1. Health Res Policy Syst. 2025 Oct 14;23(1):133. doi: 10.1186/s12961-025-01404-x.
A scoping review of future research trends and priorities in health systems

Background: Health systems worldwide are increasingly influenced by rapid and complex changes across various domains. Anticipating and responding to these changes is critical to ensuring the sustainability and effectiveness of health systems. Future-oriented research plays a key role in informing policy and planning, especially in the face of emerging global health challenges. This study aimed to identify and synthesize the emerging trends and mega-trends shaping the future of health system research across different contexts and countries.

Methods: A scoping review was conducted in 2024 following the Joanna Briggs Institute (JBI) methodology. Systematic searches were performed in three major databases - PubMed, Web of Science and Scopus - up to 8 November 2024. Inclusion criteria focussed on English-language articles that addressed future trends or priorities in health systems research. Data were analysed qualitatively and categorized using the Social, Technological, Economic, Environmental, Political, and Values (Legal) (STEEPV) framework .

Results: From 5414 initially retrieved records and after 3 phases of screening, 22 studies met the eligibility criteria. The analysis revealed six major categories influencing future health systems research: sociocultural, technological, economic, environmental, political and values (legal) factors. Sociocultural and economic dimensions were the most frequently cited drivers. Key issues identified included ageing populations, technological innovations (e.g. artificial intelligence (AI), telemedicine), climate change, rising healthcare costs, political decision-making and legal-regulatory frameworks.

Conclusions: The future of health systems research is multifaceted and shaped by intersecting global trends. Understanding these dimensions can guide policymakers and researchers in setting priorities, designing adaptive strategies and enhancing the resilience and responsiveness of health systems. Comprehensive and coordinated planning at the macro level is essential for addressing upcoming challenges and optimizing health outcomes.

2. Int J Qual Stud Health Well-being. 2025 Dec;20(1):2556350. doi: 10.1080/17482631.2025.2556350. Epub 2025 Oct 1.
Planning and conducting cross-cultural qualitative research: a methodological framework and resources for health researchers

Purpose: The aim of this review was to develop a methodological framework that could be applied during the design and conduct of cross-cultural qualitative research with people from culturally and linguistically diverse backgrounds in health contexts or settings.

Methods: Developing the methodological framework in this study consisted of three phases. In Phase 1, a literature review was undertaken to identify relevant evidence by searching bibliographic databases, online sources and relevant journals. In Phase 2, methodological and ethical concepts, issues and considerations were summarized, synthesized and consolidated into a framework. In Phase 3, the methodological framework was refined by applying it to a cross-cultural qualitative study.

Results: The resulting methodological framework proposes two stages (preparation and action) and eleven key steps for designing, conducting and reporting cross-cultural qualitative research. Other practical resources (i.e. glossary of terms and detailed prompt tool) for health researchers that can be used with the framework are also presented.

Conclusions: This article presents a methodological framework that can guide high-quality cross-cultural qualitative research and is intended for use by health researchers, especially those new to cross-cultural qualitative research. It has the potential to improve the inclusivity and cultural responsiveness of qualitative research.

3. J Eval Clin Pract. 2025 Oct;31(7):e70298. doi: 10.1111/jep.70298.
Understanding and Managing Confounders, Mediators and Colliders in Research

Rationale: Researchers often make causal inferences about relationships among variables and constructs. However, third-variable effects may obscure the relationship among studied variables. Third-variable effects generally include confounders and mediators, but recently there has been an emerging discussion on colliders.

Aim: To provide a concise introduction of confounders, colliders, and mediators for health researchers and outline strategies for minimising the impact of confounders, colliders and mediators in quantitative research.

Methods: Methodological literature from biostatistics textbooks, methodology papers, and methodological reviews published in nursing, health, psychological and behavioural sciences.

