Review Article

Drug Utilization Studies – An Overview

Shalini S¹²*, Ravichandran V¹, Mohanty BK³, Dhanaraj SK¹ and Saraswathi R²⁴
¹Faculty of Pharmacy, AIMST University, Semeling, Malaysia.
²Department of Pharmacy, Karpagam University, Coimbatore, India.
³Faculty of Medicine, AIMST University, Semeling, Malaysia.
⁴AlShifa College of Pharmacy, Perinthalmanna, India.

ABSTRACT: Aspire of the Drug Utilization Studies (DUS) is to appraise factors related to the prescribing, dispensing, administering and taking of medication, and it’s associated. Since the middle of twentieth century, interest in DUS has been escalating, first for market-only purposes, then for appraising the quality of medical prescription and comparing patterns of use of specific drugs. The scope of DUS is to evaluate the current state and future trends of drug usage, to estimate roughly disease pervasiveness, drug expenditures, aptness of prescriptions and adherence to evidence-based recommendations. The increasing magnitude of DUS as a valuable investigation resource in pharmacoepidemiology has been bridging it with other health allied areas, such as public health, rational use of drug, evidence based drug use, pharmacovigilance, pharmacoconomics, eco-pharmacovigilance and pharmacogenetics.

KEYWORDS: Drug utilization studies; drug utilization evaluation; epidemiology; pharmacoepidemiology; drug utilization research

Introduction

Nowadays drug utilization studies (DUS) are used as potential tool in the evaluation of healthcare systems. Drug utilization studies are powerful exploratory tools to ascertain the role of drugs in society. They create a sound sociomedical and health economic basis for healthcare decision making (Baksaas and Lunde, 1986; Nehru et al., 2005). DUS is defined as “the marketing, distribution, prescription and use of drugs in a society, with special emphasis on the resulting medical, social and economic consequences” (WHO expert committee, 1977). Drug utilization becomes, as such, essential for elderly care, although, the incorrect use of medicines is one of the greatest problems experienced by this population (Loyola et al., 2005; Romano-Lieber et al., 2002). The elderly often use more than one drug, which may lead to drug interactions, adverse effects, concomitant use of other therapies and drug redundancy, and the use of drugs without therapeutic value. These events are, for the most part, related to pharmacodynamic and pharmacokinetic changes that occur at this age (Braga et al., 2004; Brekke et al., 2006). It is important to realize that inappropriate use of drugs represent a potential hazard to the patients and an unnecessary expense (Hawkey et al., 1990). This necessitates a periodic review of pattern of drug utilization to ensure safe and effective treatment.

Drugs play an important role in improving human health and promoting well-being. However, to produce the desired effect, they have to be safe and efficacious and have to be used rationally. Drug use is a complex process. Optimal benefits of drug therapy in patient care may not be achieved because of under use, overuse or misuse of drugs. In any country, a large number of sociocultural factors contribute to the way drugs are used. Illiteracy, poverty, use of multiple healthcare systems, drug advertising and promotion, sale of prescription drugs without prescription, unbiased drug information are some of the sociocultural factors (Sathvik, 2004). Pattern of use can explain the extent and profiles of drug use and its trend, quality of use audits, comparing the use of drugs with national, regional and local guidelines or formularies.

The boost in the marketing of new drugs, wide variations in the pattern of drug prescribing and consumption, growing concern about the delayed adverse effects, increasing concerns regarding the cost of drugs and volume of prescription, all contribute to the increasing importance of DUS. Studies on drug utilization focus on the factors related to prescribing, dispensing, administering of medication, its beneficial or adverse effects etc (Lunde and Baksaas, 1988; Strom and Stephen, 2005; Costa et al., 2001).

