medicines utilization

<table>
<thead>
<tr>
<th>Potential data sources</th>
<th>Data types</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Procurement data</td>
</tr>
<tr>
<td>Customs or import offices</td>
<td>Aggregated</td>
</tr>
<tr>
<td>Manufacturers</td>
<td>Aggregated</td>
</tr>
<tr>
<td>Wholesalers</td>
<td>Aggregated</td>
</tr>
<tr>
<td>Hospitals</td>
<td>Aggregated</td>
</tr>
<tr>
<td>Medical practices</td>
<td>Patient level</td>
</tr>
<tr>
<td>Pharmacies</td>
<td>Aggregated</td>
</tr>
<tr>
<td>Medicines outlets</td>
<td>Aggregated</td>
</tr>
<tr>
<td>Health insurance agencies</td>
<td>Aggregated or patient level</td>
</tr>
<tr>
<td>Reimbursement agencies</td>
<td>Aggregated or patient level</td>
</tr>
<tr>
<td>National statistics agencies</td>
<td>Patient level</td>
</tr>
<tr>
<td>Research agencies</td>
<td>Patient level</td>
</tr>
<tr>
<td>Commercial data companies</td>
<td>Aggregated</td>
</tr>
</tbody>
</table>

unique code that is specific to an individual product or medicine. A detailed description of coding is not included in this manual; however, WHO supports the Anatomical Therapeutic Chemical (ATC) classification which provides a unique code for medicines at the level of the individual chemicals (2). The code is not specific for different pharmaceutical formulations of the same type of medicine. For details of how to use the WHO ATC classification for coding medicines data, refer to the web site for the ATC/DDD Toolkit for Drug Utilization Monitoring and Research (3).

Data on medicines utilization may be recorded in paper or electronic forms. The analytical methods described in this manual are applicable to the analysis of medicines regardless of the form in which the data are recorded. In general, electronic data sets are easier to use and, where paper records exist, it may be worth developing an electronic, aggregated data set from the paper record, as many of the analytical methods described in this manual can be automated to produce routine reports. Data sets containing information about medicines can be very large. In general, aggregated data sets require fewer computing resources than individual patient-level data sets; the latter, if applicable to the whole country, will require considerable computing resources. If computing resources are limited, it is best to obtain extracts of data for the analysis of interest. Data extracts can usually be handled and analysed using a standard personal computer.
ANALYSES

In undertaking analyses, it is important to start with a clear question or purpose. Box 1 provides examples of the types of questions that commonly require answers to enable a sustainable pharmaceutical policy.

Many of these questions can be answered using simple methods to analyse medicine utilization or expenditure. Sections 4 and 5 provide details of methods that are frequently used by agencies that assess medicines utilization to support pharmaceutical programmes, such as ABC analysis, drug utilization 90% (DU90%) or vital, essential and non-essential (VEN) analysis. Section 4 focuses on methods that can be used with aggregated data sets, while section 5 describes the methods that can be used where patient-level data are available. All of the methods in section 4 can also be used with patient-level data. This manual describes the method and its purpose, its advantages and limitations, as well as the data sources that can be used. The purpose and description section will help in selecting the methods required for the question of interest.

In planning an analysis, it worth considering what measure of medicine use is required. Measures of medicine use can include an assessment of the amount of medicine procured, prescribed, supplied or used. The unit of measurement can include counts, volume or cost, and all of these units can be expressed as rates. The relevant population is commonly used as the denominator where rates are calculated. Health service use, such rates per 100 bed days or rates per 100 doctor visits, are also suitable denominators in some instances. Section 3 includes further detail on the measures of medicine use that can be used, with a focus on how to calculate measures of volume.

Another consideration for determining what analyses to undertake is the data set available. Many of the key questions to support pharmaceutical policy can be answered using aggregated data, particularly where the data are available for the whole programme or where the data sample is representative of the programme. Some questions can only be answered using patient-level data and so cannot be answered if only aggregated data sets are available. Examples of questions that can be answered with the different methods of analysis described in this manual are shown in Tables 2 and 3.

Box 1 | Questions that could be addressed by analyses of medicine utilization

- What is the extent of medicine use?  
  What is the extent of medicine use overall?  
  What is the extent of medicine use for a particular class of medicines or for an individual medicine?
- Are the medicines that are most commonly used the medicines that are needed?  
  Are the most frequently used medicines those that are used to treat diseases that are most prevalent?
- Are medicines being used in accordance with formulary listings?  
  What is the effect of new listings or delistings?  
  What is the effect of changes to listings?  
  What is the effect of restricted listings?  
  Is medicine use in accordance with the predicted use of the medicine?
- What is the effect on the budget of the medicine?
- What is the extent of use of generic medicines?
- What is the effect of co-payments on medicine use?
- What is the effect of other policy initiatives, e.g. the implementation of reference pricing, therapeutic premium or brand premium policies, changes in amounts supplied, changes to refill authorization requirements, changes to who can prescribe, changes to the eligible populations?
- Does medicine use vary by region, age, gender or ethnicity?
- Is medicine use consistent with standard treatment guidelines?
- What is the extent of under-use, over-use or inappropriate selection of medicines?
- What is the extent of concurrent use, interactions or duplication of therapy?
- What is the level of compliance and persistence with therapy?
Table 2 gives examples of questions that can be answered using the methods with aggregated data, while Table 3 gives examples of questions that can be answered using the methods with patient-level data. All of the methods given in Table 2 can also be used to analyse patient-level data.

Table 2 | Examples of questions about medicine use and the methods of analysis that could be used to help answer the questions where aggregated data sets are available

<table>
<thead>
<tr>
<th>Question</th>
<th>ABC analysis, DU90%, or VEN analysis</th>
<th>Time series and segmented regression</th>
<th>Forecasting</th>
<th>Indicator ratios</th>
</tr>
</thead>
<tbody>
<tr>
<td>Are the medicines that are most commonly used the medicines that are needed?</td>
<td>✔</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Are the most frequently used medicines those that are used to treat diseases that are most prevalent?</td>
<td>✔</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>What is the expected growth in the pharmaceutical market overall or for a specific class of product?</td>
<td></td>
<td></td>
<td>✔</td>
<td></td>
</tr>
<tr>
<td>What is the effect of new listings or delistings?</td>
<td></td>
<td></td>
<td>✔</td>
<td></td>
</tr>
<tr>
<td>What is the effect of changes to restrictions for listings?</td>
<td></td>
<td></td>
<td>✔</td>
<td></td>
</tr>
<tr>
<td>What is the effect of co-payments?</td>
<td></td>
<td></td>
<td>✔</td>
<td></td>
</tr>
<tr>
<td>What is the extent of under-use, over-use or inappropriate selection of medicines?</td>
<td></td>
<td></td>
<td></td>
<td>✔</td>
</tr>
</tbody>
</table>

DU90%: drug utilization 90%; VEN: vital, essential and non-essential.

Table 3 | Examples of questions about medicine use and the methods of analysis that could be used to help answer the questions where patient-level data sets are available

<table>
<thead>
<tr>
<th>Question</th>
<th>Prevalence and incidence estimates</th>
<th>Duration index</th>
<th>Waiting time distribution</th>
<th>Patient level indicators</th>
<th>Compliance measures</th>
</tr>
</thead>
<tbody>
<tr>
<td>Is medicine use consistent with the expected prevalence and incidence of the disease?</td>
<td>✔</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>What is the extent of under-use, over-use or inappropriate selection of medicine?</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>✔</td>
</tr>
<tr>
<td>How long are people staying on therapy?</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>✔</td>
</tr>
<tr>
<td>How compliant are people with therapy?</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>✔</td>
</tr>
</tbody>
</table>
Another factor to consider is the time period over which data are available. Where data only relate to one time period, analyses will be limited to cross-sectional analyses, whereas when the same type of data have been collected over multiple time periods, longitudinal analyses are possible. Cross-sectional analyses of medicine use during a specified period of time are suitable for answering questions such as “what are the medicines that are most frequently used?” while data over many periods of time are needed to assess trends in medication use or to determine the effect of changes in policy or changes to listings. Table 4 gives an overview of the methods of analysis that can be used with the different data sources and highlights those that can be used with cross-sectional data and those that require longitudinal data.

Table 4 | Methods to analyse medicine utilization or expenditure and types of data required

<table>
<thead>
<tr>
<th>Method</th>
<th>Data requirements</th>
<th>Procurement or sales data</th>
<th>Aggregated dispensing, prescribing, or claims data</th>
<th>Patient level dispensing, prescribing or claims data</th>
<th>Survey dataa</th>
</tr>
</thead>
<tbody>
<tr>
<td>ABC analysis</td>
<td>Cross-sectional</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>DU90%</td>
<td>Cross-sectional</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>VEN analysis</td>
<td>Cross-sectional</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Time series trends</td>
<td>Longitudinal</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Segmented regression</td>
<td>Longitudinal</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Forecasting</td>
<td>Longitudinal</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Indicator ratios</td>
<td>Cross-sectional or longitudinal</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Prevalence and incidence estimates</td>
<td>Longitudinal or surveyb</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Duration indexa</td>
<td>Longitudinal</td>
<td>✓</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Waiting time distributiona</td>
<td>Longitudinal</td>
<td>✓</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lorenz curvesa</td>
<td>Longitudinal</td>
<td>✓</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Exposure durationa</td>
<td>Longitudinal</td>
<td>✓</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Patient-level indicators</td>
<td>Longitudinal or surveyb</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Compliance measures</td>
<td>Longitudinal or surveyb</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
</tbody>
</table>

a Developed for use with electronic patient-level dispensing or prescribing data. Requires at least one year of data.
b If the survey includes relevant questions and is representative of the population/programme surveyed.