Conclusions: Understanding third-variable effects is crucial to conducting rigorous research and drawing valid causal inferences from research data. Health researchers should embrace both theory and model-based thinking as a foundational element of their methodology. This involves explicitly theorising the underlying causal structures before data collection and analysis using Directed Acyclic Graphs which are useful for visually representing hypothesised causal pathways and their relationships with potential third variables.

4. Allergy. 2025 Oct;80(10):2755-2766. doi: 10.1111/all.70013. Epub 2025 Aug 23.
Statistical Analysis in Allergy and Immunology: A Review With Practical Examples

Statistical analysis plays a critical role in biomedical research, ensuring that data are interpreted appropriately and that conclusions are both valid and reproducible. In allergy and immunology, where studies increasingly rely on complex data structures and analytical approaches, clarity on biostatistical methods is essential to support transparency and scientific rigor. However, inconsistent statistical reporting and misuse of analytical techniques remain persistent challenges in the field. This review provides a structured and practice-oriented overview of key statistical aspects relevant to research in allergy and immunology Drawing upon recent peer-reviewed articles in these disciplines, we highlight best practices in the transparent reporting of statistical methods, verification of underlying assumptions, and interpretation of statistical significance in the context of clinical relevance. Each section is illustrated with practical examples to demonstrate sound analytical reasoning and to guide researchers, reviewers, and educators in improving statistical standards across the field.

5. J Biopharm Stat. 2025 Oct;35(6):1143-1160. doi: 10.1080/10543406.2025.2489288. Epub 2025 Apr 26.
Comparison of continuous, binary, and ordinal endpoints

Selecting the primary endpoint has been one of the most challenging tasks in the design of clinical trials. Typical endpoints include binary, continuous or time-to-event endpoints. The primary endpoint for many clinical trials is binary and is defined based on a threshold of a continuous endpoint. Many such trials could lack study power. It could be challenging to decide the appropriate threshold to define the binary endpoints; the best guess could be wrong, and the study will lose its power when that happens. For this reason, we propose to use an ordinal endpoint defined by two or more cut points as a primary or secondary efficacy endpoint when facing such challenges, to spread the risk from comparing treatment differences at a single cut point to multiple cut points. This way the study could maintain its power even if the results differ from the initial expectations. In this paper, we evaluate the performance of continuous, binary, and ordinal endpoints via extensive simulation studies. Furthermore, we compare the three types of endpoints across many clinical trials. Overall, we demonstrate that there may be some situations where the use of ordinal categorical endpoints, based on clinical and statistical considerations, could offer advantages as a primary or secondary efficacy endpoint.Disclaimer: This article has been reviewed by FDA and determined not to be consistent with the Agency's views or policies. It reflects only the views and opinions of the authors.

6. Clin Chim Acta. 2025 Oct 17:579:120655. doi: 10.1016/j.cca.2025.120655. Online ahead of print.
Putting clinical studies into better perspective by defining accuracy when effect size is small

Objectives: In recent years, computational techniques have improved to where tens and even thousands of observations can be rapidly analyzed on computers. Large numbers of observations may improve statistical certainty but may increase clinical/epidemiological uncertainty when the effect size is so called "modest" or even "moderate," because, although p-values may reach significance, clinical discrimination may be poor. Moreover, when the effect size is small, studies show that the conclusions may be faulty depending on unknown confounders, sample selection, the statistical models used for calculation, and other factors. Although clinical/epidemiological results may be viewed as efficacy or effectiveness, one may ask whether or not such results can be translated into measures of accuracy. The objective here is to show how indices such as risk ratio or odds ratio can be translated into more absolute parameters that better define clinical usefulness.

Content: In this review, techniques are discussed that may help providers place statistical results into a perspective that allows for better decision making. Examples are given and calculations are described whereby commonly provided more relative statistics, such as risk, hazard and odds ratios can easily be converted/examined in more absolute terms by converting to or calculating diagnostic statistics or number needed to treat/be exposed (NNT/NNE) that provides a better practical perspective.