*For correspondence: S. Shalini,
E-mail: shalinam@rediffmail.com
In the United States drug utilization research has been primarily developed at an institutional level or as a part of local health programs (Strom and Stephen, 2005). European drug utilization studies have been developed to describe and compare the patterns of use of specific groups of drugs (Gama, 2008). It is important to understand the interrelationships of the different domains as there are number of terms which have come into use such as epidemiology, pharmacoepidemiology, pharmacosurveillance, pharmacovigilance (Sjoqvist and Brikett, 2003).

Epidemiology is “the study of the distribution and determinants of health-related states and events in the population”. Pharmacoepidemiology is the epidemiological method used to study the clinical use of drugs in populations and it is defined as “the study of the use and effects of drugs in large number of people (Strom and Stephen, 2005) with the purpose of supporting the rational and cost-effective use of drugs in the population thereby improving health outcomes” (Sjoqvist and Brikett, 2003). Pharmacosurveillance and pharmacovigilance are the terms used which refers to the monitoring of safety of drugs such as spontaneous adverse effect reporting systems, case-control and cohort studies.

Pharmacoepidemiology may be drug-oriented, with emphasis on safety and effectiveness of drugs or it may be utilization-oriented which aims to improve the quality of drug therapy through intervention. It describes the extent, nature and determinants of drug exposure. Thus drug utilization research becomes an essential part of pharmacoepidemiology. Drug utilization derives its importance in pharmacoepidemiology from the fact that it provides the methodological rigor for defining the data needed in pharmacoepidemiological research.

It initially focused on the safety of individual drugs and also includes the studies of beneficial effects of these drugs. As it assesses drug effects in large heterogeneous populations for longer periods (Strom and Stephen, 2005), it makes useful contribution towards knowledge on safety and effectiveness of drugs (Sjoqvist and Brikett, 2003).

**Scope of drug utilization studies**

Drug use evaluation (DUE) aims to understand how and why drugs are used so as to improve appropriate drug use and the health outcome (Sathvik, 2004). DUS can be aimed to analyze the present and the developmental trends of drug usage at various levels of the health care system, whether national, local or institutional. DUS may evaluate drug use at a population level, based on the demographic details (Gama, 2008). These studies are used to calculate the reported adverse drug reactions, to monitor the utilization of various categories of drugs, to monitor the regulatory activities. Drug utilization data may be used to produce crude estimates of disease prevalence, such as cardiovascular disease (Psaty et al., 2006), diabetes (Duarte-Ramos and Cabrita, 2006). Drug utilization data may be also used to plan drug importation, production, and distribution, and to estimate drug expenditures. They can document the extent of inappropriate prescribing of drugs activities (Gama, 2008). DUE helps the healthcare system to understand, interpret and improve prescription, administration and use of medications (Sathvik, 2004). DUS are particularly interesting if focused on the most frequently used and misused groups of therapeutic drugs, such as antibiotics, chemotherapeutic agents, or those that constitute important therapeutic innovations (Krivoy et al., 2007).

**Why is drug utilization research necessary?**

The aim is to facilitate the rational use of drugs in populations. In individual patients, the rational drug use implies the prescription of a well-documented drug in an optimal dose on right indication at an affordable price. It is important to realize that inappropriate use of drugs represent a potential hazard to the patients and an unnecessary expense (Hawkey et al., 1990). It is difficult to understand the rational use of drug without the knowledge on how drugs are being prescribed.

Drug utilization research contributes to rational drug use by describing the drug use pattern and interventions. This understands how drugs are being used by making estimates of number of patients exposed to drugs, describing and estimating to what extent the drugs are used at certain area, whether overused or underused, describing the pattern of drug use etc. It compares the observed patterns of drug use with current recommendations or guidelines. Feed back is provided to the prescribers based on the drug utilization data collected. Drug utilization research enables to assess whether interventions undertaken improves the drug use by monitoring and evaluating patterns of drug use (Sjoqvist and Brikett, 2003).