DU90%: drug utilization 90%; VEN: vital, essential and non-essential.
When undertaking analyses for the first time, it is recommended that initial work focus on using aggregated data to gain an understanding of the extent of medicine use and expenditure. This is most easily achieved by doing an ABC analysis, DU90% or VEN analysis. Subsequent analyses can examine changes in medicine use over time and the effect of changes in listings and policies on medicine use. Analysing changes over time requires a longitudinal data set. Re-analysis over time using ABC analysis, DU90% or VEN analysis can help identify changes to medicine use over time. Time series analyses examining the use of specific medicines, classes of medicines, or indicator ratios, all of which can be done using aggregated data, are also suitable for examining changes. Where patient-level data are available or where data sets develop over time, additional analyses and methods can be considered; however, the majority of analyses required to support a national or regional pharmaceutical programme can be done with representative, aggregated data.

Analysis of medicine utilization and expenditure to support pharmaceutical policy is best established as an ongoing activity. The results of analyses should be routinely reported within the medicine utilization unit, to the expert advisory committee and to the agency responsible for the programme supporting access to pharmaceuticals. An iterative process that includes stakeholder review of the analysis and interpretation of results within the context of the goals and objectives of the pharmaceutical policy will build a comprehensive picture over time of the patterns of medicine utilization and expenditure.

For many of the methods, comparative analyses can facilitate interpretation of results, for example, where comparisons are made across health sectors, across regions within the country, or across countries. When making comparisons across countries, consideration should be given to the similarity of data collections, population profiles and health systems. Country comparisons are best made when the data sources are the same, so that the same measure can be used, and where health systems and population profiles are similar.

The subsequent sections of this manual provide more detail on data sources (Section 2), measures of medicine use (Section 3), analysis methods suitable for use with aggregated data (Section 4) and analysis methods suitable for use with patient-level data (Section 5). Additional detail on methods can be found in the guidance documents listed in Section 6, while web links to examples of analyses of medicine utilization reported by countries are included in Section 7.
SECTION 2: SOURCES OF DATA ON MEDICINE UTILIZATION

SALES OR PROCUREMENT DATA

Description: Data on the sale or purchase of pharmaceutical products by relevant businesses or organizations.

Potential data sources:
- pharmaceutical import records from pharmaceutical regulatory agencies or custom offices,
- medicine production records from local manufacturers,
- sales records from manufacturers or wholesalers,
- procurement records from hospitals,
- procurement records from pharmacies or other medicines outlets.

Information usually available:
- name of medicine,
- dosage form,
- strength,
- quantity (sales units),
- cost (ex-manufacturer, ex-wholesaler).

Advantages: These data can provide information about changes in aggregated medicine utilization. Usually they include over-the-counter medicines. These data sources have often been used to describe total quantities of specific medicines or medicine classes in circulation for defined periods and have been successfully used in low- and middle-income countries.

Limitations: The data may not be comprehensive and may be subject to fluctuations in capturing products with changing procurement practices. The data will include stock purchased but never supplied. Data may include parallel trade stock movements.

DISPENSING DATA

Description: Data on licensed medicines supplied to a patient by a dispensing officer (pharmacist or a doctor in a dispensing practice).

Potential data sources:
- pharmacies,
- medicine outlets or doctor dispensing practice records (electronic or manual form).

Where reimbursement of dispensing occurs, centralized data might be held by the payer (i.e. private insurer or government).

Information usually available:
- patient identifier,
- name of medicine dispensed,
- dosage form,
- strength,
- quantity of medicines dispensed,
- cost of each medicine dispensed.

Advantages: There is often a legal requirement to document dispensing, thus data are usually recorded at the patient level. The data might include over-the-counter medicines and medicines supplied by a pharmacist that do not require a prescription from a physician but do require a dispensing record.

A routine audit of all medicines dispensed by a representative sample of pharmacies in a country will provide a comprehensive database of all types of medicines.

Limitations: The quantity of medicines dispensed will be subject to availability and this may vary depending on the procurement practice. In many instances, the data do not contain information about the problem, condition
or diagnosis for which the medicines are dispensed, however, this is available in some data sets. Data may or may not be able to be linked to a prescriber.

The data do not take into account compliance with therapy, thus dispensing data may not reflect the actual use (consumption) of medicines.

**PRESCRIBING DATA**

**Description:** Data on licensed medicines prescribed by a health care professional.

**Potential data sources:**
- health professionals’ records,
- databases of electronic medical records of outpatient or inpatient prescriptions.

**Information usually available:**
- patient identifier,
- patient demographics (e.g. age, gender),
- name of the medicine prescribed,
- dosage form,
- strength,
- dose prescribed,
- frequency of administration,
- reasons for prescribing (i.e. specific problem or condition),
- type of prescriber (e.g. medical specialist, general practitioner).

**Advantages:** Where diagnoses are available, information on condition-specific prescribing can be determined. Data may be able to be used to identify relevant characteristics of patients and general practitioners associated with the use of specific medicines. Duration of use, comorbidities, adverse events or reason for stopping the medicine may be available in some data sets.

**Limitations:** Medicines prescribed might not be dispensed or used. Prescribing databases may not include a representative sample of prescribers; therefore, they may not be suitable for monitoring medicine utilization at the national level.

**HEALTH CLAIMS DATA**

**Description:** Health claims data for medicines that are subsidized or reimbursed by the government or private insurers.

**Potential data sources:**
- data held in either electronic or paper form by insurers or agencies subsidizing medicine costs; insurers may be private health insurance companies or government agencies.

**Information usually available:**
- name of medicine,
- dosage form,
- strength,
- quantity of medicine dispensed,
- cost of each medicine dispensed.

**Advantages:** The data provide information about aggregated medicine utilization for the insured population. Data may allow analyses at different levels of the health system (e.g. regional, national or individual). While not included in all data sets, some contain unique patient identifiers enabling patient-level analyses to be done.

**Limitations:** The data are collected for administrative purposes and thus may not include all relevant information for studies on medicine utilization. Data do not usually include over-the-counter medicines or prescribed medicines that are not subsidized or reimbursed. There are no data on medicines prescribed but never dispensed. The data are limited to the people covered by the subsidy or reimbursement programme, thus those segments of the population that are not covered by the programme are excluded. The databases do not capture information on medicines that are not covered by the subsidy or reimbursement programme. Where subsidy and reimbursement programmes limit or cap the medication costs that are subsidized or reimbursed, use and costs beyond the caps will not be included, leading to an underestimation of medicine use or costs. Where patient co-payments exist, medicines priced at a level equal to or lower than the co-payment may not be captured. Changes in medicine prices and co-payment prices over time may result in fluctuations in the medicines included in the data set.
COMMUNITY OR HOUSEHOLD SURVEY DATA

**Description:** Cross-sectional health surveys containing questions on the use of medicines.

**Potential data sources:**
- national or provincial health surveys,
- health surveys by research groups.

**Information usually available:**
- name of medicine,
- dosage form,
- strength,
- dose used,
- frequency of administration,
- duration of use,
- reason for use.

**Advantages:** Such surveys provide patient-level data on medicine utilization and reflect actual medicine utilization in practice. These data could be aggregated for a defined population. Repeat surveys can be done over time to enable longitudinal analyses.

**Limitations:** Collection of the data is time-consuming and labour-intensive. The data may be subject to reporting bias and low response rates. When surveys are repeated, question formats need to be consistent over the entire series of surveys, otherwise there is limited capacity for valid longitudinal analysis.

COMMERCIAL MEDICINE UTILIZATION DATA

**Description:** Commercial companies may collect information on sales from manufacturers and wholesalers, and prescription or dispensing data from medical practitioners, community pharmacies or hospitals.

**Potential data sources:**
- IMS health (IQVIA).

**Information usually available:**
- name of medicine,
- dosage form,
- strength,
- quantity,
- cost,
- indication where medical data are collected from a representative sample of health professionals.

**Advantages:** The data can provide information about changes in aggregated medicine utilization. Data are registered by medicine and formulations in a standardized way. Data from more than one source can be combined (e.g. both manufacturers' reports and hospital and pharmacy surveys), which may improve estimates of medicine use. The data have been used in low- and middle-income countries for pharmaceutical policy evaluation.

**Limitations:** Data are not freely available to government departments and researchers, and there are costs associated with their use. No individual-level data are available. Medicines are classified according to the anatomical classification developed by the European Pharmaceutical Market Research Association (EphMRA) and the Pharmaceutical Business Intelligence and Research Group (PBIRG) (EphMRA/PBIRG) (4). This coding classification has a similar anatomical structure to the WHO ATC system (2) but it does not include pharmacological or chemical subgroups. The coding system is also product based rather than substance based and the same product can appear in multiple categories (4). For these reasons, analyses using the EphMRA/PBIRG system cannot be directly compared with analyses using the ATC classification.

Sales data are estimates of national sales based on sampled hospital data or on wholesaler or manufacturer data. Changes over time in sampled hospitals or participating wholesalers and manufacturers may lead to fluctuations in the products included and biased estimates of change. It may not be possible to determine missing data. Data on the value of sales are expressed in constant United States dollars and disregard discounts and rebates; therefore, the sales value may not reflect actual spending by third-party payers.
AMALGAMATED DATA SOURCES

Description: Data sets built from two or more sources of data, where one data source complements the other so that improved estimates of overall medicines utilization or expenditure can be made.

Potential data sources:
- any combination of the data sources described previously, where common data elements are held.

Information usually available:
- name of medicine,
- dosage form,
- strength,
- quantity,
- cost.

