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REVIEW

Explicating the Roles of Clinicians and Statisticians in Clinical Research

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Abstract

Clinical research is foundational in advancing prevention, diagnosis, treatment, and prognosis prediction of diseases, demanding the highest quality of evidence. The caliber of a clinical study hinges on the relevance of its research question and is bolstered by its internal and external validity. These pillars of quality are best achieved through the synergistic collaboration between clinical investigators and statisticians throughout the research process. This letter outlines an ideal collaborative model by detailing the distinct yet complementary roles of clinicians and statisticians in the design, implementation, and publication of clinical research.

Introduction

Clinical research is driven by needs from clinical practice, mainly including identifying causes and risk factors of diseases, assessing the accuracy of methods in screening or diagnosing a disease, assessing the efficacy and safety of a treatment, and evaluating or predicting the prognosis of patients (Aparasu et al., 2020).

High-quality clinical research is characterized by its adequacy in design, conduct, analysis, and reporting, making findings with both good internal and external validity. The internal validity is ensured by well-controlled type I and type II errors in hypothesis testing and various biases that likely occur during the study's design, implementation, data analysis, and reporting. The external validity, the generalizability of the study conclusion, is determined mainly by eligibility criteria for participant recruitment defined by the clinical investigator. All these features present in a study report can be achieved via the cooperation of clinical investigators and statisticians throughout the entire study process, including the design phase, implementation phase, analysis, and reporting degree.

Clinicians, as investigators, play a pivotal role in initiating clinical studies by formulating relevant questions and establishing the necessity and rationale for the study. They are also responsible for interpreting the findings and their implications, translating them into improvements in clinical

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practice. Thus, they ensure the research question's relevance to the study's context, a primary consideration for any scientific journal.

The involvement of a statistician is essential in ensuring the study's internal and external validity throughout its duration. They aid in transforming research questions into testable hypotheses, employing the four components: patient/population, intervention/treatment, comparison/comparator, and outcome. In partnership with clinical investigators, statisticians help formulate scientifically sound and feasible protocols. They recommend study designs based on available resources and objectives, such as randomized controlled trials (RCTs), prospective non-randomized controlled trials, or retrospective cohort studies, depending on the study's aim of evaluating treatment effects.

This commentary aims to clarify these roles further and highlight the crucial intersections where collaboration influences the trajectory of a study. We advocate for a partnership between clinical investigators and statisticians from the study's inception to the publication of its results. This collaboration entails a clear division of responsibilities at every study phase (Figure 1). The diagram visually encapsulates their intertwined roles in the research process.

Raising a Research Question

The journey begins with clinicians, represented in orange, who identify areas where clinical practice raises questions that warrant investigation. Their insights, derived from direct patient care and understanding of disease processes, initiate the research with a query that embodies clinical relevance and scientific curiosity.

Framing the Hypothesis, Choosing a Study Design

Here, represented in blue, statisticians refine the research question into a precise hypothesis. Through communication with clinical investigators, their expertise becomes crucial in selecting an appropriate study design that robustly and feasibly answers the clinical question, and the corresponding reporting guideline will be followed when reporting the findings (Assel, 2019).

Protocol Development

This phase, marked by clinician and statistician collaboration, involves converting the research plan into a detailed protocol

