

# The STRATOS initiative - TG8 Report

TG8 co-Chairs

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**STR**engthening **AN**alytical **TH**inking for **OB**servational **ST**udies

- New TG8 members
- Recent TG8 in-person meeting
- TG8 publications
- Selected presentations by TG8 members at STRATOS sessions
- Ongoing and new TG8 projects

# New TG8 Members

- Frederico Ambrogi, Milan (also a member of TG9)
- Hein Putter, Leiden

# Recent TG8 in-person meeting

In July 2022, most TG8 members met in-person during the IBC conference in Riga, Latvia.

Discussions focused mostly on the goals and general approach for the new TG8 project on **multi-state modeling**.

- 1 Andersen PK, Perme MP, van Houwelingen HC, Cook RJ, Joly P, Martinussen T, Taylor JMG, Abrahamowicz M, Therneau TM. Analysis of time-to-event for observational studies: Guidance to the use of intensity models. *Statistics in Medicine*. 2021 Jan; 40(1): 185– 211. doi.org/10.1002/sim.8757.\*
- 2 McLernon DJ, Giardiello D, Van Calster B, Wynants L, van Geloven N, van Smeden M, Therneau T, Steyerberg EW; Topic Groups 6 and 8 of the STRATOS Initiative. Assessing Performance and Clinical Usefulness in Prediction Models With Survival Outcomes: Practical Guidance for Cox Proportional Hazards Models. *Annals of Internal Medicine* 2023 Jan;176(1):105-114. doi: 10.7326/M22-0844.
- 3 Andersen PK, Abrahamowicz M, Therneau TM, on behalf of STRATOS TG8 (2019): STREngthening Analytical Thinking for Observational Studies (STRATOS): Introducing the Survival Analysis Topic Group (TG8). *Biometric Bulletin*. 2019;36(3): 12-13.

\*This paper was identified by the publisher (Wiley) as one of the Most Cited among all articles published in *Statistics in Medicine* in 2021.

# Selected Presentations by TG8 Members at STRATOS Invited Sessions or Mini-Symposia

- 1 Abrahamowicz M. (with Richard Cook, Malka Gorfine, Pierre Joly, Dr. on behalf of TG8). Selected challenges in multivariable time-to-event analyses. Invited Session "Various issues in multivariable model building". Royal Statistical Society (RSS) International Conference. Manchester, UK. September 6-9, 2021.
- 2 Therneau T (on behalf of TG6 & TG8). Assessing performance of survival predictions models. Invited Session "Prediction with observational data: STRATOS perspective". 31st International Biometric Conference (IBC), Riga, Latvia, July 10-15, 2022.
- 3 Andersen P K. President's Invited Speaker. The Joy of Pseudo-Values. 42nd Annual Conference of the International Society for Clinical Biostatistics (ISCB), Lyon, France, July 18-22, 2021. (NOT a STRATOS talk. . .).
- 4 Therneau T. Hazard models for long term outcomes, with application to dementia. Invited Symposium "Statistical Challenges in Observational Research and Guidance Recommendations from the STRATOS Initiative". Annual conference of the Society for Epidemiological Research (SER) (Virtual), San Diego, CA, USA, June 22, 2021.
- 5 Abrahamowicz M. Multiple analytical challenges in observational studies of health: goals and approaches of the STRATOS initiative. Invited Symposium "Statistical Challenges in Observational Research and Guidance Recommendations from the STRATOS Initiative". Annual conference of the Society for Epidemiological Research (SER) (Virtual), San Diego, CA, USA, June 22, 2021.

# Ongoing and New TG8 Projects

Selected challenges in multivariable regression analyses of time-to-event data.

Michal Abrahamowicz, Richard Cook, Malka Gorfine, Pierre Joly (& possibly, Maja Pohar Perme, Frederico Ambrogi, and other TG8 members.)

The overarching goal is to increase the researchers awareness and understanding of the full spectrum of modeling options available for multivariable regression analyses of censored survival data. Whereas applications of survival analysis are dominated by Cox PH model, alternative regression models (AFT and additive hazards) have recently become increasingly most popular. Yet, empirical criteria to assess which model is more appropriate for a given dataset are not well developed. Furthermore, there is a need to develop and validate efficient and accurate methods to assess the validity of the underlying assumptions that postulate that the respective measure of the association (hazard ratio, event time ratio or hazards difference) remain constant over time and, if necessary, to re-model the data to account for time-dependent (TD) effects. Furthermore, flexible modeling of non-linear effects of continuous covariates has to be addressed, possibly jointly with their TD effects. We aim at reviewing both the relevant statistical models, including their flexible extensions that avoid some conventional restrictive assumptions, and the software available for model fitting and regression diagnostics. Initially we focus on time-invariant covariates, but later will discuss further challenges related to modeling time-varying covariates. Additional issues related to variable selection, choice of the estimands and causal inference, and prediction, will be also addressed. Both real-world and simulated data will be used to illustrate implementation of different models, as well as interpretation and comparison of their results.

## Multistate survival models

Malka Gorfine, Per Kragh Andersen, Terry Therneau, Jeremy Taylor, Hein Putter, Maja Pohar Perme, Michal Abrahamowicz, Richard Cook, Pierre Joly, possibly other TG8 members.

Multistate survival models can effectively capture an individual's progression through different states until reaching a terminal state, with events defined as the transitions between states. Previous reviews of multistate regression models have included a range of Cox-type models for each transition, either Markovian or semi-Markovian, and available software as of 2009. Currently, we are preparing a paper that summarizes the latest useful advancements in multistate survival analysis, encompassing new practical techniques and software tools. These developments comprise estimands and their interpretation, pseudo values, frailty approach, interval censoring, time-varying covariates, and time-dependent effects.

# Suggested Topics for Potential (Future) Inter-TG Collaborations

- With TG1: imputing **missing values** in survival analyses.
- With TG2: **variable selection** and functional forms in survival analyses, possibly with time-varying covariates.
- With TG3: **initial data analyses** for survival data with time-varying covariates/exposures.
- With TG7: choice of the **causal estimands** in survival analysis.
- With TG9: survival analysis for HD data.

# The End

Questions? Comments?