Advantages: These data sets provide more robust estimates of overall use if the combination of data sources minimizes gaps in data collection.

Limitations: They only enable analyses at the level where the data are representative of the population/programme analysed.

Examples

Between 1990 and 2012, Australia’s national pharmaceutical claims data set only held data for medicines reimbursed by the government. Medicines for which consumers paid the full price were not included, thus private prescriptions and medicines that cost less than the consumer co-payment limit were not in the national data set. To overcome this limitation, a survey of 200 community pharmacies that were representative of community pharmacies nationally was carried out each year so that national estimates of the use of private prescriptions and prescriptions below the co-payment limit could be obtained. By combining information from the two data sets, national estimates of community prescription and medicine use could be made (5). Since 1990, estimates on use and costs based on these data sources have been published annually in Australian statistics on medicines (6). The community pharmacy survey was only representative at the national level, so estimates at state or regional levels could not be made.

Malaysia adopted a similar approach when it established its national medicines utilization and expenditure data set. The initial survey on national medicines use was made up of data from a number of sources, including procurement records from the Ministry of Health central tender process, procurement records of local hospitals run by the Ministry of Health, procurement records from private hospitals, prescribing data based on surveys from general practitioners in private practice and from public sector primary health care practices, as well as survey data from private retail pharmacies. Collectively, the data were used to produce national estimates of medicine utilization and costs, which were subsequently published in Malaysian statistics on medicines 2004 (7).

EXAMPLES OF DATA SETS

AGGREGATED DATA

Having sourced data for analysis, data need to be organized so that they can be analysed. The minimum data set required to undertake analyses where aggregated data are available is:
- a variable that identifies the medicine (name or code), its strength, form and pack size,
- a variable that identifies the time period (day, week, month, quarter or year),
- a variable that is a measure of the quantity sold, purchased, prescribed or dispensed.
SECTION 2: SOURCES OF DATA ON MEDICINE UTILIZATION

Methods to analyse medicine utilization and expenditure to support pharmaceutical policy implementation

The quantity unit should always be of the same type; for example, always a count of units, or always a count of prescriptions dispensed or always a count of people receiving the medicine. The time periods should be equivalent (e.g. all months or all years) or should be able to be standardized to equivalent time periods. A variable that includes costs enables expenditure analyses to be done. For calculating the defined daily dose (DDD) indicators, a variable that details the DDD for each product is required.

Table 5 shows an example of a data set for aggregated data.

Table 5 | Example of a data set for aggregated data (for the analysis methods included in this manual)

<table>
<thead>
<tr>
<th>Medicine name</th>
<th>Medicine strength</th>
<th>Form</th>
<th>Pack size</th>
<th>Product code</th>
<th>ATC code</th>
<th>DDD</th>
<th>Time period</th>
<th>Quantity</th>
<th>Cost (AUD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Omeprazole</td>
<td>20 mg</td>
<td>Tablet</td>
<td>30</td>
<td>08333N</td>
<td>A02BC01</td>
<td>20 mg</td>
<td>2006</td>
<td>300</td>
<td>10 310</td>
</tr>
<tr>
<td>Omeprazole</td>
<td>20 mg</td>
<td>Tablet</td>
<td>30</td>
<td>08333N</td>
<td>A02BC01</td>
<td>20 mg</td>
<td>2007</td>
<td>345</td>
<td>11 960</td>
</tr>
<tr>
<td>Omeprazole</td>
<td>20 mg</td>
<td>Tablet</td>
<td>30</td>
<td>08333N</td>
<td>A02BC01</td>
<td>20 mg</td>
<td>2008</td>
<td>362</td>
<td>10 465</td>
</tr>
<tr>
<td>Omeprazole</td>
<td>20 mg</td>
<td>Tablet</td>
<td>30</td>
<td>08333N</td>
<td>A02BC01</td>
<td>20 mg</td>
<td>2009</td>
<td>389</td>
<td>11 410</td>
</tr>
</tbody>
</table>

ATC: Anatomical Therapeutic Chemical; DDD: defined daily dose; AUD: Australian dollar.

PATIENT-LEVEL DATA

The minimum data set required to undertake analyses where patient-level data are available is:

- a variable that identifies the patient and is maintained across the data set,
- a variable that identifies the medicine (name or code), its strength and form,
- a variable that identifies the date the medicine was supplied to the patient.

A variable that identifies the quantity of medicine supplied to the patient as well as the DDD amount will enable the DDD indicators to be measured. A variable that includes costs enables expenditure to be measured.

Table 6 shows an example of a data set for patient-level data.

Table 6 | Example of a data set for individual patient-level data (for the analysis methods included in this manual)

<table>
<thead>
<tr>
<th>Patient ID</th>
<th>Medicine name</th>
<th>Strength</th>
<th>Form</th>
<th>Product code</th>
<th>ATC code</th>
<th>DDD Date supplied</th>
<th>Quantity</th>
<th>Cost (AUD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>20106</td>
<td>Amoxicillin</td>
<td>250 mg</td>
<td>Capsule</td>
<td>01884E</td>
<td>J01CA04</td>
<td>03APR2006</td>
<td>20</td>
<td>7.87</td>
</tr>
<tr>
<td>20106</td>
<td>Omeprazole</td>
<td>20 mg</td>
<td>Tablet</td>
<td>08333N</td>
<td>A02BC01</td>
<td>03APR2006</td>
<td>30</td>
<td>34.38</td>
</tr>
<tr>
<td>20106</td>
<td>Omeprazole</td>
<td>20 mg</td>
<td>Tablet</td>
<td>08333N</td>
<td>A02BC01</td>
<td>10APR2006</td>
<td>30</td>
<td>34.38</td>
</tr>
<tr>
<td>20106</td>
<td>Omeprazole</td>
<td>20 mg</td>
<td>Tablet</td>
<td>08333N</td>
<td>A02BC01</td>
<td>24APR2006</td>
<td>30</td>
<td>34.38</td>
</tr>
<tr>
<td>20173</td>
<td>Atenolol</td>
<td>50 mg</td>
<td>Tablet</td>
<td>1081X</td>
<td>C07AB03</td>
<td>02MAY2006</td>
<td>30</td>
<td>10.06</td>
</tr>
<tr>
<td>20173</td>
<td>Omeprazole</td>
<td>20 mg</td>
<td>Tablet</td>
<td>08333N</td>
<td>A02BC01</td>
<td>02MAY2006</td>
<td>30</td>
<td>34.38</td>
</tr>
</tbody>
</table>

ATC: Anatomical Therapeutic Chemical; DDD: defined daily dose; AUD: Australian dollar.
SECTION 3: MEASURES OF MEDICINE UTILIZATION

Measures of medicine utilization can include an assessment of the amount of medicine procured, sold, prescribed, dispensed, supplied or used.

The unit of measurement can include:
- counts,
- volume,
- costs.

The measures can generally be applied whether the data are available as units of stock, prescriptions written, prescriptions dispensed or units of medicines supplied. Where individual patient-level data are available, measures may include counts of people receiving the medicines and counts of people starting new medicines.

The volume measures that have been developed use the DDD or prescribed daily dose, and these are described in more detail below.

**Rates and denominators:** When examining changes in the use of medicine over time, it is helpful to express the unit of measurement as a rate. All of the measurement units can be expressed as rates. The most commonly used denominator is the population to which the data are applicable, with rates commonly expressed per 100 or per 1000 persons per period of time. Changes in the population may result in substantial changes in medicine use. Expressing measures of medicine utilization as a population rate standardizes use to a population and accounts for any underlying population changes that may influence the result.

In some instances, the overall utilization of the health service may be a suitable alternative denominator. For example, the rate per 100 bed days is a denominator that can be used with data from hospitals, while the rate per 100 patient encounters is a denominator that can be used for data from medical practices. Expressing measures of medicine utilization as a rate of health service use accounts for any change in the number of health services provided that may influence the result.

**DEFINED DAILY DOSE**

**Purpose:** To provide a standardized measure of the overall volume of medicines provided.

**Description:** The standard for the measure is the defined daily dose (DDD), which is an internationally set standard that is “the assumed average maintenance dose per day for a drug used for its main indication in adults” (8). Information on the principles for DDD assignment is given on the website of the WHO Collaborating Centre for Drug Statistics Methodology (www.whocc.no). The DDD is linked to the ATC classification, and a website for the ATC/DDD toolkit is available for drug utilization monitoring and research (3).

One measure of utilization is known as the DDD per 1000 population per day (DDD/1000 per day) (8)

\[
\text{DDD/1000 per day} = \frac{\text{Mass (strength)} \times \text{Quantity} \times \text{Number of dispensings (packs)} \times 1000}{\text{DDD} \times \text{Population} \times \text{Number of days}}
\]

Where Mass = mass or strength of the product; Quantity = quantity in the pack supplied; and DDD is the defined daily dose. The population refers to the population that is relevant to the data that have been used. Number of days is the count of days in the time period (e.g. 365 for 1 year) (9).

The measure may also be expressed as DDD/1000 per year (8). When measuring medicine use within hospitals, the measure is usually expressed as DDD/100 bed days (8).
**Advantages:** The measure enables comparisons of use within and across classes of medicines despite products having different strengths or different pack sizes. Because it is a volume measure, it overcomes limitations in longitudinal analyses where product strengths or pack sizes change over time, enabling assessment of changes in use over time and the effects of interventions or policy changes. The estimate is most useful for medicines used long term and when there is good agreement between the average prescribed daily dose and the DDD. If the DDD accurately reflects the actual dose used in practice, then the DDD/1000 per day is equivalent to a measure of point prevalence (10). Similarly, if the DDD accurately reflects the actual dose used in practice, then the DDD/1000 per year is equivalent to the number of days of the year, on average, for which the population was treated (8). This measure has also been described as a measure of “therapeutic intensity” in a population (10).