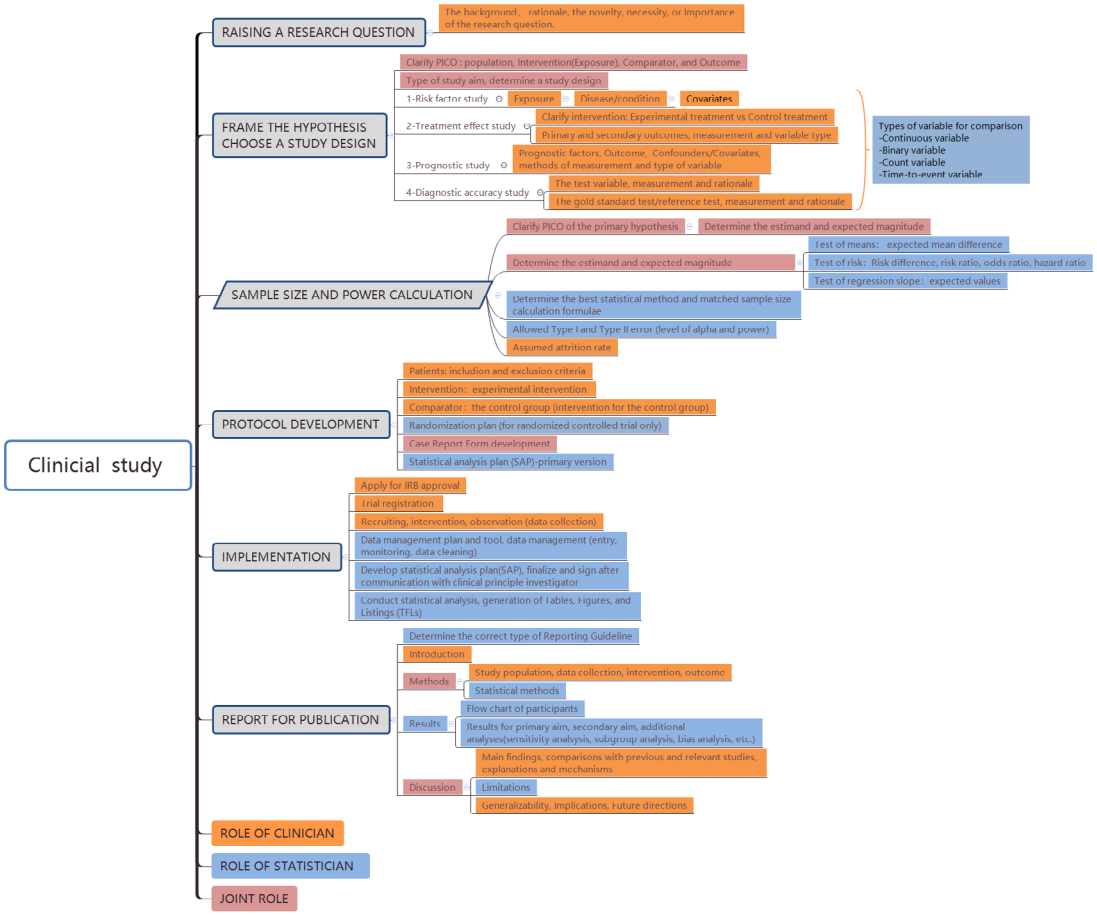

Figure 1. Responsibilities of clinical investigators and statisticians in clinical research

structured in the PICO format. Clinicians will determine patient/population, intervention/treatment, comparison/comparator, and outcome, while the statistician will outline data management and statistical analysis methods. The clinicians' knowledge of patient demographics and clinical interventions merges with the statisticians' insight into comparative groups and analysis methods. This collaboration, especially considering potential biases, ensures the protocol's robustness.

Sample Size Calculation and Statistical Analysis Plan

In this phase, statisticians lead the sample size calculation, using discussions with clinicians to determine critical parameters like expected estimands and variation. Together, they scale the study to be sufficiently powered and achievable, aiming to detect meaningful outcomes without wasting resources. Developing a statistical analysis plan (SAP) following guidelines is also the statistician's responsibility, aiming to minimize bias of statistical analysis and maintain quality during implementation(Cummings et al, 2003;
Editors ICoMJ, 2022). A crucial intersection emerges where clinicians and statisticians must align their knowledge. They sign off on the plan's final version and publish it before data locking.

Implementation

The execution of the study protocol marks this stage. Clinicians lead patient recruitment and data collection, while statisticians oversee the integrity and preliminary analysis of the data. The success of this stage relies on the meticulous planning of previous steps. Ensuring consistency across the IRB-approved protocol, trial registry, and manuscript "Methods" section is vital for publishing high-quality research.

Reporting

Adhering to international reporting guidelines is imperative. Statisticians should prepare critical sections like the "Methods" statistical analysis and the entire "Results" report. The International Committee of Medical Journal Editors (ICMJE) mandates the registration of clinical studies in a public trial registry and uploading a detailed SAP before database lockup to prevent analysis bias (Centre, 2022). In the final stage, clinicians and statisticians collectively interpret the results and the study's implications for broader clinical practice.

Despite the widespread acknowledgment of statisticians' importance in clinical research(Pocock, 2004; Greenwood, 1948), their involvement is often confined to sample size calculation or data analysis, particularly in observational studies. By delineating the roles of clinicians and statisticians at each step of clinical research, we aim to encourage closer collaboration between these professional groups, thereby enhancing the quality of clinical research.

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Conflict of Interests

No

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