



DRUG UTILIZATION RESEARCH: NEED OF THE HOUR

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ABSTRACT

Drug utilization studies involves the whole process starting from the prescriptions to the dispensing of drugs, to the administering of the prescribed drugs in a patient and finally to study the after- effects of drugs. Drug Utilization Research is a highly neglected topic in India. The interest in drug utilization studies has been escalating. This concept may be extended from the moment a drug is manufactured till its final utilization or disposal. Earlier it was conducted only as a market research but now they are conducted as part of audit programs in some countries and for studying the quality of prescriptions and medications in this country. Here we discuss the understanding of drug utilization studies, its various types, and its importance in the society, the socio-cultural, medical and economic aspects of the research.

KEYWORDS: Drug utilization studies, Drug utilization review, incremental cost- effectiveness ratio, pharmacoconomics, qualitative drug utilization study, quantitative drug utilization study, quality-adjusted life year.



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INTRODUCTION

In today's profit-oriented world, it has become essential to evaluate the healthcare systems to ensure that they focus more on providing better healthcare to patients than making money. Drug Utilization Research is a highly neglected topic. Drug utilization study (DUS) is one such tool to evaluate the healthcare systems and to ascertain the role of drugs. The WHO expert committee described the DUS as "the marketing, distribution, prescription and use of drugs in a society, with special emphasis on the resulting medical, social and economic consequences"¹. The most important medical consequence is that the problem faced by people mainly the elderly, is the use of multiple drugs (polypharmacy); not only from allopathic system of medicine but also alternative systems (polypathy) like Ayurveda, Unani and Homeopathy. This may lead to unwanted drug interactions causing adverse reactions and subsequent use of other therapeutic drugs, which may not even be as effective. These reactions get prominent as various pharmacodynamic and pharmacokinetic changes occur as the age progresses^{2, 3, 4}.

Excessive prescriptions of non-essential drugs by licensed physicians is another issue, the monitoring of which isn't possible in everyday life and there aren't enough funds to audit all the prescriptions that are dispatched in India. Also side-effects caused by these non-essential drugs cannot be over-looked for the safety of the patients. Prescriptions of branded drugs instead of generic ones adds to the net cost of healthcare, even though the effects of both the type of drugs is similar. In India, patients don't tend to question the prescriptions, rather doctors are considered to be above all. Correspondingly, the pharmacists don't ask the patient about the need of the drugs and only follow the doctors' prescriptions. Therefore, it is important to realize that periodic inspections are required to ensure safety and efficacy of treatment towards the patient and avoiding the unnecessary adverse events. Therefore, the safety and efficacy of the drugs depend on the interaction between the patients, the physician with the drugs as demonstrated in the figure below (Figure 1).

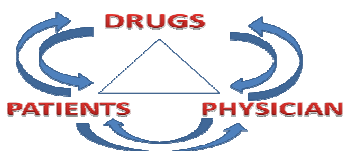


Figure 1
The triangle of drug safety and efficacy. Each component interacts with the other two to maintain the drug safety and efficacy.

To maximize benefits, drugs have to be used rationally, in order to promote human well-being. Socio-cultural factors also play a major role in the need for DUE (Drug Use Evaluation), especially in India. The over-use, misuse and under-use of prescribed drugs are very common. When the drugs are dispensed by the pharmacists, some patients might come back for more medicine when not required, some might not complete their set doses and some might keep it for similar illnesses in the future. Illiteracy and ignorance in rural populations and some classes of people in the urban sectors lead to the misuse of drugs in a

large way. Taking medical advice from people who are not licensed physicians also plays a role. Poverty causes people to ignore physician's medical advice and not follow the course of doses, as it becomes more expensive to complete the treatment. The use of multiple healthcare systems causes prescriptions of similar generic drugs under different brand names by different physicians thus, leading to confusion among patients. Promotions and advertisements of drugs on national television and sale of prescription drugs without prescriptions are some socio-cultural factors worth mentioning⁵. The