**Example**

In a one-year period (365 days), 200 000 prescriptions of diazepam 5 mg tablets in packs of 50 are provided. The DDD of diazepam is 10 mg. The population in the area where the prescriptions were supplied is 5 million persons. Based on these numbers, the DDD/1000 per day would be:

\[
\frac{5 \times 50 \times 200\,000 \times 1\,000}{10 \times 5\,000\,000 \times 365} = 2.74
\]

The DDD/1000 per day is commonly used to compare medicine use across medicines, health settings or countries. Fig. 2 shows an example of the comparison of medicine use by DDD/1000 per day for different types of respiratory medicines in the public and private sectors in Malaysia. The data show that there is a much higher use of inhaled beta-2 agonist therapy in the public sector than the private sector. Within the private sector there is more use of oral beta-2 agonist therapy than inhaled beta-2 agonist therapy. Analyses such as this flag opportunities for intervention or further assessment when the results are not consistent with expected practice.

**Fig. 2 | Use of respiratory medicines in public and private sectors, Malaysia, 2005**

[Bar chart showing DDD/1000 per day for different types of respiratory medicines in public and private sectors.]
Example

Fig. 3 provides an example of a cross-sectional analysis using the DDD/1000 per day where the results are compared for different countries. Lipid lowering therapy is indicated for most people with diabetes, as well as for people at risk of cardiovascular disease. In 2005, the overall volume of diabetes therapy was 36 DDD/1000 per day in Malaysia compared with 43 DDD/1000 per day in Australia. The ratio of lipid lowering therapy to diabetes therapy was significantly different across countries. Analyses such as this can be useful to generate hypotheses as to whether the use of therapies is in keeping with expected use.

The DDD/1000/day has been commonly used in cross sectional studies comparing antibiotic utilization across Europe (12-14). The Organization for Economic Cooperation and Development (OECD) regularly publishes medicine utilization results as DDD/1000/day for the OECD countries (15), enabling comparisons across participating countries and across time.

Fig. 3 | Use of lipid lowering and diabetes therapy in Malaysia and Australia

Limitations: The DDD is based on the average assumed dose for the main indication in adults. Therefore, when applied to medicines that are mostly used in children or across indications where doses vary substantially, the volume of use does not reflect the point prevalence and changes in volume of use over time may be difficult to interpret in specific populations, for example in children or the elderly. Furthermore, comparisons across medicine groups may be confounded if the main indications for medicines of similar pharmacological or chemical classes are different.

Suitable types of data: Estimation of the DDD requires data on the quantity per pack, number of packs and product strength information. Procurement data, sales data, dispensing data, prescribing data or health claims data may all be appropriate.

Data period: Cross-sectional or longitudinal.
**PRESCRIBED DAILY DOSE**

**Purpose:** To provide a measure of the amount of medicine used per day for a specified population or indication.

**Description:** The prescribed daily dose is defined as the average daily dose prescribed. It needs to be calculated from a representative sample of prescriptions. The prescribed daily dose can be determined from studies of prescriptions, or medical or pharmacy records. The prescribed daily dose will give the average daily amount of a medicine that is actually prescribed. When calculating the prescribed daily dose for a specific indication, it is important to limit the calculations to prescriptions relevant to the diagnosis for which the medicine is used. Similarly, when assessing the prescribed daily dose for age groups, only prescriptions relevant to the age group should be included.

**Advantages:** Where analysis of medication use is in a population or for an indication that does not reflect the DDD indication and population, the prescribed daily dose may be more appropriate. For example, when examining medicine utilization in children, the prescribed daily dose could be an alternative measure because the DDD reflects the average assumed dose for the main indication in adults. Similarly, the prescribed daily dose may be more appropriate if examining medicine use for indications other than the main indication, or if the dose range is wide and varies for different indications.

**Limitations:** The prescribed daily dose is not commonly used as a standard. Comparisons using the prescribed daily dose are limited to the settings in which this measure has been calculated or is known. The prescribed daily dose can change over time, which may limit its suitability for longitudinal analyses. It can also differ from one country to another so it is rarely suitable for cross-country comparisons. In addition, the prescribed daily dose can vary according to both the illness treated and national policies and practices. For example, the prescribed daily dose of an anti-infective medicine may vary according to the severity of the infection. In general, estimates of utilization of medicine using the prescribed daily dose are not suitable for comparison with utilization estimates calculated with the DDD. When there is a substantial discrepancy between the prescribed daily dose and the DDD, it is important to take this into consideration when evaluating and interpreting medicine utilization figures that use these two measures.

**Suitable types of data:** Estimation of the prescribed daily dose requires a data type where the prescribed dose is available. Prescribing data, dispensing data or health claims records may all be appropriate.

**Data period:** Cross-sectional or longitudinal.

---

**Example**

An example where it might be preferable to calculate the prescribed daily dose rather than use the defined daily dose would be an assessment of tricyclic antidepressants in the elderly, where the prescribed dose is likely to be lower to treat neuropathic pain or incontinence than the much higher defined daily dose that is based on the indication for the treatment of major depression. A similar example is the use of antipsychotics in the elderly for the treatment of behavioural symptoms of dementia, again a situation where lower doses are used rather than the much higher defined daily dose based on the indication to treat schizophrenia. Assessment of medicines in children, where weight-based dosing is often used, is another example where prescribed daily doses may provide a better estimate of the extent of use in children. In these cases, the prescribed daily dose would better reflect the actual use in specific populations.
SECTION 4: METHODS FOR ASSESSING MEDICINE UTILIZATION USING AGGREGATED DATA

ABC ANALYSIS

Purpose: To determine which medicines account for the majority of either:
- medicine use (by volume, packs, dispensings or DDD/1000 per day),
- medicine budget (cost).

Description: ABC analysis (16) can be used to support procurement (ensuring purchase of needed medicines), stock control (ensuring products are purchased in appropriate volumes) and assessment of the appropriateness of use (e.g. are the majority of medicines used, the medicines that are most needed?)

Based on counts or total costs of medicines or medicine classes, an ABC classification is developed where medicines are classed as:

A = top 10 to 19% of medicines which account for approximately two thirds of the total cost or total volume
B = top 20 to 30% of medicines which account for approximately one quarter of the total cost or total volume
C = remaining 51 to 70% of medicines that account for approximately 10% of total cost or total volume.

The ABC analysis can be presented as total cumulative volume or total cumulative cost.

The results of the ABC analysis should be interpreted within a framework assessing, for example: whether the most frequently used or costly medicines are consistent with the most prevalent diseases; whether the most frequently used medicines are first-line agents; or whether the most frequently used medicines are generic products.

Measures that can be used: Counts, volume or expenditure. Measures expressed as rates are also suitable.

Advantages: ABC analysis enables easy identification of the most commonly used or most costly medicines or medicine classes. It can be calculated: at the macro or micro level; by product level, medicine level, therapeutic class or therapeutic group; and based on monetary value, stock volume (e.g. numbers of packs, numbers of prescriptions), or medicine volume (e.g. DDD/1000 per day). A coding system such as WHO ATC classification (2) is required to do an analysis of therapeutic class or group.

Limitations: If used without a framework for assessment of results, it may limit identification of under-used, over-used or inappropriately used medicines.

Suitable types of data: Procurement data, sales data, dispensing data, prescribing data, health claims data, representative survey data.

Data period: Cross-sectional.
Example

The ABC analysis for Australia (Fig. 4) shows that medicines affecting the cardiovascular system, the nervous system, and the alimentary tract and metabolism account for two thirds of Australia’s medicine use. Australia continually monitors medicine expenditure and prescriptions, and publishes reports which identify the level of medicine use by cost and volume every 12 months (6).

**Fig. 4 | ABC analysis, Australia, 2014 based on therapeutic groups and total cumulative percentage volume**

Source: Calculated from dispensing claims data reported in the Pharmaceutical Benefits Scheme for expenditure and prescriptions 12 months to 30 June 2014 (17).

**DRUG UTILIZATION 90%**

**Purpose:** To identify the medicines that contribute to 90% of total medicine utilization.

**Description:** Drug utilization 90% (DU90%) calculations are based on the DDD/1000 per day and can be used to assess whether the most commonly used medicines (by volume) are consistent with the medicines recommended in standard treatment guidelines (18). A variation on this analysis is the drug cost 90% (DC90%) which identifies the medicines contributing to 90% of total medicine costs.

**Measures that can be used:** Counts, volume or expenditure. Rates of these measures can also be used.

**Advantages:** DU90% calculations enable easy identification of the most common or most costly medicines. DU90% and DC90% can be calculated at the macro or micro level, product level and medicine level, and by therapeutic class or therapeutic group. A coding system such as the WHO ATC classification is required to do an analysis of therapeutic class or group.

**Limitations:** Essential medicines that are used for uncommon or rare conditions will not be monitored.

**Suitable types of data:** Procurement data, sales data, dispensing data, prescribing data, health claims data, representative survey data.

**Data period:** Cross-sectional.
Example

The DU90% has been used in Sweden as part of the evaluation of compliance with the recommendations of the essential medicines list (19). Another example is presented in Fig. 5, which shows a portion of a DU90% analysis of Malaysia’s medicine use in 2004. The medicines in blue are highlighted for potential review as they are oral antihistamines, three of which are in the top 35 medicines, by volume. This high level of use may warrant review to consider the appropriateness of use.