**Types of DUS** (WHO, 2003; Einarsson et al., 1999; Lee and Bergman, 2000)

DUS can be targeted towards any of the following links in the drug-use chain:

- the *systems and structures* surrounding drug use (e.g. how drugs are ordered, delivered and administered in a hospital or health care facility);
- the *processes* of drug use (e.g. what drugs are used and how they are used and does their use comply with the relevant criteria, guidelines or restrictions); and
- the *outcomes* of drug use (e.g. efficacy, adverse drug reactions and the use of resources such as drugs, laboratory tests, hospital beds or procedures).
Cross-sectional studies

Cross-sectional data provide a “snapshot” of drug use at a particular time. Such studies might be used for making comparisons with similar data collected over the same period in a different country, health facility or ward, and could be drug-based, problem-based, indication-based, prescriber-based or patient-based. Alternatively, a cross-sectional study can be carried out before and after an intervention. Studies can simply measure drug use, or can assess drug use in relation to guidelines or restrictions.

Longitudinal studies

Longitudinal data is required for the purpose of studying the trends of drug use which is often the interest of Public health authorities. Drug-based longitudinal data can be on total drug use as obtained through a claims database, or the data may be based on a statistically valid sample of pharmacies or medical practices. Longitudinal data are often obtained from repeated cross-sectional surveys i.e., IMS (Intercontinental Medical Statistics) and practice-based data are of this type. Data collection is continuous, but the practitioners surveyed, and therefore the patients are continually changing. Such data give information about overall trends, but not about prescribing trends for individual practitioners or practices.

Continuous longitudinal studies

In some cases continuous longitudinal data at the individual practitioner and patient level can be obtained. Claims databases are often able to follow individual patients using a unique (but anonymous) identifier. These data can provide information about concordance with treatment based on the period between prescriptions, co-prescribing, duration of treatment, and so on. As electronic prescribing becomes more common, databases are being developed to provide continuous longitudinal data comprising full medical and prescribing information at the individual patient level. Such databases are very powerful, and can address a range of issues including reasons for changes in therapy, adverse effects and health outcomes.

Types of drug use information

Types of information required depend on the problem being evaluated. These include information on overall drug use or use of drug groups, generic or specific products. Information about the patient, prescriber and the condition being treated will be required. To ensure whether drugs are used efficiently and economically, data on drug costs will be required. Types of information can be categorized as follows: (Sjoqvist and Brikett, 2003; WHO, 2003a).

(a) Drug based information

Detailed information is usually required to answer clinically important questions which may involve aggregation of drug use at various levels, and information on indications, doses and dosage regimens.

(b) Problem based information

The question must be addressed to know more about the problem that is being managed instead of knowing about the particular group of drugs used for any condition.

(c) Patient information

Demographics and other information about the patient will be useful for the studies. The age distribution has critical importance in some cases e.g., to know whether the drug is being used in an age group different from that in which clinical trials were performed. The co-morbidities of the patient group may be important in determining treatment choice and adverse effects. For example in the management of hypertension in asthma patients, beta blockers should be avoided.

(d) Prescriber information

The differences in the drug prescribing often lack rational explanations. This type of information helps to determine the prescribing behavior which is often helpful to understand how and why drugs are prescribed.

Drug utilization evaluation (DUE)

DUE is defined as an authorized, structured, ongoing review of physician prescribing, pharmacist dispensing and patient use of medication. DUE is an ongoing, systematic process designed to maintain the appropriate and effective use of drugs (Sathvik, 2004; Joint Commission, 1995). DUE programs play a key role in helping managed health care systems to understand, interpret, and improve the prescribing, administration, and use of medications. It involves a comprehensive review of patients’ prescription and medication data before, during, and after dispensing to ensure appropriate medication decision making and positive patient outcomes.

DUE studies ensures whether the drugs are used appropriately, safely, and effectively to improve patient health status (Palumbo and ober, 1995). DUE is typically classified into three different categories: prospective, concurrent and retrospective.