Conclusions: As described, statistically significant studies with small effect sizes are always suspect but may be converted or viewed in parameters that allow observers to better evaluate the results in term of accuracy. This may provide a more practical perspective.

7. Stat Med. 2025 Oct;44(23-24):e70282. doi: 10.1002/sim.70282.
Sensitivity Analyses for Missing in Repeatedly Measured Outcome Data

We discuss practical aspects of conducting sensitivity analyses for missing data with a repeatedly measured outcome. Our motivation is a SMART trial with a repeatedly measured outcome subject to missingness. We discuss and describe delta-based controlled imputation approaches to conducting sensitivity analyses for such trials that typically use linear mixed models for their primary analysis. We find that delta-based sensitivity analyses for trials with repeatedly measured outcome variables are enhanced by using MICE for the imputation. Further, including last-observed-before-time covariates is critical for a repeatedly observed outcome. We also develop some novel metrics for judging the adequacy of sensitivity analyses.

Trial Registration: Tailoring Mobile Health Technology to Reduce Obesity and Improve Cardiovascular Health in Resource-Limited Neighborhood Environments: NCT03288207.

8. PLoS Comput Biol. 2025 Oct 3;21(10):e1013515. doi: 10.1371/journal.pcbi.1013515. eCollection 2025 Oct.
A Bayesian model for repeated cross-sectional epidemic prevalence survey data

Epidemic prevalence surveys monitor the spread of an infectious disease by regularly testing representative samples of a population for infection. State-of-the-art Bayesian approaches for analysing epidemic survey data were constructed independently and under pressure during the COVID-19 pandemic. In this paper, we compare two existing approaches (one leveraging Bayesian P-splines and the other approximate Gaussian processes) with a novel approach (leveraging a random walk and fit using sequential Monte Carlo) for smoothing and performing inference on epidemic survey data. We use our simpler approach to investigate the impact of survey design and underlying epidemic dynamics on the quality of estimates. We then incorporate these considerations into the existing approaches and compare all three on simulated data and on real-world data from the SARS-CoV-2 REACT-1 prevalence study in England. All three approaches, once appropriate considerations are made, produce similar estimates of infection prevalence; however, estimates of the growth rate and instantaneous reproduction number are more sensitive to underlying assumptions. Interactive notebooks applying all three approaches are also provided alongside recommendations on hyperparameter selection and other practical guidance, with some cases resulting in orders-of-magnitude faster runtime.

9. Stat Med. 2025 Oct;44(23-24):e70299. doi: 10.1002/sim.70299.
Measuring Agreement in Diagnostics: A Practical Guide for Researchers

Healthcare professionals routinely perform clinical examinations and diagnostic assessments. How the findings of these assessments are interpreted can have significant implications for patient care and outcomes. A recent systematic review on reliability and agreement studies in intrapartum fetal heart rate monitoring highlighted three methodological issues: (1) confusion between the concepts of agreement and reliability, (2) lack of clarity on how agreement and reliability measures are calculated when more than two raters are involved, and (3) confidence intervals seldom reported. This paper aims to clarify how agreement measures can be computed and interpreted when the outcome is binary (e.g., normal/abnormal test result). Using a motivating example in which five experienced obstetricians assessed 20 CTGs, we demonstrate how agreement can be defined, computed, and interpreted in various scenarios. The paper further explains the relationship between agreement measures and the concept of reliability, the distinction between intra- and inter-observer studies, and approaches to make statistical inference and sample size calculations. Particular emphasis is placed on the proportion of agreement, the proportion of specific agreement and kappa coefficients. A shiny application has also been developed to support researchers in their agreement studies. This work completes existing tools such as the Guidelines for Reporting Reliability and Agreement Studies (GRRAS), the Quality Appraisal Tool for Studies of Diagnostic Reliability (QAREL) and STARD guidelines for reporting diagnostic accuracy studies. It is intended to help researchers improve the methodological quality of studies that evaluate the agreement of clinical tests.