Fig. 5 | Drug utilization 90% for Malaysia, 2004 (only top 35 medicines included)

Source: (7).

VITAL, ESSENTIAL, NON-ESSENTIAL ANALYSIS

**Purpose:** To determine the proportion of medicine volume or cost used for vital, essential and non-essential (VEN) medicines.

**Description:** Medicines need to be classified according to the following criteria (16):

- **Vital:** “potentially life-saving or crucial to providing basic health services”;
- **Essential:** “effective against less severe but significant forms of disease, but not absolutely vital to providing basic health care”;
- **Non-essential:** “used for minor or self-limited illnesses; these may or may not be formulary items and efficacious, but they are the least important items stocked”.

A similar method, intrinsic value analysis, categorizes medicines according to the strength of evidence for
clinical effectiveness (20). Categorization of medicines should be done by a panel of experts such as an existing medication and therapeutics committee or a clinical pharmacology group specifically established for that purpose.

Once categorized, medicines can be examined by the ABC analysis or DU90%. The results of a VEN analysis should be interpreted within a framework assessing whether the most frequently used or costly medicines are consistent with the essential medicines, or whether vital medicines are always in stock.

**Measures that can be used:** Counts, volumes or expenditure. Rates of these measures can also be used.

**Advantages:** VEN analysis can be done at the macro or micro level, and at the level of the medicine or medicine class.

**Limitations:** It may be difficult to classify some medicines where multiple indications exist. Some medicines may need to be classified by indication.

**Suitable types of data:** Procurement data, sales data, dispensing data, prescribing data, health claims data, representative survey data.

**Data period:** Cross-sectional.

---

**Example**

Table 7 shows that the medicines most commonly used by volume in Malaysia in 2004 were for diabetes, cardiovascular diseases and airways diseases, which is consistent with the prevalence of chronic diseases in the country. Chlorphenamine, an antihistamine, is in the top 10, which may be for coughs and colds as these are a common reason for presentation to clinics, however, this medicine can be considered non-essential. Thus, the analysis provides an opportunity to consider the appropriateness of procurement and use.

**Table 7 | Top 10 medicines used in Malaysia, 2004**

<table>
<thead>
<tr>
<th>Rank</th>
<th>ATC code</th>
<th>Medicine</th>
<th>DDD/1000 per day</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>A10B B01</td>
<td>Glibenclamide</td>
<td>14.5</td>
</tr>
<tr>
<td>2</td>
<td>C07A B03</td>
<td>Atenolol</td>
<td>13.1</td>
</tr>
<tr>
<td>3</td>
<td>A10B A02</td>
<td>Metformin</td>
<td>11.7</td>
</tr>
<tr>
<td>4</td>
<td>C07A B02</td>
<td>Metoprolol</td>
<td>11.0</td>
</tr>
<tr>
<td>5</td>
<td>C08C A05</td>
<td>Nifedipine</td>
<td>9.9</td>
</tr>
<tr>
<td>6</td>
<td>C10A A01</td>
<td>Simvastatin</td>
<td>7.9</td>
</tr>
<tr>
<td>7</td>
<td>C08C A01</td>
<td>Amlodipine</td>
<td>6.6</td>
</tr>
<tr>
<td>8</td>
<td>R03A C02</td>
<td>Salbutamol</td>
<td>6.3</td>
</tr>
<tr>
<td>9</td>
<td>R06A B04</td>
<td>Chlorphenamine</td>
<td>5.7</td>
</tr>
<tr>
<td>10</td>
<td>A10B B09</td>
<td>Gliclazide</td>
<td>5.6</td>
</tr>
</tbody>
</table>

ATC: Anatomical Therapeutic Chemical; DDD: defined daily dose.

Source: (7)
TIME SERIES TRENDS

Purpose: To examine changes in medicine use over time.

Description: Aggregate measures of medicine use or cost are calculated per unit of time (e.g. day, week, month, year). Time series trends can be created from counts or volumes of medicines procured or dispensed, or the sum of costs (21). Volumes and costs can also be standardized to the population (e.g. prescriptions per 1000 population).

Measures that can be used: Rates of counts, volume or expenditure.

Advantages: Time series trends provide a clear graphical representation of trends in the use of medicines, which can be standardized to the population and interpreted with minimal training. Visual inspection, rather than statistical analysis, is sufficient to identify time points associated with large changes in utilization. Time series analysis enables comparisons of use over time, which can be used to determine the effect of listings, delistings and policy changes (e.g. changes in co-payments, pricing, restrictions). This method can also be used for forecasting.

Limitations: Time series analysis may be affected by seasonality. Use of a moving average can remove the seasonality effect. Where person data are not available, it cannot be ascertained if changes in use are because of changes in the numbers of people getting the medicine or changes in the amount of medicine used per person. Similarly, where individual unit data or individual prescription data are not available (i.e. where only aggregate costs or aggregate units are available), the components influencing the change may be difficult to interpret.

Suitable types of data: Procurement data, sales data, dispensing data, prescribing data, health claims data, representative survey data.

Data period: Longitudinal.

Examples

Time series trends have been used by many countries to evaluate medicine utilization and the effect of policy or listing changes. For example, time series trends on medicine use are routinely analysed by Australia’s Drug Utilisation Sub Committee (22). Time series analysis has been used to evaluate the effect of adding restrictions to listings, such as requiring an authorization prior to writing a prescription (23,24), the effect of pricing policy (25,26), and the changing use of generic medicines (27) and changing expenditure (28). Time series trends of antibiotic use have been used to evaluate the effect of programmes to improve the use of antibiotics in Slovenia (29) and to examine use in India (30).

Fig. 6 shows a time series for non-steroidal anti-inflammatory agents in Australia. The figure shows the rate per 1000 population of non-steroidal anti-inflammatory prescriptions dispensed in Australia for each calendar month between 2001 and 2012. Visual inspection of the prescription trend is sufficient to identify a substantial decrease in prescriptions dispensed from late 2004 onward. Upon investigation it was determined that rofecoxib, a widely used treatment for osteoarthritis, was delisted because of safety concerns in October 2004. The use of non-steroidal anti-inflammatories did not recover to the 2004 levels in the following years to 2012.

Visual inspection of the data also shows significant variation at the end of each calendar year. This is due to the Australian pharmaceutical safety net (31). Individuals or families receive medicine at a lower cost or at no cost if they have reached the safety net threshold (which is based on out-of-pocket patient costs) within a calendar year. For some medicines, stockpiling takes place whereby people get extra dispensings in December while they are on the safety net, with a subsequent fall in dispensings in January, when co-payments are re-established at standard rates until a new safety net threshold is reached. Converting the trend to a moving average provides a smoother trend without the influence of the safety net variation.
The blue line is a 12-month moving annual average which results in a similarly shaped line without the variation. Note, however, that the steepness of the fall associated with rofecoxib withdrawal is also less apparent as the averaging technique results in the effect being averaged over time.

**SEGMENTED REGRESSION ANALYSIS**

**Purpose:** To quantify changes in medicine use over time.

**Description:** Segmented regression analysis builds upon time series analysis, allowing differences in utilization trends before and after a specified intervention or change point to be quantified (21). As with time series analysis, aggregate measures of medication use or cost are calculated per unit of time (e.g. day, week, month, year) and graphically displayed over time.

Basic segmented regression models assume a linear relationship between time and utilization, creating a line of best fit (least squares regression line) for the portion of the time series before and after the intervention point. This approach is suitable for continuous utilization measures such as numbers of prescriptions or cost. The general formula for this is:

\[ Y_t = \beta_0 + \beta_1 \times \text{time}_t + \beta_2 \times \text{intervention}_t + \beta_3 \times \text{time after intervention}_t + e_t \]

Where \( Y \) is the number (or cost) of prescriptions in time unit \( t \); \( \text{time} \) is a continuous variable indicating the number of time units from the start of the observation period; \( \text{intervention} \) is a binary variable indicating the time period before or after the change point; \( \text{time after intervention} \) is a continuous variable counting the number of time units after the change point; and \( e \) is the error.
Methods to analyse medicine utilization and expenditure to support pharmaceutical policy implementation

SECTION 4: METHODS FOR ASSESSING MEDICINE UTILIZATION USING AGGREGATED DATA

The term representing the random variation not explained by the model (21). The resulting line of best fit can be graphed with the time series (see example).

The output from segmented regression analysis quantifies:

- the mean change (by time units) in utilization prior to the intervention point;
- the immediate rise or fall in utilization in the time unit immediately following the intervention point (the level change); and
- the change in the underlying trend (by time unit) of the post-intervention trend compared with the pre-intervention trend.

Seasonality can be accounted for using ARIMA (autoregressive integrated moving average) models or lag terms (21,33), which are available in the main statistical software packages. When non-continuous measures (e.g. population-adjusted rates, DDD/1000 per day) are available, non-linear regression models are appropriate.

Measures that can be used: Counts, volume or expenditure. Rates of these measures can also be used.

Advantages: Segmented regression analysis quantifies changes in utilization occurring after a specified change point such as a policy intervention, price increase or new listing. The analysis accounts for the baseline utilization trend occurring before the change point (including underlying population growth and ageing), thereby incorporating the effect of historical events. Segmented regression analysis can adjust for seasonal variation.

Limitations: A clear change point needs to be determined before starting the analysis (i.e. the analysis will not identify the change point). A minimum number of data points is required either side of the intervention point; 20 is preferable, particularly if monthly data with seasonal patterns are used (21,33).

Suitable types of data: Procurement data, sales data, dispensing data, prescribing data, health claims data.

Data period: Longitudinal.