Prospective DUE

Prospective review involves evaluating a patient's planned drug therapy before a medication is dispensed. In this process the pharmacist can identify and resolve problems before the patient receives the medication. Pharmacists routinely perform prospective reviews by assessing a prescription medication's dosage and its directions and
reviewing patient information for possible drug interactions or duplicate therapy (APhA, 1995). A prospective study watches for outcomes, such as the development of a disease, during the study period and relates this to other factors such as suspected risk or protection factor(s).

Prospective DUE commonly addresses drug-disease contraindications, therapeutic interchange, generic substitution, incorrect drug dosage, inappropriate duration of drug treatment, drug-allergy interactions and clinical abuse/misuse. All efforts should be made to avoid sources of bias such as the loss of individuals to follow up during the study. Prospective studies usually have fewer potential sources of bias and confounding than retrospective studies.

**Concurrent DUE**

Concurrent review is performed during the course of treatment and involves the ongoing monitoring of drug therapy to ensure positive patient outcomes. It presents pharmacists with the opportunity to alert prescribers to potential problems and to intervene in areas such as drug-drug interactions, duplicate therapy, and excessive or insufficient dosing. This type of review allows therapy to be altered for a patient if necessary (APhA, 1995).

Concurrent DUE commonly addresses drug-drug interactions, excessive doses, high or low dosages, duplicate therapy, drug-disease interactions, over and under utilization, drug-age precautions, drug-gender precautions, and drug-pregnancy precautions.

**Retrospective DUE**

A retrospective DUE is the simplest to perform since drug therapy is reviewed after the patient has received the medication. A retrospective review may detect patterns in prescribing, dispensing, or administering drugs to prevent recurrence of inappropriate use or abuse and serves as a means for developing prospective standards and target interventions. In retrospective DUE, patient medical charts or computerized records are screened to determine whether the drug therapy met approved criteria and aids prescribers in improving care for their patients, individually and within groups of patients, such as those with diabetes, asthma, or high blood pressure (APhA, 1995).

Retrospective DUE commonly addresses the issues such as therapeutic appropriateness, over and under utilization, appropriate generic use, therapeutic duplication, drug-disease contraindications, drug-drug interactions, incorrect drug dosage, inappropriate duration of treatment, and clinical abuse/misuse.

Using DUE information, pharmacists can identify prescribing trends in patient populations and initiate action to improve drug therapy for groups of patients, as well as individuals. Although a retrospective design is usually discouraged when a prospective study is feasible, a retrospective study can serve a useful purpose as a pilot study that is completed in anticipation of a prospective study. There are 3 general types of retrospective study: case report, case series, and case-control study (Hess, 2004).

A case report is a report of one unusual and/or instructive case (eg, symptoms not previously observed with a given medical condition, or an unexpected or new combination of medical conditions in one case), whereas a case series is a report of multiple similar unusual or instructive cases. A retrospective case series can be used to study a disease that occurs infrequently or to generate a hypothesis that can be tested more rigorously in a prospective study.

A case-control study, although retrospective, is superior to a case series because of the presence of a control group. The degree of exposure to a possible risk factor is then compared between the two groups. The case-control study design assumes that

(i) cases differ from controls only in having the disease,

(ii) exposure should be equally distributed between cases and controls if the exposure does not cause the disease, and

(iii) greater exposure among cases would indicate that exposure increases the risk of the disease.

The exposure is determined retrospectively. Ideally, the data collectors are unaware of whether a subject is a case or a control, and the data collectors should be unaware of the study hypothesis. The cases and the controls must be assessed for exposure in the same way.

Most sources of error due to confounding and bias are more common in retrospective studies than in prospective studies. For this reason, retrospective investigations are often criticized. Special care should be taken to avoid sources of bias and confounding in retrospective studies.

**Sources of drug utilization data**

(Sjöqvist and Birkett, 2003; WHO, 2003a)

The drug-use chain includes the processes of drug acquisition, storage, distribution, prescribing, patient compliance and the review of outcome of treatment. Data is collected at national, regional or local level and may be derived from quantitative or qualitative studies.

