WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
SJIF Impact Factor 8.084
Volume 9, Issue 5, 2596-2604. Review Article ISSN 2277– 7105

EPIDEMIOLOGY STUDY OVERVIEW AND MITIGATION OF CDM CHALLENGES IN EPIDEMIOLOGICAL STUDIES

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Article Received on
19 March 2020,

Revised on 11 April 2020,
Accepted on 01 May 2020,

DOI: 10.20959/wjpr20205-17549

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ABSTRACT

Epidemiology involves the scientific study of disease/infection patterns among populations in time and space. The study of cholera in London and its relationship to water supply (John Snow 1855) is widely considered to be the first epidemiological study (Baker et al. 1999). Epidemiology studies provide concrete evidence linking exposure to the incidence of the disease/infection in a population. It can provide accurate estimates of the magnitude of risk related to a specific level of dose or exposure. Epidemiology studies can quantify probabilities that observed relationships took place by chance factors and also possess the potential to control for other risk factors or/and cofounders of the outcome illness being observed. Epidemiology studies used for the setting up of guidelines or evaluation must be of high quality. This will ensure confidence in the validity of the results. In this paper, we provide an overview of the impact of epidemiology trials, different types of epidemiology trial designs, its objectives, challenges of clinical data management in epidemiological studies and suggest effective solutions to ease data management activities.

KEYWORDS: Epidemiology trials, Observational study, Interventional study, Clinical data management, Data collection.

INTRODUCTION

The word epidemiology is derived from the Greek words *epi* = upon, among; *demos* = people, district; *logos* = study, word, discourse which means ‘study of what is upon/on the people’. Epidemiology is the study of distribution of events/diseases in human population and use of these studies to prevent such distribution of events/diseases. To further explain in

detail, epidemiology would involve the investigation of disease frequency, patterns, and its effect on population.[1] Studying epidemiology is associated with activities such as identifying risk factors, history of disease, high risk for disease, complex problems related to health, efficacy & effectiveness of health programs, more information about health program & communication.[2]

Epidemic, endemics, & pandemics are words that are commonly used to describe epidemiology in detail. Epidemic means incidence of diseases/events and health issues related to such events that are identified in more than normal expectancy/level in certain population or area. However, endemics means ongoing, frequent incidence of disease with a certain rate of distribution/spread in a region/population. If endemic is affecting or spreading in specific region/population/country/continent, then it is called as pandemic. Based upon the mode of spread, epidemic has types such as common source epidemics and propagated epidemics which might have direct or indirect mode of transfer from one individual to another.[2]

Over the past years, the primary focus of clinical trials was on core stream diseases which impact the larger populations. Epidemiology is a type of clinical study that examines the effect of disease across a regional or global population.

According to a new market research study, the Global Clinical Trials Market Size has been estimated at USD 18.4 Billion in 2019 and is projected to reach USD 26.9 Billion by 2024 at a CAGR of 7.83% during the forecast period from 2019 to 2024.[3]

The purpose of Epidemic disease clinical trials is to identify the occurrence/frequency and causes of health problem/issues, prevention of these health problems and assessing different treatments. Different types of clinical trial design will be castoff to achieve required purpose.

Epidemiology Clinical Trials Overview

Epidemiology studies have multiple elements such as selection of study population, exposure, evaluation of this exposure, relation between exposure and disease, efficient treatment to prevent/control which should be assessed.[4] It is crucial to adopt the right clinical trial design to meet requirements of a trial. Common issues related to the conduct of an epidemiology clinical trial are selection bias, recall bias, information bias & confounding.[5] These issues will be controlled or managed by study design of trial.

Epidemiology clinical trial design has 2 main types:

- Observational studies
- Interventional studies (experimental studies)

1. **Observational Study:** is divided into cohort, case control, cross sectional, ecological & descriptive study.