Example

Large changes in medicine utilization can be seen from time series trends (see the example of Fig. 6). Time series trends, however, do not quantify the size of the change and where smaller changes in utilization occur, it may be necessary to quantify the size of the change to determine the effect. Segmented regression enables quantification of the size of the change but it does require more specialist analytical skills and the advice of a statistician is recommended. For a worked example of a segmented regression analysis, see Wagner et al., 2002 (21).

Fig. 7 shows a hypothetical example of a small change in the use of a medicine as a result of a price change. The time series graph shows the volume of prescriptions of Medicine A dispensed each month over a four-year period. The price of Medicine A was increased in January 2013 and segmented regression analysis has been used to compare the volume of prescriptions of Medicine A in the period before (January 2010–December 2012) and after (January 2013–December 2014), the change point. In this analysis example, which was done using statistical software, the results indicated that dispensing of Medicine A was increasing on average by 507 prescriptions per month before the price increase. Immediately after the price increase, prescriptions fell by 2,262 prescriptions (a significant level change, $P = 0.025$). For each month after the change point, there were, on average, 214 fewer prescriptions of Medicine A dispensed each month (a significant trend change, $P = 0.005$). These results suggest that the January 2013 price increase had an immediate and ongoing effect on dispensing of Medicine A.
**FORECASTING**

**Purpose:** To estimate future medicine utilization.

**Description:** Forecasting builds upon time series analysis by creating a line of best fit for utilization at historical (existing) time points and extrapolating the line of best fit forward to estimate utilization at future time points (34). As with time series analysis, aggregate measures of medicine use or cost are calculated per unit of time (e.g., day, week, month, year) and graphically displayed. The line of best fit can be created using simple linear regression (34). Alternatively, models accounting for seasonality and based on polynomial, exponential or logarithmic functions can be used, if they better represent the historical data (as determined by an $R^2$ value close to 1).

Crude predictions can be made from the line of best fit for time points extending beyond historical data. Predictions can also be adjusted for the estimated effect of foreseeable factors likely to affect utilization, such as new listings, delistings or policy changes (34).

Simple forecasting can be done using the trendline function in Microsoft Excel. For a description of more complex forecasting methods and instructions for conducting analyses with the statistics software, “R”, refer to Hyndman and Athanasopoulos (33).

**Measures that can be used:** Counts, volume or expenditure. Rates of these measures can also be used.

**Advantages:** Forecasting enumerates likely medicine utilization in the future. This may help budget planning and stock control. Predictions do not need to be adjusted for population growth or population ageing as these are accounted for in the historical trend.

**Limitations:** Predicted medicine utilization is an approximate estimate. Where the line of best fit does not adequately account for the historical trend (i.e. $R^2$
is small), extrapolated time points are unlikely to be reliable. The reliability of extrapolated time points is likely to decrease the further forward in time they go beyond the historical data. The reliability of estimates can be affected by unforeseeable events.

**Suitable types of data:** Procurement data, sales data, dispensing data, prescribing data, health claims data, representative survey data.

**Data period:** Longitudinal.

---

**Example**

Forecasting is often used to support assessments of the budget impact of medicines (35–37), with current market use of medicines used to forecast future use of medicines. Fig. 8 shows an example of forecasting. It shows the number of prescriptions of vascular endothelial growth factor (VEGF) inhibitor dispensed in Australia annually between 2008 and 2014 (historical data are the red data points), with approximately 250 000 prescriptions dispensed in 2014. The line of best fit (trendline) calculated for these historical data points had an \( R^2 \) value of 0.966 (close to 1), indicating that the line of best fit represented these data well. The line of best fit was extrapolated for a further three years. The crude predictions from the line of best fit (blue data points) indicate that annual prescription volumes are likely to reach 300 000 by 2017.

**Fig. 8 | Forecast of future use of VEGF inhibitors in Australia**

![Fig. 8 | Forecast of future use of VEGF inhibitors in Australia](image-url)

Source: Calculated from Pharmaceutical Benefits Schedule item reports online statistics (32).
INDICATOR RATIOS

Purpose: To monitor medicine use using ratios of specified medicines.

Description: The basic calculation for indicator ratios is:

\[
\frac{\text{Utilization of specified medicine (a)}}{\text{Utilization of specified medicine (b)}}
\]

Specified medicines can be individual medicines or therapeutic classes or groups if appropriate. Medicine utilization can be assessed by volume (procurement or dispensing), cost or a population-standardized unit. Indicator ratios can be considered at one time point, or over time. Criteria for selecting indicator medicines should be based on procurement, pricing or standard treatment guidelines using a framework such as that outlined below (38,39).

Supporting use of generic medicines
1) where medicine (a) is the generic medicine and medicine (b) is the branded product (or generic and branded);

Supporting cost-effective use of medicines
2) where medicine (a) is more cost-effective than medicine (b) when used for the same indication;

Supporting judicious and appropriate selection of medicines
3) where medicine (a) is the first-line therapy and medicine (b) is the second-line therapy as identified in standard treatment guidelines.

Where data sets do not contain information on indication, preferred treatments can only be selected where one medicine dose or form is preferable to another in all circumstances of its use or where it is known that the main indication for use represents the majority of prescribing.

4) where medicine (a) is a medicine that is known to be under-used and medicine (b) is a medicine which is used for the same indications and the level of use is thought to be appropriate.

It is preferable that medicine (b) is a medicine used for the same indications as (a) because changing disease prevalence can confound trends in medication use. If the comparator medicine used in this ratio is indicated for the same conditions, then the influence of changing disease prevalence is limited to some extent.

5) where medicine (b) is a medicine that is known to be over-used and medicine (a) is a medicine which is used for the same indications and the level of use is thought to be appropriate or medicine (a) is considered the preferred treatment to the over-used medication.

The over-used medication has been identified as the denominator in this instance so the results of all ratio measurements are consistent in that an increasing ratio would be considered evidence of improving medication use, while a decreasing ratio would be considered evidence of worsening medication use.

Supporting safe and efficacious use of medicines
6) where medicine (a) is considered safer than medicine (b) when used for the same indication.

7) where medicine (a) is considered more efficacious than medicine (b) when used for the same indication.

8) where medicine (a) is the lower strength product and medicine (b) is all other products of that medicine.

9) where medicine (a) is the medicine with the simpler regimen and medicine (b) includes all other products or medicines in the class.

For all these indicators, the measure can be limited to medication use in specified groups where patient-level data or area data are available (e.g. age, gender, location).

Measures that can be used: Counts, volume or expenditure. Rates of these measures can also be used.

Advantages: Indicator ratios can be calculated at the macro or micro level. Comparisons within and across countries may also be informative.

Limitations: Indicator ratios cannot generally be used where the medicine has multiple indications for use.

Suitable types of data: Procurement data, sales data, dispensing data, prescribing data, health claims data, representative survey data.

Data period: Cross-sectional or longitudinal.
Examples

Ratio indicators have been used in Sweden to monitor compliance with recommendations in the essential medicines list (19). One indicator from the Swedish evaluation was the use of angiotensin converting enzyme (ACE) inhibitor as a percentage of all renin angiotensin aldosterone system agents, because the essential medicines list aimed to restrict use of angiotensin II receptor blockers to patients intolerant of ACE inhibitors (19). Another example was simvastatin use as a proportion of use of all statin prescriptions because simvastatin was the preferred therapy (19). Ratio indicators have also been used to monitor the effect of Australia’s national strategy for quality use of medicines (40). Ratios have included the use of paracetamol as a proportion of all simple analgesic use, use of narrow spectrum antibiotics as a proportion of all antibiotic use, and use of low-risk medicines for diabetes compared with high-risk medicines (40).

Fig. 9 shows the ratio of gliclazide use to glibenclamide use in Australia from 1990 to 2005. The rationale for this indicator was that gliclazide was preferred to glibenclamide in the elderly because it has a shorter half-life and was less likely to cause hypoglycaemia (41). The figure shows an increasing ratio which indicates that the use is in the direction of the preferred therapy, with glibenclamide use declining relative to gliclazide. Other medicines for diabetes are increasingly being used (data not shown), which explains the declining volume of use of these two medicines after 2000.

SECTION 5: METHODS FOR ASSESSING MEDICINE UTILIZATION USING PATIENT-LEVEL DATA

PREVALENCE AND INCIDENCE COUNTS

Purpose: To estimate period prevalence and incidence of a population (10).

Description:

\[
\text{Period prevalence} = \frac{\text{Number of persons dispensed the medicine in the period}}{\text{Population}}
\]

Where the population refers to the population that is relevant to the data that have been used.

For example:

One year prevalence, 2014 = \[
\frac{\text{Number of persons dispensed the medicine in 2014}}{\text{Population at 30 June 2014}}
\]

\[
\text{Incidence} = \frac{\text{Number of new users in the period}}{\text{Population}}
\]

Where the population refers to the population that is relevant to the data that have been used.

For example:

Incidence for 2014 = \[
\frac{\text{Number of new users in 2014}}{\text{Population at 30 June 2014}}
\]

Where new users are those with no dispensings in the previous one-year period (i.e. no dispensings in 2013).

Advantages: Prevalence and incidence counts enable comparisons over time. It can be useful to compare these estimates with period prevalence and incidence estimates from other sources, such as national health surveys or epidemiological studies of prevalence and incidence from the same populations because discrepancies may identify over- or under-use of medicines.

Limitations: This method is only applicable as a measure of prevalence or incidence where medicine use is indicative of a diagnosis (e.g. diabetes medicines as an indicator of diabetes).

Suitable types of data: Patient-level dispensing data, prescribing data or health claims data. The variables required are patient identifier, medicine identifier and date of supply. Representative survey data that include relevant questions can also be used.