10. Stat Med. 2025 Oct;44(23-24):e70284. doi: 10.1002/sim.70284.
A New Test for Assessing the Covariate Effect in ROC Curves

The ROC curve is a statistical tool that analyzes the accuracy of a diagnostic test in which a variable is used to decide whether an individual is healthy or not. Along with that diagnostic variable, it is usual to have information on some other covariates. In some situations, it is advisable to incorporate that information into the study, as the performance of the ROC curves can be affected by them. Using the covariate-adjusted, the covariate-specific, or the pooled ROC curves, we discuss the implications of excluding or including the covariates in the analysis. Motivated by the above, a new test for comparing the covariate-adjusted and the pooled ROC curve is proposed, and the problem is illustrated by analyzing a real database.

11. J Biopharm Stat. 2025 Oct;35(6):1106-1125. doi: 10.1080/10543406.2025.2489286. Epub 2025 Apr 29.
Application of complete N-of-1 trial design in bioequivalence-biosimilar drug development

Biosimilars play a crucial role in increasing the accessibility and affordability of biological therapies; thus, precise and reliable assessment methods are essential for their regulatory approval and clinical adoption. Currently, the 2-sequence 2-period crossover design is recommended for two-treatment biosimilar studies. However, such designs may be inadequate for the practical assessment when multiple test or reference products are involved, particularly in scenarios such as: (1) bridging biosimilar results across regulatory regions (e.g. the European Union, Canada, and United States), or (2) evaluating biosimilarity across different dosage forms or routes of administration. To address these challenges, multi-treatment designs such as Latin-square design, Williams design, and balanced incomplete block design can be considered. More recently, the complete N-of-1 trial design, which contains all permutations of treatments with replacement, has gained attention in biosimilar drug development, especially with the presence of carryover effects. However, detailed statistical methodologies and comprehensive performance comparisons of these designs are lacking in the context of multi-formulation studies. This study employs a linear mixed-effects model to estimate the contrast of treatment effects across three drug products within the framework of the designs under investigation. Subsequently, the relationship between sample size and relative efficiency is explored under same significance level and statistical power. The findings indicate that, for a given sample size, the complete N-of-1 design consistently achieves the lowest estimation variance relative to the alternative designs, thereby representing a more efficient design for biosimilar assessment under the conditions examined.

12. Lifetime Data Anal. 2025 Oct;31(4):810-829. doi: 10.1007/s10985-025-09672-z. Epub 2025 Oct 15.
Statistical methods for composite analysis of recurrent and terminal events in clinical trials

In many clinical trials, one is interested in evaluating the treatment effect based on different types of outcomes, including recurrent and terminal events. The most popular approach is the time-to-first-event analysis (TTFE), based on the composite outcome of the time to the first event among all events of interest. The motivation for the composite outcome approach is to increase the number of events and potentially increase power. Other composite outcome or composite analysis methods are also studied in the literature, but are less adopted in practice. In this article, we first review the mainstream composite analysis methods and classify them into three categories: (A) Composite-outcome Methods, which combine multiple events into a composite outcome before analysis, e.g., combining events into a time-to-event outcome in TTFE and into a single recurrent event process in the combined-recurrent-event analysis (CRE); (B) Joint-analysis Methods, which test for the recurrent event process and the terminal event jointly, e.g., Joint Frailty Model (JFM), Ghosh-Lin Method (GL), and Nelsen-Aalen Method (NA); (C) Win-ratio type Methods that account for the ordering of two types of events, e.g., Win-fraction Regression (WR). We conduct comprehensive simulation studies to evaluate the performance of various types of methods in terms of type I error control and power under a wide range of scenarios. We found that the non-parametric joint testing approach (GL/NA) and CRE have overall the best performance. However, TTFE and WR exhibit relatively low power. Also, adding events that have no or weak association with treatment usually decreases power.

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