- **Cohort studies** compare subject with exposure factor versus those without exposure factor. Though these cohort studies are expensive, complex and time consuming, these are useful for studies of common outcome and rare exposure.
- **Case control observational studies** compare exposure and outcome in disease cases against control (no disease) case in same population. These studies are cost effective, time efficient and more appropriate for rare disease study. A major disadvantage would be recall bias resulting in miscalculation of exposure and selection bias.
- **Cross sectional studies** where exposure and health status are determined simultaneously. Data is collected from individual level about case and control. Since historical data is involved, chances of recall bias are high.
- **Ecological studies** measure the link of exposure and outcome within the group only. A large number of population and data is involved.[4]
- **Descriptive studies** mainly collect data in single or multiple cases which gather health data over specific duration. Example is survey data. It is mainly used for hypothesis. Being cheaper and quick is an attribute of these studies.

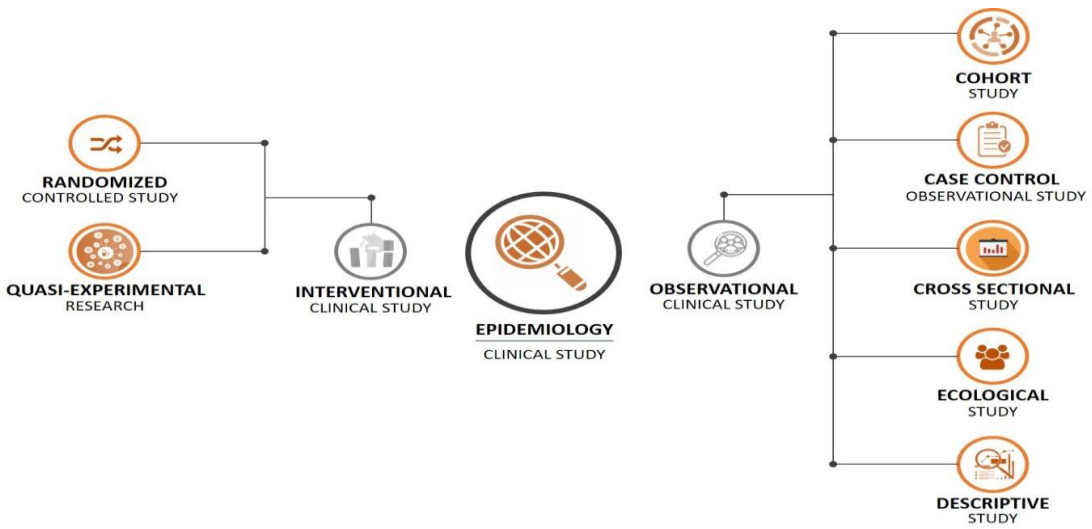

Fig 1: Types of Epidemiology Clinical Trial Design.

2. **Interventional Studies (Experimental studies)** further classified into randomized controlled trial and quasi experiments.

- **Randomized Controlled Trial (RCT)** studies allocate subject randomly to experiment treatment, or control treatment or placebo. Sometimes, a placebo may be used as a comparator for the new medicine or treatment. However, in some cases, use of placebo or sham treatment may be considered unethical. The use of a placebo is generally agreed to be unethical when it is likely to result in irreversible harm, death, or other serious morbidity.[6,7,8] RCT will help to overcome the problem of confounding and bias. Statistical analysis is a key factor in these studies that will help capture significant difference between two groups.

RCT may be further classified into.

1. **Open label** (a study in which both the health providers and patients are aware of the treatment or drug being given)
2. **Single blind** (a study in which only the researcher doing the study knows which treatment/intervention the participant is receiving until the trial is over)
3. **Double blind** (study in which neither the patient nor the health providers know who is receiving a particular treatment)

- **Quasi-experimental research** is research that resembles experimental research but isn't true experimental research. Participants are not randomly assigned to conditions or orders of conditions, although the independent variable is manipulated. Quasi-experimental research eliminates the directionality problem because the independent variable is manipulated before the dependent variable is measured.

Since there is no randomization involved, likely due to differences between conditions, quasi-experimental research does not eliminate the problem of confounding variables.