Data period: At least one year of patient-level dispensing, prescribing or health claims data are required. Survey data can be cross-sectional.

Example

Prevalence rates have been used to compare antibiotic use across countries (42) and can be used to determine if the amount of medicine being used is in line with expectations of use where the overall prevalence or incidence of a disease is known. For example, if the population with diabetes is known, then a prevalence count of people receiving diabetes medicines gives insight into the percentage of the population with diabetes that are treated with medicines. Prevalence and incidence counts can also be helpful for assessments of budget impact (37), where information on the number of people currently being treated or the number of new people starting treatment can be used to estimate likely future treatment rates.
DURATION INDEX

**Purpose:** To estimate the average duration of medicine use.

**Description:** The average duration of medicine use can be calculated using the point prevalence and incidence data where new medicine use indicates the development of the condition (10). Where data on medicine use are available, this can be calculated using the following formula.

\[ D = \frac{P}{(1-P) \times I} \]

Where \( D \) = average duration of medicine use; \( P \) = point prevalence; \( I \) = incidence. The DDD/1000 per day can be used as the measure for point prevalence (10).

**Advantages:** The duration index can give an approximation of the duration of use based on only one year of data. It is simple to calculate without the need for advanced statistical methods.

**Limitations:** Using the DDD/1000 per day as a substitute for point prevalence is only possible if the DDD reflects the prescribed daily dose in practice. Age variations in prevalence and incidence will bias the results to lower values. While it is possible to calculate age-specific durations of use, they cannot be easily interpreted (10).

**Suitable types of data:** Patient-level dispensing data, prescribing data or health claims data.

---

Data period: At least one year of patient-level dispensing, prescribing or health claims data are required.

Example

To calculate the duration index, a prior calculation of the DDD/1000 per day is required (see Section 3 page 14), as well as an analysis of the incident population (see page 29). The example below estimates the length of time people stay on antidepressant medicines based on the duration index, where the overall volume of use is 97 DDD/1000 per day and the incidence is 26 per 1000 persons. The result of an estimated duration longer than 4 years, suggests considerable long-term use of antidepressant medicines. Further examples can be found in the paper by Hallas, 2005 (10).

Estimating the duration of antidepressant medicine use (\( D \)) with:

- DDD/1000 per day (used as the measure of point prevalence) = 97
- Incidence per 1000 = 26

\[ D = \frac{0.097}{(1-0.097) \times 0.026} \]

\[ = 4.2 \text{ years} \]

---

LORENZ CURVE

**Purpose:** To determine the proportion of persons accounting for the majority of medicine use.

**Description:** The Lorenz curve is a graphical tool that illustrates the cumulative percentage of medicine use by the cumulative percentage of medicine users (10).

It is a similar analysis to the total cumulative value curves built from ABC analyses; however, where the ABC analyses identify which medicines account for the majority of use compared to all medicine use, the Lorenz curve identifies the proportion of persons who account for the most and least use of a medicine or class of medicines.

**Advantages:** This analysis enables the identification of medicines that may be under- or over-used.

**Limitations:** The interpretation can be limited when the use varies by disease severity.

**Data sources:** Patient-level dispensing data, prescribing data or health claims data. The variables required are patient identifier, medicine identifier and date of supply.

**Data period:** At least one year of patient-level dispensing, prescribing or health claims data are required.
Example

Fig. 10 shows hypothetical examples of Lorenz curves for two different medicines. Medicine A has equal distribution of medicine supply (every person gets the same volume in the period measured), while for Medicine B, 20% of users receive 50% of the medicine as illustrated by the rectangle, while 30% of users account for less than 10% of use. This may be appropriate where there is different disease severity, but may indicate over-use or under-use where similar treatment is expected. Other examples of Lorenz curves can be found in Hallas, 2005 (10).

Fig. 10 | Hypothetical examples of Lorenz curves: A) for a medicine used uniformly by the population and B) for a medicine used more frequently by some members of the population and less frequently by others

WAITING TIME DISTRIBUTIONS

Purpose: A graphical tool to support estimates of prevalence, incidence and time to refill of a prescription. In addition, visual inspection of the graphic can identify time points associated with large changes in utilization.

Description: The waiting time distribution is a count of the first prescription in the data set for a person for either a product, medicine or class plotted across time (e.g. months, weeks, days). The counts are plotted in a histogram, with each person only counted once. As the count is of the first prescription for an individual in the data set, existing users (prevalent users) who fill prescriptions regularly are captured in the first portion of the histogram, with the time in which most prevalent users are captured dependent on usual supply quantities (e.g. if supply quantities are one month’s supply, most prevalent users will appear within the first two or three months of analysis), while new users (incident users) will be captured later in time. Thus, the histogram represents a curve and the area under the curve represents the period prevalence. The steady state section of the histogram can be used to determine incidence rates (10). The point prevalence can be calculated by subtracting the steady state area from the area under the curve (10). Similar to the duration index (page 30), the duration of use can be calculated as the ratio of point prevalence and incidence. Visual inspection of the histogram can reveal seasonality, as well as changes in access (e.g. stock outs, and the effect of listings and delistings; see examples below). For a complete description of other measures that can be estimated from the histogram, see Hallas, 2005 (10).
**Methods to analyse medicine utilization and expenditure to support pharmaceutical policy implementation**

**SECTION 5: METHODS FOR ASSESSING MEDICINE UTILIZATION USING PATIENT-LEVEL DATA**

**Advantages:** It is a rapid assessment measure that can be used to estimate several parameters at once and guide the need for further analyses.

**Limitations:** Measures are an approximation only. Visual inspection requires a trained observer to ensure correct interpretation.

**Data sources:** Patient-level dispensing data, prescribing data or health claims data. The variables required are patient identifier, medicine identifier and date of supply.

**Data period:** At least one year of patient-level dispensing, prescribing or health claims data are required.

**Examples**

Fig. 11 shows a hypothetical waiting time distribution. The graph is a count of persons when they receive their first dispensing of the medicine. The initial months are highest as this represents a period in which existing users obtain a refill of their prescription. Summing these counts gives an estimate of the prevalent population, which in this example is approximately 25,000 persons. The time period where the trend stabilizes (from month 5 onwards) is the period representing incident users, which in this example equates to approximately 1,000 new users per month. This tool can be used to support additional analyses, including prescription sequence symmetry analysis, which is a method for signal detection in medication safety (details are given in Appendix 2).

**Fig. 11 | Hypothetical waiting time distribution**

Waiting time distributions can also show variation in practice. Fig. 12 shows a waiting time distribution for celecoxib in Australia from 2000 to 2010. There is a spike in the number of new users of celecoxib in October 2004. This corresponds to the time that rofecoxib was withdrawn from the market and the waiting time distribution highlights that there was a therapeutic shift to celecoxib. While not presented, a spike in incident use of some of the other non-steroidal anti-inflammatory agents would show which other products therapy had shifted to.
Fig. 12 | Waiting time distribution for celecoxib

Fig. 13 shows a proportion of a waiting time distribution for prochlorperazine. In this example the effect of a stock out problem can be seen, with a much lower number of people receiving the medicine in month 15, and then the number returning to pre-existing levels, which highlights that the stock out issue was resolved within the month.

Fig. 13 | Proportion of a waiting time distribution for prochlorperazine

Source: Calculated from data supplied by the Australian Government Department of Veterans’ Affairs.
PRESCRIPTION DURATION

Purpose: To estimate the duration of a prescription supply in data sets where dosage information is not available.

Description: Where data sets do not have information on days supplied or this cannot be calculated from the data because dosage information is not available, exposure durations for prescription supply can be estimated. This is done by examining the time, usually in days, between refills of prescriptions amongst persons receiving multiple prescriptions for the same product. Persons receiving single prescriptions are excluded from the analysis. The output can be graphed as counts of persons against time between prescription refill and as cumulative percentage of time between prescription refills. A cut-off, based on clinical knowledge and the cumulative percentage, is used to determine duration. For example, the exposure duration can be selected based on the time period within which 50%, 75%, 80% or 90% of people return for a refill of their prescription. Graphical presentation of the cumulative distribution may assist in selection of the cut-off to be applied. A variation of the method uses the prevalent pool from the waiting time distribution (43). The waiting time distribution is calculated using the prevalent population only, which is defined as those who filled one or more prescriptions in the previous year (43). The cumulative percentage of persons is calculated and a cumulative percentage distribution produced. A cut-off is then applied to assign duration, such as the period of time in which 80% of people have returned to refill their prescription (43).

Examples

Figs 14 and 15 show the graphical output of a prescription duration estimate for simvastatin, one as counts (Fig. 14) and the second as a cumulative distribution (Fig. 15). Fig. 14 shows the most common refill interval is 28 days, while the cumulative distribution (Fig. 15) shows that 50% of people have refilled their prescription within 31 days and 75% have refilled their prescription within 36 days. Using this as the basis for prescription duration suggests that prescriptions last for one month.

Fig. 14 | Time between refills of prescriptions for simvastatin

Source: Calculated from data supplied by the Australian Government Department of Veterans’ Affairs.
Advantages: This is a standard method that can be used for all medicines used on a long-term basis where dosage information or days supplied are not available.

Limitations: The method is not suitable for medicines that are used for a short time. The results can be confounded for medicines that can be used in the short or long term. They can also be confounded for medicines that have variable dosing schedules and pack sizes supplied are standard.

Data sources: Patient-level dispensing data, prescribing data or health claims data. The variables required are patient identifier, medicine identifier and date of supply.

Data period: Longitudinal.

