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Editorial
Novel Statistical Methods and Designs for Clinical Trials

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1. INTRODUCTION

Clinical trials are essential for advancing medical knowledge and improving patient care. The complexities involved has spurred the development of a wide range of statistical methods and trial designs, all aimed at maximizing efficiency, interpretability, and likelihood of success, all while ensuring patient safety. This special issue of the journal is dedicated to "Novel Statistical Methods and Designs for Clinical Trials," showcasing a selection of thought-provoking papers that push the boundary of the statistical innovation in clinical research and drug devvelopment.

2. RESEARCH ARTICLES

Huang and Dasgupta [3] address a critical challenge in cancer research: the construction of biomarker panels for early detection. Employing a novel approach that integrates logic-regression and multiple imputations, the authors tackle the pervasive missing data in clinical trials, offering superior alternatives to traditional methods. Their pragmatic solution, demonstrated through pancreatic cyst data, representing a significant advancement in robust and adaptable biomarker identification.

Qiu and Wong [6] tackle the complex designs in dose-response studies. They introduce the particle swarm optimization (PSO) as a groundbreaking method within continuation-ratio models defined over compact dose intervals. Their simulation study boldly juxtaposes PSO against established algorithms, highlighting its potential superiority for estimating model parameters and critical functions like the most effective dose (MED) and the maximum tolerated dose (MTD).

Edefonti et al. [1] delivers a comprehensive review of recent methodological strategies for analyzing dietary patterns and cancer risk in nutritional epidemiology studies. navigating through a variety of multivariate statistical methods, from the classical *a posteriori* patterns to the latest in Bayesian and Frequentist frameworks, the authors emphasize reproducibility and the integration of sophisticated statistical techniques, thereby extending the horizon of dietary pattern analysis.

With the advancements in cancer genomics, basket trials have become a focal point in oncology research. Huang et al. [2] broaden the application of Bayesian methods to basket trials with treatment and control arms. Through the adaptation of hierarchical models and a compelling argument favoring Bayesian methods over traditional Frequentist methods, the authors shed new light on basket trial designs in rare diseases.

Liu et al. [4] present the Ti3+3 design as an innovation in toxicity profiling for early-phase trials. By transcending the binary endpoint limitation and considering multiple toxicity grades and types, the authors offer a simple yet potent alternative to contemporary designs, promising refined dose escalation decisions while adhering to operating characteristics essential for patient safety. More importantly, it addresses an important question of modeling toxicity beyond the DLT from the recent FDA Project Optimus.

Pan et al. [5] delve into the progressive notion of platform trials, elucidating strategies for integrating new experimental arms post-trial activation. With meticulously outlined approaches to error control and optimization of experimental design, this work serves as a guidebook for the challenging problems in pediatric osteosarcoma studies, underscored by the publication of an accompanying R package.

Sidi et al. [7] propose an original framework addressing the perennial dilemma in non-inferiority trials: the selection of the non-inferiority margin. By combining expert opinion with trial data and respecting the mandated survey margins, the authors pave the way for more informed and sound decisions concerning new treatments, potentially transforming the landscape of non-inferiority trials.

In diagnostics, Wang [8] confronts the commonly neglected issue of indeterminate imaging data, highlighting its relevance and potential informative nature. With a meticulous definition of estimands and imputation strategies, this contribution aim to enrich the planning and analysis of imaging drug trials – a fundamental step toward precision medicine.

Ye et al. [9] meticulously examine the statistical intricacies of master protocols, emphasizing the implications of a shared control in multiplex therapeutic evaluations. The authors dissect the simultaneous false-decision error, providing reassurance regarding the adequacy of pre-set false

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discovery rates as the existing error rate controls in master protocol designs, thus offering clarity amidst complexity.

Zhou and Ji [10] revisit Bayesian sequential clinical trial designs, delving into the nuances of interim analyses and their impact on trial integrity. Their work offers a profound understanding of sequential designs for clinical trials grounded in fundamental statistical principles. This study serves as a compass for statisticians navigating the planning of practical trials involving sequential decision makings.

3. REMARK

We hope that this special issue, featuring eleven diverse and innovative research papers, will serve as a catalyst further exploration and innovation in the field of clinical trial designs and data science. The methodologies and insights presented within these papers have the potential to revolutionize clinical trial design, conduct, and analysis in our data-driven world. We encourage you to delve into these papers to discover the latest advancements and ideas on experimental designs in data science.

The assembled contributions in this special issue represent a convergence of statistical innovation and clinical prudence. As guest editors, we are honored to present this dynamic amalgamation of papers that enrich the armamentarium of clinical trial designs. We anticipate that these novel methods will shape the future of clinical trial methodologies, leading to accelerated development of treatments and improved patient outcomes.

We invite the readership not only to scrutinize but also to employ these novel designs and methods, thereby influence the trajectory of clinical trials as we move into a more data-intense and patient-centric paradigm of healthcare.

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