growing interest in DUE is because of the increase in the cost of new drugs that are being introduced in the market, the variations in the drug prescription patterns, marketing of new drugs without knowing its side-effects, polypharmacy (multiple drugs in a single prescription) and the use of FDCs (Fixed dose combinations)^{6, 7, 8}. Different countries have got a different approach towards drug utilization research (DUR), for example, United States have developed DUR at an institutional level as part of health programs⁷. In European countries, use of specific groups of drugs is compared⁸. In a large population, the study of the use and effects of drugs using epidemiological methods is termed as pharmacoepidemiology⁷. Monitoring of the safety of drugs by adverse event reporting system is carried out by pharmacosurveillance and pharmacovigilance^{9, 10}. Sjoqvist and Brikett, 2003¹⁰, added the purpose of rational and cost-effective use of drugs to improve the health outcomes into this definition. Studies such as case-control and cohort studies are included in the system. Pharmacovigilance involves the safety and efficacy of the drugs and also to improve the overall quality of the drug therapy. DUR is an essential part of pharmacoepidemiology, as the latter derives its crude data and methodologies from DUR for research⁶. Previously, DUR was only about accessing the safety and use of individual drugs in the society; however, now it is making contributions to modern knowledge of different drugs used in the society today¹⁰. The extent of rational or irrational drug use can only be determined by observing its pattern of use, by performing regular audits and comparing the local drug use at a national and international level. This will be great pointer to determine our standing.

Importance of Drug Utilization Research

The most important point here is to promote rational use of drugs. It encourages the doctors to prescribe a legal drug at an optimal dose and affordable price. Because the inappropriate use of drugs could pose a dangerous threat to the life of the patient^{11, 12}. Understanding and applying rational drug use is difficult and hence it is important to rely on DUS. Drug utilization research contributes to

the knowledge of the way drugs are used in the society; whether the drug is being prescribed correctly, whether the drug is been taken in right amount of dosages and not misused, whether the drug is available at an affordable price or not. DUS compares the current trends of drug use to the recommendations provided by the WHO. The most important outcome of a DUS is that it provides with valuable feedback about the prescriptions to the doctors. It also assesses whether a particular intervention affects the drug use in the population by examining the drug use pattern¹⁰.

The main objectives of drug utilization research are identification of the problems in medicine use, analysis of the problem, analysis of the consequences of such problem. These objectives differ with different groups of people, as they want different alternatives⁷. For example, health authorities want the DUR to be differently analyzed in a way that would support the understanding of the drugs for common people. However, the drug manufacturers would want the DUR analysis to shed some light on the economics of drug use. Other groups of professionals include clinical professionals, social scientists, academicians, media and finally we; the consumers. DUR programs allow comparing of two different health providers by comparing their approach to treating a particular disease. These comparisons are instrumental in bringing about a change in the prescription habits of the physicians and thus, improve healthcare in the process. Data obtained from the DUR studies could also help in developing educational programs or seminars or symposiums required at healthcare institutes to educate the staff about the advantages and disadvantages of the rational use of drugs and healthy prescription habits.

Types of Drug Utilization Studies/ Drug Utilization Reviews

Drug utilization studies can be of two types: Qualitative and Quantitative.

Qualitative & Quantitative DUR/ DUS

Drug utilization studies can either be *qualitative* or *quantitative*. In the *quantitative* study of the DUR/DUS, the purpose of the

study is to use quantification of the present trends of drug use at different levels of our healthcare system and also to quantify it against the time duration of the use. Drug statistics that come out from time to time are a result of quantitative DUR. This quantified statistical data can be used to calculate the amount of drug utilization by age, gender and social status of people and used to investigate the under- and over-use of drugs in certain areas than other. This quantified data can also be used as a denominator in calculating the rates of adverse drug reactions that have been reported and also to monitor the use of restricted drugs (for eg., narcotic pain-killers, sedatives and psychotropic drugs), to observe the international or national formularies for any changes in the listing of drugs, as markers for monitoring the disease prevalence in the community. Lastly, it decides an action-plan for the importation, production, distribution of drugs and to calculate the total expenditure on drugs. *Qualitative* DUR/DUS, on the other hand, analyzes the need for the suitability of drug utilization research. For example, does the drug utilization in a particular case justify the drug prescription in that case? Appropriateness of drug utilization is an added concept in the qualitative DUR. Criteria for drug utilization could be based on the daily dose, indications for use and the duration of a course of therapy. Another major criterion for failure of drug prescription is the prescription of wrong drugs even when safer alternatives are available in the market. There is something called as DUR programs, which has to be clearly distinguished from DUR studies. DUR studies are not conducted routinely, and are performed only once to find out the hidden problems with drug prescriptions and utilization in the society. Very little feedback is produced as a result of the DUR studies⁷. Different study methods, with respect to time, are also employed in DUR studies. They are generally observational research methods:

- *Cross-sectional*: where the use of drugs is studied at a single point in time. The use of drugs is also examined before and after intervention to improve prescriptions in large hospitals^{12, 13}. Some researchers performed a cross-sectional study at the

paediatric unit of a university hospital to determine the extent of the use of unlicensed and off-label drugs in children under the age of 14 years. Prescriptions were analysed to see the class of drugs that were mostly prescribed from November 2007 to January 2008. A higher number of unlicensed drugs were found in the prescriptions¹⁴.

- *Prospective*: A prospective DUS (pDUS) examines a patient's drug therapy before he/she has received the medication. This process allows the pharmacist to identify and rectify any issues impending to the medication relating to the standard of care of the patient. Pharmacists practice this daily routine to study drug interactions and side-effects before dispensing drugs to a patient. Prospective drug review takes care of the following issues: Drug interactions, Substituted generic drugs, incorrect dosages of the prescribed drugs, Duration of the drug treatment, Allergic reactions owing to the prescribed drug, Misuse or overuse of drugs, Excessive prescribing of the same drug. An example of this type of DUR can be demonstrated in a study conducted in 1996, where, a medical ward and surgical ward at a children's hospital were prospectively followed for 13 weeks to observe the pattern of unlicensed or off-label drug prescriptions in child healthcare. It was found that around 25% of the prescription drugs were unlicensed¹⁵.
- *Retrospective*: Retrospective DUS (rDUS) examines the drug therapy after the patient has received it. The rDUS can identify patterns in prescriptions and drug dispensing and can prevent the overuse and abuse of certain drugs. It scrutinizes the prescriptions and compares it with patient medical records to see if the drugs worked. This helps to improve the prescriptions further and hence, improving patient care. The rDUS addresses the following issues^{16, 17, 18, 19}: Drug-drug interactions, Overuse and misuse of drugs, Appropriateness of the drug prescriptions for a particular disease, Duplication of drug therapy, Prescribed dosages and its duration. A retrospective analysis was conducted on the case records of patients

who had received anti-depressants at the psychiatric OPD of a tertiary care hospital from January 2006 to December 2006. The types of anti-depressant prescribed were also noted along with the rationality in prescriptions of drugs²⁰.

- **Concurrent:** Concurrent DUS (cDUS) is carried out during the treatment of the patient. This study monitors patient outcomes because of the drug therapy being administered to him/her. This type of study is also referred to as case management. Similar to the pDUS, the pharmacists can inform the clinicians about any adverse events arising because of the prescribed drug use as the patient here is closely monitored. cDUS not only checks for adverse events, it also alerts about the proper utilization and dosing of the prescribed drug. This allows for changes or alterations in the patients therapy. These studies usually take place at larger institutions, where the 'wait and watch' principle can be followed. The issues that are addressed by cDUS are: Drug-drug interactions, Amount of dosage, under or over use of drugs, Age, gender and pregnancy precautions^{13, 16, 17, 18}. In a study in 2006, 300 randomly selected groups of patients were followed to observe their case files and the treatment regimes. Results of tests performed for diagnoses and adverse drug reactions, if any, were also taken into account. This study was a concurrent and qualitative drug utilization study as the patients were followed from the time of admission to the time of discharge²¹.

CONSEQUENCES OF DRUG UTILIZATION

According to the WHO definition of drug utilization research, there are social, economic and medical consequences related to the DUR. They are discussed as following:

Socio-cultural factors²²

Social and cultural factors play a major role, as they might be responsible for the patient's behavior towards the acceptance and use of certain drugs because of the impact of the society. Cultural factors involve people's perceptions towards the available drugs in the

market and how they can be used. Patients' response towards placebo effect is a good example, as the effect is influenced by the surroundings and the society in which the placebo is administered.

Self-medication is a major socio-cultural factor and thus, a perceived threat to the society. Self-medication is used in the cases where medical help is not available or unaffordable. It is used when the illness is not serious enough to seek doctor's help. The only reason people choose self-medication is because it has helped them in the past and that they might think that the doctor's prescriptions are not helping them in the recovering of their illness. Another possible reason could also be that they have kept record of their previous prescriptions and this time they want to save on the doctor's bill by self-medicating on the same illness.

