

The Increasing Role of Pragmatic Clinical Trials and Real-World Data in Healthcare Research

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Introduction

Healthcare systems are institutions that deliver healthcare services to meet the health needs of individuals or a community. Healthcare services are delivered in defined settings, such as hospitals, long-term care facilities, or clinics. Healthcare research is defined as the creation of knowledge by performing studies in healthcare settings. This type of research is performed by multidisciplinary teams of healthcare practitioners with the primary goal of generating new knowledge that will improve the quality of patient care. During the planning phase of a healthcare study, it is important to select an optimal study design. In this perspective, definitions of common study designs will be reviewed and the increasing role of pragmatic clinical trials and real-world data in healthcare research will be described.

Interventional & Observational Studies

Healthcare research can be classified as interventional or observational according to the role that the investigator plays during the performance of the study. In interventional studies, the investigator performs a treatment or other intervention to study patients in the setting of a clinical trial. Then, the investigator evaluates whether the study intervention causes an outcome of interest. In observational studies, the investigator does not perform any active patient intervention. The most common observational designs include the cohort study, the case-control study, and the cross-sectional study.

Clinical Trials & Clinical Studies

Another broad way to classify healthcare research is into clinical trials and clinical studies. The National Institutes of Health define a clinical trial as a study

in which patients are prospectively assigned to one or more interventions to evaluate the effects of those interventions on clinical outcomes.[1] In a clinical trial, the study intervention is prospectively assigned to particular patients according to the study protocol. In observational studies, investigators may collect data on interventions and evaluate the effects of interventions on outcomes, but these interventions were not prospectively assigned according to a study protocol. Hence, observational studies are clinical studies (**Figure 1**).

Randomized Clinical Trials & Pragmatic Clinical Trials

Clinical trials can be further classified according to the selection of study participants as randomized clinical trials (RCT) or pragmatic clinical trials (PCT) (**Figure 1**). In RCTs, participants are selected based on strict inclusion and exclusion criteria defined in the study protocol. This creates a highly defined study population. This population is then randomized to receive the intervention or placebo. The RCT is an optimal design to evaluate the efficacy of an intervention on a particular outcome. In this type of clinical trial, the study population is very restrictive, and the intervention delivered to this carefully selected population is applied under ideal protocol-defined conditions. Because of the above, data generated in RCTs is not easily translated to the real world.

PCTs select a diverse population of study participants. In this type of clinical trial, the study population reflects real life patients. The interventions that are compared in PCTs are the ones used in routine patient care. Since the compared interventions are real-world alternatives, the study results can be readily applied to improve clinical practice or inform policy decisions. Another important characteristic of PCTs is that the study

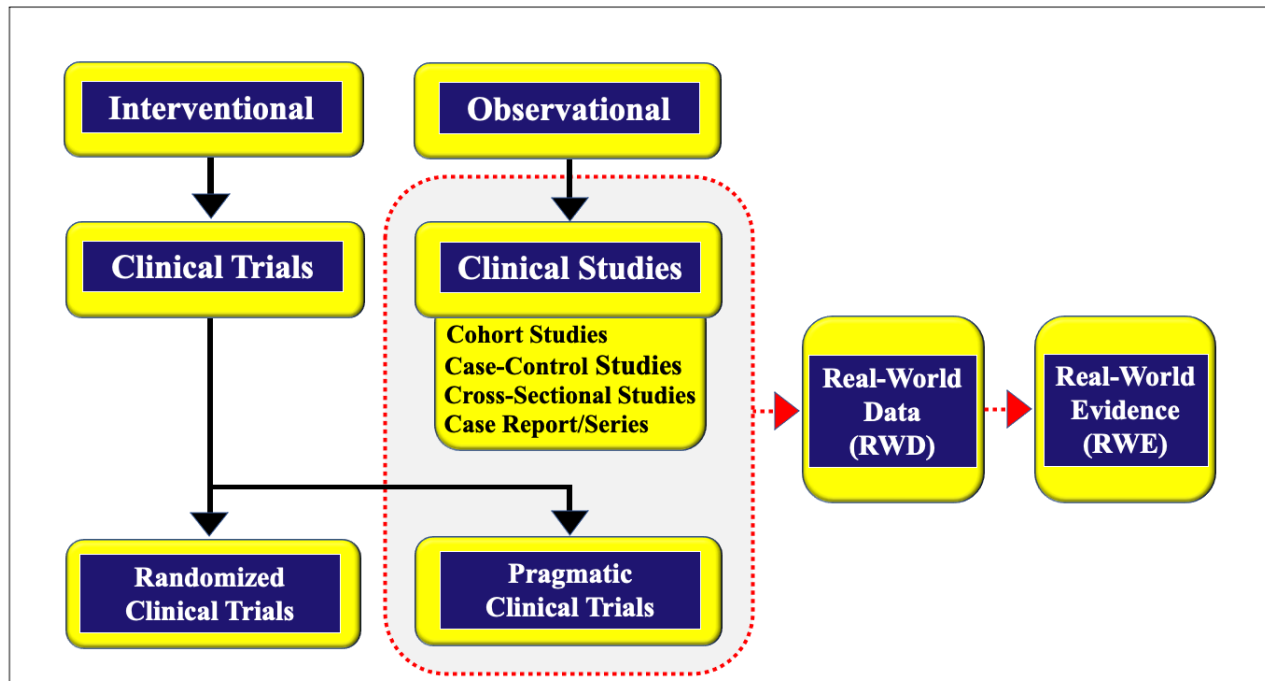


Figure 1. Overview of clinical study designs.

is constructed around the normal operations of the healthcare system, and data are collected around normal, or routine, patient care activities. In both RCTs and PCTs, an intervention is prospectively applied to patients. In the RCT, the intervention is applied by the investigator, and in the PCT, the intervention is applied as part of routine patient care. In RCTs, individual study patients are randomized to a particular intervention versus a placebo. In PCTs, randomization may occur based on a hospital, clinic, or group of patients. This type of randomization is defined as cluster randomization.

Randomized Clinical Trials & Real-World Data

An additional way to classify healthcare research is based on the origin of the data collected as part of the study. Randomized clinical trials require data that are collected outside of routine clinical care. In these trials, study protocols require particular measures that are not part of standard care. Real-world data (RWD), on the other hand, is defined as study data collected during routine patient care. To obtain RWD, the study protocol needs to be designed so that data can be easily collected

during regular healthcare setting activities, such as hospital stays or clinic visits. Since data on routine care are regularly included in electronic medical records (EMRs), a common source of RWD is data from EMRs. Other sources of RWD include government datasets, disease registries, or patient-source data from questionnaires or wearable devices. New evidence generated from studies using RWD is defined as real-world evidence (RWE).[2] The Food and Drug Administration is now making regulatory decisions, such as approving new therapeutics, based on RWE.[3] RWD and RWE can be generated by observational studies and pragmatic clinical trials (Figure 1).

Conclusions

Since RWD is generated based on actual patient care, RWE can be readily implemented into patient care improvement activities. Because RWD and RWE facilitate the rapid translation of research findings into clinical practice, they are playing an increasing role in healthcare systems' decisions.[4] Clinical investigators performing research in healthcare settings should become familiar with research activities involving RWD and RWE.

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