Review Article

# Pharmacoepidemiology: An Overview on Methods and Effects

**Ankur Rohilla[1]*, Priyanka[1], Pooja[1], Akshma Singh[1], Amarjeet Dahiya[1] and Gurfateh Singh[2]**

[1]Department of Pharmaceutical Sciences, Shri Gopi Chand Group of Institutions, Baghpat, Uttar Pradesh, India
[2]Sachdeva College of Pharmacy, Gharuan, Kharar, Mohali, Punjab, India

**ABSTRACT**
Pharmacoepidemiology (PCE) is the study of the use of and the effects of drugs in large numbers of people. Moreover, the PCE can be referred to as the transparent application of epidemiological methods through pharmacological treatment of conditions in order to understand the conditions to be treated. The PCE research has evolved as an important discipline that analyzes information on adverse drug events, drug utilization patterns, drug efficacy, and post-marketing surveillance research. In addition, the PCE includes the application of principles of epidemiology to the study of drug use and outcomes in large populations; providing an estimate of the probability of beneficial effects in populations; the probability of adverse effects in populations; and other parameters which relates to use of drugs alongwith methods for continual monitoring for unwanted effects and other safety-related aspects of drugs. The present review highlights about various methodologies and effects possessed by of PCE.

**Keywords:** Pharmacoepidemiology, Epidemiology, Adverse Drug Events.

## INTRODUCTION

Pharmacoepidemiology (PCE) can be defined as the study of use and effects of drugs in large groups of general population.[1-2] PCE was first described in the year 1984, when it was proposed that a new discipline was necessary in order to integrate epidemiology and drug-related events. PCE has been considered to make use of both pharmacology and epidemiology, and, hence PCE acts as a bridge between pharmacology and epidemiology.[3-4] It has been widely accepted that pharmacology is the study of the effect of drugs and clinical pharmacology is the study of effect of drugs on man, whereas, epidemiology is the study of the distribution and resulting determinants of diseases on populations. Further, the epidemiological studies can be divided into descriptive epidemiology, which describes the incidence and prevalence of diseases; and analytic epidemiology, which includes observational studies like case-control and cohort studies, and experimental studies which include clinical trials or randomized clinical trials.[5-6] Furthermore, the PCE benefits from the methodology developed in general epidemiology and develop them for applications of methodology unique to needs of PCE.[6] Moreover, PCE supports the optimal use of medications and helps clinicians make better-informed drug therapy decisions, which can be evidenced from the recent withdrawals of marketed medications due to adverse events. Additionally, PCE provides valuable information about clinical and economical outcomes of drugs and biologics, especially after their permission for clinical use.[7] PCE has been reported to possess a number of roles in various areas like data supplementation in premarketing studies; quantitation of the incidence of drug effects; discovery of undetected drug effects; analysis of cost-effectiveness of drugs; drug utilization patterns and adherence profiles; assessment of effects of drug overdoses and reassurance of drug safety; and the association between medication use and outcomes.[7-8] However, the pharmacy professionals possess an important role in

conducting the pharmacoepidemiological studies due to their capability of understanding and utilizing the fundamental pharmacoepidemiological concepts and methods in their routine practice.[9-10] This contention is supported by the fact that the patients and health care providers rely on pharmacists to appropriately evaluate the benefits and risks of drug therapy, and, hence indicates a need for PCE training and education for general public. This review article discusses about the aims of objectives of conducting PCE studies. Moreover, various methodologies adopted for conducting PCE studies have been discussed in the present review.

## AIMS AND OBJECTIVES OF PHARMACOEPIDEMIOLOGY

It has been documented that PCE analyzes information on adverse drug events, drug utilization patterns, drug efficacy, and post-marketing surveillance [4]. PCE has been noted to own various aims which include determining the distribution of disease; examining the determinants of a disease; and judging whether a given exposure causes or prevents disease possess.[7] However, the PCE is primarily essential for evaluating the drugs safety and effectiveness to give active treatment, but other objectives of PCE have also been documented which involve, the measurement of population-based benefits and risks of drug use; assessment of the benefit-risk ratio; analysis of prescribing of drugs and its determining factors; and the implementation of PCE knowledge into action.[11] In addition, analyzing the people's actual use of drugs and its determinants; describing and analysing the economics of drug use; and advising the decision-makers over the drug use, accounts for other potent objectives of PCE. Moreover, PCE can play an important and useful role for helping to find out the advantages, benefits and risk factors, health care system, high profile withdrawing of drugs for safety reason followed by the principles and major warnings for drugs existing in the market.[8-12]