Quantitative data may be obtained from collected data or from surveys and may be used to describe the present situation and the trends in prescribing and drug use at various levels of the health care system. Qualitative studies assess the appropriateness of drug utilization and generally link the data to reasons for prescribing i.e., indications.
Such studies are referred as Drug utilization evaluation or Drug utilization review. The process is a “therapeutic audit” based on defined criteria and is used to improve the quality of therapeutic care.

There is an increasing interest in economic impact of clinical care and medical technology. This has developed a discipline which is dedicated to study how pharmacotherapeutic methods influence resource utilization in health care termed as pharmacoeconomics.

The sources of drug utilization data vary from country to country. Data may be collected on drug sales, drug movement at various levels of drug distribution chain, medical billing data or samples of prescriptions. The information on sales available through pharmacy records is the measure most frequently used in drug utilization studies (Duarte-Ramos and Cabrita, 2006; Boethius and Wilman, 1977; Hartz et al., 2007). They provide detailed information on the drugs but data on the consumer is usually very limited. This could be improved if a patient is allowed to purchase drugs at only one designated pharmacy (Neutel and Walop, 2000).

Data obtained from health facilities may be used to measure the drug use and also to generate indicators that provide information on prescribing habits and aspects of health care. These indicators can determine the problems in drug use; provide mechanism for monitoring, and to motivate health care providers to follow the established standard health care guidelines. Prescription and dispensing data are useful to determine some of the quality indicators of drug use recommended by WHO which includes average number of drugs per prescription, percentage of drugs prescribed by generic name or trade name, percentage of antibiotic prescribed, percentage of injections prescribed, percentage of drugs prescribed from essential drug list, average drug cost per prescription, etc (Sjøqvist and Birkett, 2003).

Increase interest in efficient use of health care resources has resulted in the establishment of computer databases for studies on drug utilization. Some of the databases can generate statistics for patterns of drug utilization and adverse drug reactions. The databases may be international, national or local in scope (WHO, 2003a).

Databases currently available for drug utilization studies may be classified as diagnosis-linked or non-diagnosis-linked. Diagnosis-linked data enable drug use to be analyzed according to patient demographics, therapeutic groups, disease or conditions, indications and outcomes (Gama, 2008; WHO, 2003a). A useful analysis requires an understanding of the sources and organization of the data. Databases available currently lack information on morbidity and are used in descriptive studies of patterns of drug consumption (Gama, 2008).

Drug regulatory agencies have the legal responsibility to ensure the availability of safe, efficacious and good-quality drugs in the country. Regulatory agencies also have inspection and enforcement functions and are responsible for supervising the import of drugs and drug registration. It is possible to obtain data on the number of drugs registered in a country from such agencies (WHO, 2003b).

Data may be also obtained from drug importers, wholesalers, or local manufacturers. Data from these sources can generally be used to describe total quantities of specific drugs or drug groups, origins of supplies and type, i.e., branded or generic. In the absence of data on drug production or importation, wholesalers become an important source of information on drug acquisition.

It is very difficult to obtain true estimates if documentation is incomplete and not all transactions are recorded. It is very difficult to collect comprehensive data from these sources even if there are regulatory requirements about submitting reports in some countries where medical, dental and veterinary practitioners, as well as pharmacists, can import pharmaceutical products.