EPIDEMIOLOGY CLINICAL TRIALS OBJECTIVES[1]

Listed below are few epidemiology study objectives:

- Ratio observed
- Proportion of target population
- Percentage/Occurrence of incidence proportion
- Incidence percentage
- Prevalence in overall and specific population

- Mortality rate count or percentage

The measures taken should be of public health impact.

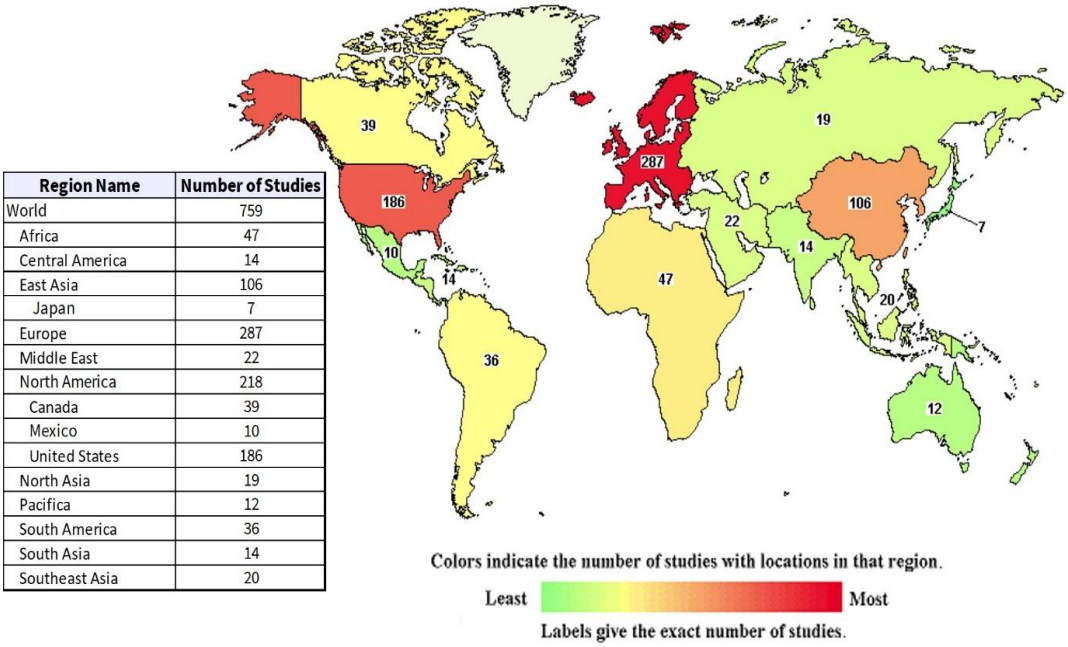

Fig 2: Global Map of Epidemiological Studies.

No of Epidemiology studies – 759 (As on 26 April 2020)

Source: https://ClinicalTrials.gov[9]

Challenges of Clinical Data Management in Epidemiological Studies

There are always some pros and cons for every Therapeutic area specific clinical trials. Listed below are some of the pros and cons for Epidemiological trials:

- Trial Implementation: Epidemiology trials are conducted more as Paper Studies and there is reduced scope of deploying EDC (electronic data capture) mainly due to Budget constraints or connectivity challenges.
- Flexibility of epidemiological study design to accommodate the changing environmental, geographical, cultural, economic factors, etc. that influence the study.
- Data volume & source: Involves large volumes of data and mostly the source of this data is in the form of Patient questionnaires or data collection techniques such as Surveys, Questionnaires and QOL (Quality of Life) Assessments, etc.
- Setup timeline: Epidemiological studies requires quick setup across domains and activities. It really needs real-time solutions for study build and postproduction changes.