## METHODOLOGY OF PHARMACOEPIDEMIOLOGY

It has been widely accepted that various methods are used to study health events associated with drug exposures. The usual approach to studying adverse reactions begins with the collection of spontaneous reports of drug-related morbidity or mortality. However, it has been a comprehensive topic of debate that a large number of study designs and methods are required in order to generate data on the uses and risks of newer and older drugs. The types of study designs used in PCE can be classified as experimental studies including clinical trials or randomized clinical trials; and observational studies including case-control and cohort studies.[5-6] The experimental studies have been frequently used to measure the importance and consequence of the alteration of a strategy or policy. The experimental studies have been noted to employ control in the assignment of individuals to exposure groups, usually through random assignment of individuals to the exposure under investigation, and then follow-up of individuals in order to detect the effects of drug exposure.[13-14] On the other hand, observational epidemiologic study designs, like case-control, cohort, and cross-sectional studies, are used extensively. In addition, large automated databases, meta-analysis, randomized controlled trials, and hybrid designs have also been documented to play an important role in PCE.[15-16] However, it ahs been noted that epidemiologic studies do not use randomization in order to determine who will receive a particular drug exposure, but the associations between exposures and diseases are determined by the use of observational study designs and statistical analysis. The observational methods are used in most situations due to the limitations in the use of experimentation because of ethics and cost.[16-17] However, the observational studies have been proven to be quicker and less costly than experimental studies, but they have been noted to possess various disadvantages like confounding by indication, which occurs when the subjects treated with the medication of interest

differ from the nontreated group on a characteristics associated with the outcome.[5-6] Currently, there is growing interest in using computerized databases containing medical care information for conducting the PCE studies. In addition, various multipurpose databases have been used for PCE studies, which include data from managed care organizations, the Medicaid program, the Medicare program, and geographically defined populations.[18-20] Such databases have been noted to possess information on patient demographics, outpatient drugs, hospital discharge diagnoses, and ambulatory care encounters.

**EFFECTS OF PHARMACOEPIDEMIOLOGY**

The effects of PCE studies can be studied as the adverse drug effects and beneficial drug effects. The adverse drug effects are based on the pharmacologic studies of the drugs, which further involve the effects like type A (Augmented) effect and type B (Bizzare) effects, whereas, the beneficial drug effect have been documented to involve unintended effects and intended effects possessed by the drug.[6,11] According to WHO, an adverse drug reaction is that reaction in which the undesirable, unwanted, unintended, harmful and pernicious effects of any drug is produced at the dose which is used in humans for treatment, diagnosis or therapy.[21-22] The probability of the occurrence of adverse drug effects ranges from 1%-44% during the hospitalization, depending upon the class of hospital, the introduction of an adverse effect, and the methodological studies performed.[23-24] The type A (augmented) effects are produced by intensifying the exaggerated pharmacological action of the drugs. Such reactions are also known as the mechanism based adverse reaction, which are predicted on the basis of the pharmacological study of the drugs, whereas, type B (Bizzare) effects are those effects which are not predicted from its pharmacological properties in the patient at the usual doses, which metabolize the drug in the normal manner.[23] Moreover, the type A effects have been considered as typically dose dependence responses, whereas, the type B responses are non dose-dependent. Further, the beneficial drug effects have been reported to include intended effects, in which the efficacy associated with the advantages and benefits of medication and treatment is determined by randomized, controlled clinical experimentation; and unintended effects, in which some recent signs and symptoms for drug medication have started with the discovery of a sudden and unexpected union between the drug exposure and the beneficial effect.[23,25]

**CONCLUSION**

Pharmacoepidemiology plays a significant role in the control and prevention of drug-induced diseases, i.e. the adverse drug reactions. Over a few years, we have seen considerable amount of applications of PCE in the regulation of clinical trials alongwith utilization of the randomized trials layout. Although the epidemiologic terms and statistics often appear in the clinical literature, but sufficient data on adequate preparation to accurately understand and interpret statistical results about drug risks and benefits is not available. Hence, further studies are demanded for the advancement, development and growth of the process which is used to estimate casuality from characterstic or individual cases reports.

