Ensuring covariate adjustment methods for TTE outcomes are fit for use

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Methodological research has “phases” too!

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Biometrical Journal

RESEARCH ARTICLE

Phases of methodological research in biostatistics—Building the evidence base for new methods

Georg Heinze[1] | Anne-Laure Boulesteix[2] | Michael Kammer[1,3] | Tim P. Morris[4] | Ian R. White[4] | on behalf of the Simulation Panel of the STRATOS initiative

The ideas offer:

1. Frustrated methodologists a way to understand why no-one is using their ideas
2. Everyone else a way to articulate their hesitation when it comes to new methods

Covariate adjustment approaches

When considering covariate adjustment approaches for continuous and binary outcome measures, methods are relatively mature (late phase).

We know a bit about:

- Convergence of estimation methods
- How wrong things can go under model misspecification
- Efficiency – can we lose? See Jack Kuipers & Giusi Moffa's recent papers
- Accuracy of variance estimation in finite samples (or lack thereof)
- Missing baseline values: problematic for conditional population-level summary measures; fine for marginal
- Missing outcome data: analysis under departures from missing-at-random

Perspective

CLINICAL TRIALS

Clinical Trials
1–13

DOI: 10.1177/17407745241251568
journals.sagepub.com/home/ctj
Sage

Covariate adjustment in randomized controlled trials: General concepts and practical considerations

Kelly Van Lancker[1], Frank Bretz[2,3] and Oliver Dukes[1]

Morris *et al. Trials* (2022) 23:328
https://doi.org/10.1186/s13063-022-06097-z

Trials

METHODOLOGY Open Access

Planning a method for covariate adjustment in individually randomised trials: a practical guide

Tim P. Morris[1,2*], A. Sarah Walker[1], Elizabeth J. Williamson[2] and Ian R. White[1]

Time-to-event: a different story

The main population-level summary measures have major cons

Measure	Pro	Con
Hazard ratio	One-number summary	Non-collapsible Proportional-hazards?
Difference in restricted mean survival time	Collapsible Interpretable(?)	Choice of horizon time Power loss? (Dominic M's talk)
Difference in survival at specified time	Collapsible Interpretable	Choice of landmark time Power loss

For estimation methods corresponding to these estimands, we need a level of knowledge comparable to continuous and binary outcomes.