Prescriptions also play a socio-cultural role in a patient's medical care. Prescriptions are made by a doctor and thus, the doctor is an important determinant in the type of drugs being used and circulated in the market. Drug utilization research, these days' focuses mainly on the doctor's prescriptions and its effects on use of drugs and in-turn the society. Our society and education system has always taught us the importance of doctors' and therefore, we never question the ability of the doctor to provide us with prescriptions of drugs that will cure our illnesses. The power of a pharmaceutical company can also influence the drugs prescriptions. Besides these, there are other factors influencing the prescriptions such as Government regulations on drugs, the results of pharma industries in certain drug trials and the demands of people suffering from certain diseases.

Another social issue arising is the patient non-compliance after the drug has been dispensed. Patient compliance comes under both medical and social aspect of drug use. Non-compliance is prominent in cases where there is prolonged drug therapy, where drug side-effects are unbearable. To improve patient compliance, physician's role is very important. He has to gain the patient's confidence, communication has to be good. Since the prescriptions are a physician's decisions, compliance is a patient's decision

and he/she will comply to the prescriptions only when they understand the advantages and disadvantages. Cultural studies have been performed more in under-developed countries than in the developed ones. A study performed on Turkish women showed that they believe that any disease could be cured with the right medicines. Some of them even think that traditional medicines might be more effective than the medicines available in the modern market. Cultural views differ markedly when it comes to treatment options²³. In another study, Germans were found to believe that low blood pressure should be treated with medicines, whereas, Anglo-Saxons thought that it was unnecessary treatment and was not required²⁴. Cultural factors also determine the perception towards drug induced conditions.

The influence of the healthcare system is prominent as they make the necessary drugs available in the market. The doctor can hence prescribe the drugs required by the

patients. Figure 2 describes the healthcare system and the role of the components in the drug use system. Firstly, the pharmaceutical companies that manufacture the medicines or drugs for use in certain diseased conditions. Secondly, the health authorities regulate/authorize the use, trade and distribution of drugs in the market. They also provide independent information about the drug when the drug is marketed. After which, it comes back to the pharmaceutical companies, who market their drugs with the help of various marketing strategies. Once the marketing is complete, the pharmaceutical companies provide the drugs to the wholesale companies who distribute it to various pharmacies and make the physicians well aware of it. The physicians prescribe these available drugs and the pharmacists dispense them to the patients. Finally, the patients take home these medicines and compliance or non-compliance follows.

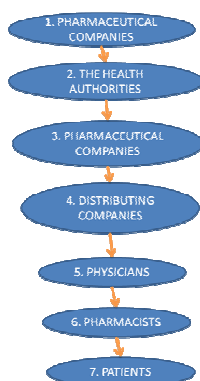


Figure 2

The healthcare system. Position of each individual entity is important for the cascade.

Medical aspects²²

Once the drugs are prescribed, dispensed and consumed, what happens next? Does the patient feel better? Is he completely cured before the course is over? Is he suffering from any side-effects? Does he seek medical attention for the management of the side-effects? All these factors comprise the medical aspects of drug utilization, along with polypharmacy and polypathy. Some diseases don't get easily affected by the drug treatment. In that case, there is nothing to be done medically, but to observe what effects that drug might have on the natural course of the

disease by the medical doctor. Patient compliance is also an important medical aspect here. Knowing how much drug has been consumed from the quantity prescribed is important. Did the patient finish his course of treatment; the prescribed medicines could get passed to someone else, even though they were not meant for them in the first place. These are some of the medical aspects in DUR. Drug utilization review could also enable physicians to compare and discuss their data with the peers, in order to improve their prescriptions for conditions in the future.

Pharmacoeconomics (economic aspects)¹⁷

Pharmacoeconomics involves the economic aspects of drug utilization. Money spent on drugs is worth mentioning because it uses a substantial part of the total healthcare costs. About 30-40% of healthcare costs in developing countries and about 10-15% of healthcare costs in developed countries. Pharmacoeconomics include the cost-minimization, cost-effectiveness, cost-benefits and cost-utility of the drugs in question.