**REFERENCES**

1. Enger C, Gately R, Ming EE, Niemcryk SJ, Williams L and McAfee AT. Pharmacoepidemiology safety study of fibrate and statin concomitant therapy. Am J Cardiol 2010;106:1594-601.
2. Nordmann S, Biard L, Ravaud P, Esposito-Farèse M and Tubach F. Case-only designs in pharmacoepidemiology: a systematic review. PLoS One 2012;7: e49444.
3. Blake KV, Prilla S, Accadebled S, Guimier M, Biscaro M and Persson I. European Medicines Agency review of post-authorisation studies with implications for the European Network of Centres for Pharmacoepidemiology and

Pharmacovigilance. Pharmacoepidemiol Drug Saf. 2011;20:1021-9.
4. Brian S. Textbook of Pharmacoepidemiology. West Sussex, England: John Wiley and Sons; 2006;3.
5. Etminan M and Samii A. Pharmacoepidemiology I: a review of pharmacoepidemiologic study designs. Pharmacotherapy. 2004;24:964-9.
6. DiPietro NA. Methods in epidemiology: observational study designs. Pharmacotherapy. 2010;30:973-84.
7. Fletcher RH, Fletcher SW and Wagner EH. Clinical Epidemiology, The Essentials, 3rd ed. Baltimore: Williams & Wilkins,1996.
8. Strom BL and Melmon KL. The use of pharmacoepidemiology to study beneficial drug effects. In: Strom BL, ed. Pharmacoepidemiology. New York: Wiley. 2005;611-28.
9. Rector TS. Pharmacoepidemiology: emerging roles for pharmacists. Am J Hosp Pharm. 1985;42:778-83.
10. Lipton HL, Byrns PJ, Soumerai SB and Chrischilles EA. Pharmacists as agents of change for rational drug therapy. Int J Technol Assess Health Care 1995;11:485-508.
11. Strom BL. ed. Pharmacoepidemiology. New York, Wiley: 1994.
12. Collett JP and Boissel JP. Pharmacoepidemiology: Epidemiologic approach to the study of drugs. Post Market Surveill 1991;5:3-14.
13. Donnan PT and Wang J. The case-crossover and case-time-control designs in pharmacoepidemiology. Pharmacoepidemiol Drug Saf. 2001;10:259-62.
14. Noordzij M, Dekker FW, Zoccali C and Jager KJ. Study designs in clinical research. Nephron Clin Pract. 2009;113: c218-21.
15. Etminan M. Pharmacoepidemiology II: the nested case-control study--a novel approach in pharmacoepidemiologic research. Pharmacotherapy. 2004;24:1105-9.
16. Shields KM, DiPietro NA and Kier KL. Principles of drug literature evaluation for observational study designs. Pharmacotherapy. 2011;31:115-27.
17. Verhamme K and Sturkenboom M. Study designs in paediatric pharmacoepidemiology. Eur J Clin Pharmacol. 2011;67:67-74.
18. Strom BL and Carson JL. Use of automated databases for pharmacoepidemiology research. Epidemiol Rev. 1990;12:87-107.
19. Hennessy S. Use of health care databases in pharmacoepidemiology. Basic Clin Pharmacol Toxicol. 2006;98:311-3.
20. Takahashi Y, Nishida Y and Asai S. Utilization of health care databases for pharmacoepidemiology. Eur J Clin Pharmacol. 2012;68:123-9.
21. Onder G, Pedone C, Landi F, Cesari M, Della Vedova C, Bernabei R and Gambassi G. Adverse drug reactions as cause of hospital admissions: results from the Italian Group of Pharmacoepidemiology in the Elderly (GIFA). J Am Geriatr Soc. 2002;50: 1962-8.
22. Franceschi M, Scarcelli C, Niro V, Seripa D, Pazienza AM and Pepe G. Prevalence, clinical features and avoidability of adverse drug reactions as cause of admission to a geriatric unit: a prospective study of 1756 patients. Drug Saf. 2008;31:545-56.
23. Koch KE. Adverse drug reactions. In: Brown T, ed. Handbook of Institutional Pharmacy Practice, 3d ed. Bethesda, MD: American Society of Hospital Pharmacists, 1992;279-91.
24. Raebel MA, Carroll NM, Andrade SE, Chester EA, Lafata JE and Feldstein A. Monitoring of drugs with a narrow therapeutic range in

ambulatory care. Am J Manag Care. 2006;12:268-74.
25. Ernst FR and Grizzle AJ. Drug-related morbidity and mortality: updating the cost-of-illness model. J Am Pharm Assoc (Wash). 2001;41:192-9.