Title: Evidence synthesis accounting for uncertainty in estimating heterogeneity

Presenter: Tim Friede

Abstract

Meta-analyses of clinical trials are a cornerstone of evidence-based medicine. In clinical medicine, often only a small number of studies, say 2 – 5, are available to address a specific research question. In these settings substantial uncertainty is attached to estimates of between-trial heterogeneity in treatment effects. However, standard methods fail to account for this uncertainty resulting in coverage probabilities well below the nominal level for confidence intervals of the overall treatment effect (Bender et al, 2018). We start by reviewing frequentist approaches that account appropriately for this uncertainty by rescaling the standard error and use of t-quantiles rather than normal quantiles in the construction of the confidence intervals (Hartung und Knapp, 2001a,b; Röver et al, 2015). As an alternative we consider Bayesian approaches to random-effects meta-analysis (Friede et al, 2017) and consider practical aspects of their implementation including the choice of priors (Röver et al, 2021, 2023) and the role of trace plots in their interpretation (Röver et al, 2024). Finally, we discuss how predictive distributions and shrinkage estimators can be used to facilitate the integration of data from different sources such as a new randomized controlled trial (RCT) and external real world data (RWD) such as clinical registries (Röver & Friede, 2020).

Some references

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Title: WATCH: A Workflow to Assess Treatment Effect Heterogeneity in Drug Development

Presenter: Björn Bornkamp

Abstract

In this talk the Workflow for Assessing Treatment effeCt Heterogeneity (WATCH) in clinical drug development will be introduced. WATCH is designed to address the challenges of investigating treatment effect heterogeneity (TEH) in randomized clinical trials, where sample size and multiplicity limit the reliability of findings. The workflow offers a general overview of how treatment effects vary by baseline covariates in the observed data and guides the interpretation of the observed findings based on external evidence and the best scientific understanding. The workflow is exploratory and not inferential/confirmatory in nature but should be preplanned before database lock and analysis start. It is focused on providing a general overview rather than a single specific finding or subgroup with a differential effect.

Title: Understanding the association between air pollution and dementia by using early biomarkers of disease and omics profiling of brain samples

Presenter: Anke Hüls

Abstract

Alzheimer's disease (AD) and related dementias (ADRD) are the 6th leading cause of death in the US, affecting over six million people, with projections reaching 13.8 million by 2060. Identifying modifiable risk factors, such as air pollution and fine particulate matter ($PM_{2.5}$), is crucial for prevention. This presentation will showcase our research on how $PM_{2.5}$ impacts the pre-clinical stage of AD/ADRD and the biological mechanisms underlying this association. Our findings aim to enhance understanding of how air pollution influences AD/ADRD risk, potentially moving us closer to establishing causality.

Title: Bayesian variable selection for multi-omics modelling and outcome prediction in precision oncology

Presenter: Manuela Zucknick

Abstract

In precision cancer medicine, the goal is to use diverse data modalities, such as (multi-) omics data, histopathology images, and clinical information, to tailor treatments and make survival predictions for patients, despite the challenge of limited sample sizes. To address this multi-response model setting with high-dimensional and heterogeneous input data, we aim to enhance model performance by leveraging data structure, designing structured priors to combine data sources, borrowing information across correlated response variables, and integrating external biological knowledge, such as drug target pathways. Our approach involves a multivariate Bayesian variable and covariance selection setup with several extensions. One such extension utilizes a Markov random field prior for latent variable selection to exploit known structures, like molecular pathways linked to specific drugs. Another recent development incorporates interaction effects with moderating variables to account for heterogeneity in the impacts of individual omics variables on outcomes.