- **Cost-minimization analysis:** This analysis calculates the drug costs to determine the least costly drug or the therapeutic modality. It focuses on the preparation and administration of doses. This method is a powerful tool for the comparison of the generic or therapeutic equivalent drugs. However, between two in-equivalent products, this method of analysis cannot be used. An effective approach would be to determine the relative prices of these two products based on their prescribed daily doses (PDDs).
- **Cost-effective analysis:** This method of analysis involves determining of cost (in monetary value), as well as the effectiveness of the drug in question. The effectiveness is generally measured by the clinical outcomes, for example the number of patients getting cured after using the drug. Determining the cost-effectiveness of a drug requires the weighing of the extra health benefit provided by the drug against the extra cost of that drug. This comparison is called the incremental cost-effectiveness ratio (ICER), which can be defined as the net incremental cost of the incremental health benefit of the drug over another drug.
- **Cost-utility analysis:** This analysis is used to determine the cost of utilities such as the quantity and quality. As this type of analysis assigns a value to the quantity and quality of life, it is often considered as controversial. It compares two drugs which have different outcomes, i.e. difference in their benefits. The ICER in this case is the incremental cost of gaining an additional quality-adjusted life year (QALY). This type integrates both, the increase in the survival

time and the changes and the quality of life, either with or without the increase in the survival time. The quality of life is expressed in the utility value on a scale of 0 (being dead) to 1 (best quality of life). Thus, an increase in one year of life (without affecting the quality of life) or an increase in the quality of life from 0.5 to 0.7 utility units for 5 years would result in a gain of 1 QALY.

- **Cost-benefit analysis:** This type of analysis involves direct calculation of the net expenditure to achieve a healthy outcome, thus classifying the costs and health outcomes in monetary terms. Similar to the cost-utility analysis, this type remains controversial as well, because of this categorization of health care outcomes and quality of life in monetary terms. Thus, it is not widely used for pharmacoeconomics purposes. Here, the willingness of patients to pay for a better quality of life is assessed.

Scope and Future of Drug Utilization Research

Drug use evaluation defines why drugs are being used and how are they used to make an improvement in the health outcome⁵. As discussed earlier, DUS is used to study the current and future trends in the healthcare system at local, national and international level. Gama, 2008⁹ demonstrated how DUS can evaluate drug use at the population level based on its demographic details. Studies like these monitor adverse drug reactions (ADRs) and report them. Disease prevalence could also be predicted by DUR data, like cardiovascular disease²⁵, and diabetes^{26, 27}. The production, distribution, expenditures and the import-export of a drug can also be deduced from the drug utilization data. Monitoring prescriptions is another use of the DUR data⁹. Currently, an increasing number of scientists are interested in applying DUS to misused drugs such as antibiotics, chemotherapeutic drugs or newer drugs to find out more about our healthcare system²⁸. Increased use of computers for the analysis of drug utilization is taking the horizons to a new level. Drug utilization reviews have a greater scope in areas such as pharmacovigilance,

pharmacoeconomics, public health and pharmacoepidemiology^{9, 13}.

Drug utilization studies are a constant quality improvement process where they:

- Assess the drug use and the prescription patterns⁵
- Work on developing a standard that describes the drug use
- Advices clinicians on prescription issues
- Promote better education about diseases, drugs and their use¹⁸
- They encourage better use of drugs and help understand the ill-effects of drug abuse and overuse^{7, 29, 30, 31}.

Thus, the DUE helps the healthcare system to promote application of the appropriate and rational use of medical drugs by the medical staff including doctors, nurses and pharmacists. It also promotes patients to ask more questions, when in doubt, to improve their understanding of the topic. The most important thing it can help with is to rationalize the allocation of the budget of a particular hospital⁵.

CONCLUSION

Drug utilization research has gained a lot of importance after the twenty-first century. They can be employed for many purposes like market research to identify the need for certain drugs required to treat a particular disease. However, the need of the hour is far different from back then. The quality of drug prescriptions has been compromised for monetary gains in recent years. Online databases have been made available to find a connection between drug utilization to the diagnosis of a disease. Pharmacoepidemiology is an important field which derives its importance from DUR studies that can shed some light on public health, pharmacoeconomics, pharmacovigilance, rational use of drugs and finally pharmacogenetics. Further, the concept may be extended from the moment a drug is manufactured till its final utilization or disposal i.e. from womb-to-tomb. Drug utilization research should involve studies pertaining to the entire life of a drug in order to improve drug utilization.

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