STRATOS initiative – progress with guidance in three topics in observational research

Introduction of the STRATOS initiative

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The STRATOS initiative, launched at ISCB 2013 ([https://www.stratos-initiative.org/en.),](https://www.stratos-initiative.org/en.) aims to provide accessible, evidence-based guidance for key topics in the design and analysis of observational studies. Guidance is intended for applied statisticians and other data analysts with varying levels of statistical expertise and experience. While the primary focus is on health sciences research, the content is also applicable in other empirical sciences. Currently, the STRATOS initiative comprises nine topic groups (TGs) and ten cross-cutting panels coordinating the activities of the initiative and working on issues common to all TG's. Since 2017, STRATOS has published a series of short articles in the Biometrical Bulletin. In this session, we will have talks from topic groups TG2 (Selection of variables and functional forms in multivariable analysis) and TG3 (Initial data analysis) and present some results from the cooperation in the Setting International Standards in Analyzing Patient-Reported Outcomes and Quality of Life Endpoints (SISAQOL-IMI) project.

Accessible structured Initial Data Analysis and Data Quality Assessments

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Initial Data Analysis (IDA) [1] and data quality assessments (DQA)[2] are critical prerequisites to the main statistical analyses that address the research questions of interest. Despite their importance for scientific studies, IDA and DQA are commonly insufficiently applied and lack transparency.

This talk provides an update on recent guidance for the comprehensive and efficient implementation of IDA and DQA. Best practice examples from observational health studies, specifically the Study of Health in Pomerania (SHIP) and the Survey of Health, Ageing and Retirement in Europe (SHARE) will be used to illustrate IDA and DQA[3]. Additionally, an extended approach to writing statistical analysis plans will be introduced, explicitly incorporating IDA elements and demonstrating their connection to subsequent main statistical analyses.

1. Huebner M, le Cessie S, Schmidt CO, Vach W. A Contemporary Conceptual Framework for Initial Data Analysis. Observational Studies 2018; 4(1): 171-92.
2. Struckmann S, Marino J, Kasbohm E, Salogni E, Schmidt CO. dataquieR 2: An updated R package for FAIR data quality assessments in observational studies and electronic health record data. Journal of Open Source Software 2024; 9(98): 6581.

3. Lusa L, Proust-Lima C, Schmidt CO, et al. Initial data analysis for longitudinal studies to build a solid foundation for reproducible analysis. PLoS ONE 2024; 19(5): e0295726.

A categorization of performance measures for estimated non-linear associations between an outcome and continuous predictors

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In regression analysis, associations between continuous predictors and the outcome are often assumed to be linear. However, accounting for non-linear associations can enhance model fit. Numerous flexible modeling techniques, such as (fractional) polynomials and spline-based methods, are available for this purpose. Such methods can be systematically compared in simulation studies, which require appropriate performance measures to assess the accuracy of estimated curves against the true data-generating functions. Crucially, selecting suitable performance measures is essential for conducting neutral simulation studies—those in which the authors, as a group, are approximately equally familiar with all compared methods and have no vested interest in any particular method.

While various performance measures for estimated non-linear associations have been proposed in the literature, a comprehensive overview is currently lacking. To fill this gap, we present a categorization of performance measures for evaluating estimated non-linear associations between an outcome and continuous predictors. This categorization includes many commonly used measures. The measures can not only be used in simulation studies, but also in application studies to compare different estimates to each other. The behavior of different performance measures is further illustrated using some examples and a Shiny app.

Analyzing Patient Reported Outcome Measures (PROMs) in oncology trials

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In 2021 STRATOS joined the EU SISAQOL-IMI consortium for the development of guidance when estimating treatment effects on PROMs in oncology trials. The estimand framework is key here and meets important challenges as many patients encounter intercurrent disease progression, treatment discontinuation and death as the terminal event. Policy oriented estimands are then designed to involve continued PROM measurements after non-terminal events occur. For single arm trials, we show how popular alternative estimands yield different answers for a different purpose 1. We focus on the two-dimensional outcome, survival time and disease outcome while alive, for a causal estimand with prime

interpretation and relevance. It overcomes limitations of 1) the (timevarying) survivor average causal effect and 2) the hypothetical estimand often presented following mixed models. For estimation, we compare `double inverse probability weighting' with `outcome regression followed by adapted standardization'. This handles censoring and death in a distinct manner under assumptions of conditional non-informative treatment, survival and censoring. An important secondary problem is the joint occurrence of missing data and intercurrent events with non-positivity and/or missingness not at random. A case study on evaluating PROMs in late stage oncology will illustrate issues, available solutions and suggestions for further research.

1. Thomassen et al. The role of the estimand framework in the analysis of patient-reported outcomes in single-arm trials: a case study in oncology. BMC Medical Research Methodology (2024);24:290.