- Data collections standard availability: No specific standards are available for data collection in epidemiological studies in comparison with regular therapeutic area wise clinical studies. For e.g. Oncology studies have fixed standard/non-standard parameters for assessment.
- Variability in data collection: It comprises of diverse patient populations involving multiple countries and different climatic conditions that could play an important role in variability in data collection for the same disease.
- Database facility for mega trial: Epidemiological studies are conducted with large sample size. Since the data generated is huge, as a result, the databases required to support these studies is limited in the market.
- Lab data challenges: Data Collection Instrument needs to be efficient and effective as End points involved may have laboratory tests. In case of local labs, challenges for Laboratory Normal range and its management/data cleaning will be prominent due to variation across regions.
- Society taboo: Data Collected will show variability and trends due to social reservations /due to society taboo, hence deploying effective discrepancy management is important. E.g. In the case of an epidemic/pandemic, affected individuals do not come forward to get themselves assessed or share their medical details.
- Subject Tracking: Subject do not follow-up/return for their clinical trial visit. This should be managed efficiently. There is a need to train investigators and site staff to encourage and maintain subject compliance to trial visit in the duration of the study.
- Budget Issues: Prospective data brings its own challenges, particularly in terms of the manpower effort and budget required to collect it.
- Timelines: Generally, most studies are of a long duration (on an average of 1 to 2 years) posing challenges to non-compliance by patients/subjects. This can adversely affect data quality and reliability.
- Monitoring of Data entry is important. Lag time in data entry due to increased volume of data generated during an epidemic/pandemic can affect the quality of data collected. Hence, it is recommended that the Sponsor monitor sites to avoid having any pending/outstanding data entry.

Few effective solutions that can ease data management activities

- Automated reminders (SMS, Email, App alerts) are helpful applications or softwares to engage with patients and encourage patient retention and participation during the trial.
- To over come the challenges faced due to flexibility in study design, the data collection platform should have a flexible study configuration accompanied with robust platform to manage post-production changes.
- Effective Data Collection Instrument creation is required - Driving CRFs (Case Report Forms) to meet study objectives – Incidence, prevalence, survivorship
- Survey software integrated with Clinical Data Management Systems (CDMS)/Electronic Data Capture (EDC) Systems to enhance data quality and effective data validation.[10]
- Automatic integration of data: eCRF required to integrate decentralized captured data (data from multiple centres spanning different and different collection modules for e.g. digital diaries, medical devices, wearable devices, and app data).[11]
- Use of technological advances in assessments e.g. sensors/wearable devices which could capture data automatically.
- Managing language translation, back translation, and transcribing data in to CDMS/EDC database appropriately is important specially the patient questionnaire.
- Some studies could be of greater duration hence effective resource management and controlling attrition of team members is important.
- Knowledge transfer and knowledge sharing within Study team is of paramount importance.
- Identify core team prior experience of managing epidemiology Studies.
- Investments in Subject Matter expertise, Analytics tools & Platforms, Knowledge Sharing and Continues Upgradation of epidemiology Understanding.
- Collaboration and Coordination between Interdepartmental Staff i.e. site staff, Medical Monitor, Data Management, Biostatistics & Medical Writing cross study.
- Use of Automation, Continuous Streamlining and making the Process Lean.
- Proactive Planning & Collaborative Approach – Volume Projection & Dynamic Resource Planning to manage workloads.

CONCLUSION

Epidemiology trials will continue to play a key role to increase our understanding of disease/infection patterns among populations. Since epidemiology studies take multiple

variables into consideration, careful selection of study design is required. Each study design has its own set of pros and cons. Choosing the appropriate trial design will significantly improve the outcomes of epidemiology studies by diminishing different bias and confounding. A well organized and conducted experimental study design will score high in managing issues of epidemiology studies. Tapping into newer means of data collection and its integration across platforms can help streamline and ease outcome interpretation. Challenges of huge, ongoing data should be resolved by selecting an application that provides integration of various variables in a consolidate database and system. The process of automation can decrease human error, ease data collection and its management while ensuring integrity and quality of clinical data. Choosing the correct study design and the right database/system can help solve the problems faced in epidemiology studies.

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