**Instruments for data collection on drug utilization**

Patient files and computer registries are widely used for collecting information on drug utilization. Home inventories, in which interviewer visits the home of the respondent are also used and considered as best method of obtaining accurate and complete data (Psaty et al., 1992; Johnson and Vollmer, 1991; Lau et al., 1997). Questionnaires, one of the easiest tools for data collection are most widely used in population surveys. In several studies questionnaire information was compared with pharmacy records (Van den Brandt et al., 1991; West et al., 1995) which is a reliable source of drug exposure, with an acceptable degree of agreement (Neutel and Walop, 2000; Johnson and Vollmer, 1991; Klungel et al., 1999; Klungel et al., 2000; Sjahid et al., 1998). Carefully constructed questionnaires can subject to recall bias due to its characteristics, and noncompliance can also influence the reliability, despite being accurate (Goodman et al., 1990). Drug utilization data collected through questionnaires is commonly used in epidemiological studies. Variations in questionnaire structure may affect recall. Therefore, it must be carefully designed, and the characteristics of the questionnaires used to obtain information on medicines need to be taken into account in the interpretation of results from studies quantifying drug utilization by self-report.

WHO specifies drug use indicators (WHO, 1993; Sutharson et al., 2003) for adoption in drug utilization studies. These indicators help us to know the shortcomings in prescription writing and allow improving the performance periodically.
Core indicators

(i) Prescribing indicators
   (a) Average number of drugs per encounter
   (b) Percentage of drugs prescribed by generic name
   (c) Percentage of encounters with an antibiotic prescribed.
   (d) Percentage of encounters with an injection prescribed
   (e) Percentage of drugs prescribed from essential drug list

(ii) Patient Care Indicators
   (a) Average consultation time
   (b) Average dispensing time
   (c) Percentage of drugs actually dispensed
   (d) Patients' knowledge of correct dosage

(iii) Facility indicators
   (a) Availability of copy of EDL: By stating yes (or) no.
   (b) Availability of key drugs

Complementary indicators
   (a) Percentage of patients treated without drugs
   (b) Average drug cost per encounter
   (c) Percentage of drug costs spent on injection

Factors That May Affect Drug Expenditure and Utilization (WHO, 1993)

Changes in total drug expenditure are affected by changes in drug prices and changes in drug utilization. Consumption of larger quantities of drugs can result in increased expenditure even if prices go down. Similarly, shifts in prescribing practices from older and often less expensive drug therapies to newer and often more expensive drug therapies result in increased costs. Numerous factors, many of which are interrelated, may affect drug expenditure, drug utilization, and ultimately health outcomes. These factors present important challenges for the development of indicators to monitor trends and results that affect not only the performance of the health care system, but also the health of the population. Some of the factors that may affect drug expenditure and utilization are prices, entry of new drug chemicals and volume of drug use.

Population related factors include changes in total population, changes in population demographics such (age, gender and ethnicity), changes in health status of a population (emergence of new disease, epidemics) and so on. System related factors include changes and transition associated with health system reform and restructuring (move towards shorter hospital stays and home/community care, shift of drug provision from hospital to community), changes in policies and programs [The extent of formulary listings, eligibility and co-payments, availability of third party (insurance coverage)].

Research and technology-related (clinical and informational) includes new treatment approaches (drugs replacing surgery, availability of more and/or improved diagnostic technology, evidence-based preventive or curative approaches in diagnosis or treatment), use of programs and technology in monitoring patients.

Pharmaceutical industry includes development of new drug products (e.g., new strengths, new drug forms and presentations), promotion of drugs to physicians, drug sampling, direct to consumer advertising.

Practice and people-related (health care providers and consumers) includes changes in prescribing and dispensing practices, number and mix of prescribers (specialists, general practitioners, nurse practitioners and others), multiple doctoring, consumers’ expectations and behavior and wastage.

Conclusion

Drug utilization derives its importance in pharmacoepidemiology from the fact that it provides the methodological rigor for defining the denominator data needed in pharmacoepidemiological research (Serradell et al., 1987). The study of drug utilization is an evolving field. The use of computerized databases that links drug utilization to diagnosis, although subject to some inherent limitation, is contributing to expansion of this area of study. DUS increases its importance in pharmacoepidemiology by bridging more closely with other areas such as public health, rational use of drugs, evidence based drug use, pharmacovigilance, pharmacoecnomics, eco pharmacovigilance and pharmacogenetics.

References