PATIENT-LEVEL INDICATORS

Purpose: To identify appropriate or inappropriate use of medicines at the patient level.

Description: Patient-level indicators aim to assess the appropriate use of medicines for the patient. Within a data set of medication use where patient-level data are available, patient-level indicators can assess appropriateness of use according to factors such as age, gender, dosage used or prescribed, where dosing information is available. The indicators can assess adherence, duration of use, number of medicines used, coadministration of recommended therapy, duplication of therapy, use of contraindicated therapies (where this can be identified by coadministered medicines) or prescribing cascades (e.g. prescription of one medicine causes side-effects for which a second medicine is prescribed and so on).

Some examples of indicators of under-treatment, age-specific treatment and use of contraindicated therapy are given below.

Monitoring under-treatment

Indicator: percentage of persons using medicines for diabetes and not using a lipid lowering agent (denominator = all persons using medicines for diabetes).

Rationale: lipid lowering therapy is recommended in diabetes patients.

Monitoring age-specific treatment

Indicator: percentage of elderly people (over 65 years) using sulfonylureas who are using glibenclamide (denominator – all persons over 65 years on sulfonylureas).

Rationale: glibenclamide is not recommended in elderly people.
Methods to analyse medicine utilization and expenditure to support pharmaceutical policy implementation

SECTION 5: METHODS FOR ASSESSING MEDICINE UTILIZATION USING PATIENT-LEVEL DATA

Monitoring contraindicated therapy

Indicator: percentage of people on medicines indicative of asthma who are co-prescribed a non-selective beta-blocker (denominator – all persons on medicines indicative of asthma).

Rationale: non-selective beta-blockers are contraindicated in asthma.

Advantages: Patient-level indicators can be monitored at the national, regional, institutional or practitioner level. They can be used for routine monitoring of changes in health care practice.

Limitations: Many patient-level indicators require information on the indication for use or patient comorbidities and so cannot be measured unless the data set contains information on reason for prescription or the data on medicines are linked to other health data sources such as medical practitioner or hospital records. Indicators that involve simple counts of numbers of medicines (e.g. polypharmacy counts of five or more medicines) may not be indicators of quality and need to be interpreted with care. Assessment of patient-level indicators are sometimes used for benchmarking but this can be a limitation as the appropriate “benchmark” or “target level” may not be known.

Data sources: Patient-level dispensing data, prescribing data or health claims data.

Data period: For the majority of indicators longitudinal data are usually required.

Example

Indicator sets of patient-level indicators have been developed for population screening of potentially inappropriate medicine use. Examples include Beers criteria (44), STOPP START criteria (45) and ACOVE indicators (46). Indicator sets have also been developed for specific diseases, including diabetes and cardiovascular disease (47–49), as well as asthma (50).

PATIENT ADHERENCE MEASURES

Purpose: To identify the extent to which utilization, refill or supply rates are consistent with expected utilization.

Description: Patient adherence measures are most frequently measured for medicines used for chronic conditions where patients can be expected to remain on medicines long term. Calculations are based on the amount of medicine supplied over a specified time interval. Alternative calculations include measures of the time patients go without therapy. Measures are best presented as a distribution and not limited to the proportion meeting a pre-specified cut-off level that denotes adherence.

Advantages: Standard measures for assessing patient adherence allow variation in refill rates of medicine use to be observed across the population. Measures can be used to examine adherence to an individual medicine or medicines within the class (i.e. includes allowances for switching medicines within a therapeutic class). Use of more than one measure is recommended (e.g. both a measure of adherence during treatment and a measure of gaps in treatment).

Example

Medication possession ratio (51):

The number of days of medicine supplied as a proportion of:

- a fixed time interval, or
- between the date of the first dispensing and the start date of the last dispensing (not including the days supplied for medicines in last supply).

Continuous measure of medication gaps (51):

\[
\frac{\text{The number of days without medicine supply}}{\text{Days in the observation period}}
\]

There are numerous methods for assessing adherence, many of which are variations on the two measures above. Further examples can be found in Lam and Fresco, 2015 (52), Andrade et al., 2006 (51) and Hess et al., 2006 (53).
Limitations: Different measures do not necessarily give the same result. Patient compliance or adherence measures assessed in routinely collected dispensing data do not reflect consumption; medicines may be dispensed but not used. Adherence measures can be biased when limited to a fixed time interval if patients who stopped or switched medicines are not accounted for at the time of change in therapy.

Data sources: Patient-level dispensing data or health claims data. Patient surveys.

Data period: Longitudinal for dispensing and health claims data. Cross-sectional surveys.
SECTION 6: GUIDANCE DOCUMENTS


SECTION 7: ANALYSES OF MEDICINE UTILIZATION PUBLISHED ON THE INTERNET

Australia
Drug Utilisation Sub Committee (DUSC) Utilisation Analysis Public release documents:
Australian Statistics on Medicines:

Canada
Canadian Institute for Health Information. Pharmaceutical Care and Utilization:

Europe
PROTECT (Pharmacoepidemiological Research on Outcomes of Therapeutics by a European Consortium). Drug Consumption Databases in Europe:
http://www.imi-protect.eu/drugConsumption.shtml

Ireland
National Centre for Pharmacoeconomics Drug Utilisation Research:
http://www.ncpe.ie/research/drug-utilisation/

Malaysia
Malaysian Statistics on Medicines:

Nordic countries
NOWbase. Nordic Welfare database:
http://nowbase.org/

Norway
Norwegian Prescription Database:
http://www.norpd.no/
Drug consumption in Norway:
http://www.legemiddelforbruk.no/english/
Norhealth:
http://www.norgeshelsa.no/norgeshelsa/?language=en

Organisation for Economic Co-operation and Development (OECD), member countries
Pharmaceutical consumption:
Pharmaceutical market:

United States of America
Medicaid. Drug Utilization Review:
Sentinel. Assessments:
https://www.sentinelinitiative.org/drugs/assessments
REFERENCES


GOVERNANCE COMMITTEE

EXAMPLE OF TERMS OF REFERENCE

1. To develop and advise on the mechanisms for the collection, analysis and interpretation of data on utilization of medicines.
2. To provide advice on analyses required and suitable methods.
3. To review the utilization of medicines.
4. To provide advice about changes in patterns of utilization of medicines as a consequence of changes in their availability or listing.
5. To advise stakeholders on the interpretation of patterns in utilization of medicines.
6. To identify potential problems and benefits related to patterns in the utilization of medicines.
7. To evaluate policy and other interventions related to the use of medicines.
8. To facilitate and promote the dissemination of information on utilization of medicines.
9. To conduct international comparisons of utilization of medicines by interaction with appropriate international bodies.

EXAMPLE OF A STANDING AGENDA

1. Declaration of potential or actual conflicts of interest
2. Minutes of the previous meeting
3. Matters arising from previous meetings
4. Data issues
   4.1 Data sources
   4.2 Data quality
   4.3 Data set requirements
5. Formulary changes
   5.1 New listings
   5.2 Delistings
   5.3 Policy changes
6. Analyses of the use of medicines and advice on methods
   6.1 Presentation of current analyses
   6.2 Selection of topics for future reviews
7. Items for information, medicine use and education
8. Correspondence
9. Other business
APPENDIX 2

PRESCRIPTION SEQUENCE SYMMETRY ANALYSIS

**Purpose:** To identify potential signals of adverse events.

**Description:** Prescription sequence symmetry analysis is a statistical and temporal graphical method which calculates a sequence ratio between two different medicines. The analysis is built on counts of the number of persons with incident use of two different medicines (one the medicine under investigation, the second a potential treatment of an adverse event) in sequence within a specified period of time (usually 12 months) (1). The sequence is calculated as:

\[
\frac{\text{Number of people with sequence A before B}}{\text{Number of people with sequence B before A}}
\]

The sequence ratio is adjusted for changes in market trends using a null sequence ratio (1).

**Advantages:** This is a rapid assessment of safety signals using only three data variables. It can be used to prioritize areas for further investigation. The method is a within-person design, thus not affected by confounders such as age, gender and comorbidities that do not change within the time period of analysis. The measure has been validated (2,3) and is complementary to signal detection methods using spontaneous reports (4).

**Limitations:** The measure uses a medicine indicator as a proxy for adverse events. This limits analyses to adverse events that are treated by medicines for which the medicine is specific to the adverse events (e.g. antidiarrhoeals as an indicator of diarrhoea). A key assumption of the method is that the adverse event must be independent of exposure. If the presence of the adverse event could influence subsequent exposure, the measure is confounded.

**Data sources:** Patient-level dispensing data. Variables required are patient identifier, medicine identifier and date of supply.

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**Example**

The example below shows prescription symmetry output for the association between amiodarone and thyroxine. Amiodarone-induced hypothyroidism is a well-known adverse event and has been reported to occur early in the course of therapy (5). Thus, we may expect to see an increase in thyroxine dispensing after starting amiodarone in persons where this adverse event occurs. The temporal pattern can be seen in Fig. A2.1, which shows many more persons starting thyroxine after amiodarone than starting thyroxine before amiodarone. The adjusted sequence ratio shows there is more than a three-fold increased risk of receiving thyroxine after amiodarone than before amiodarone (adjusted sequence ratio = 3.22, 95% confidence intervals 2.9–4.1).
Methods to analyse medicine utilization and expenditure to support pharmaceutical policy implementation

**Fig. A2.1 | Prescription sequence symmetry analysis of the use of thyroxine and amiodarone**

Adjusting sequence ratio = 3.44 (95% CI 2.9–4.1)

Counts of persons

Source: Calculated from data supplied by the Australian Government Department of Veterans’ Affairs.

**REFERENCES**


