Special interest group “Estimands in Oncology”, sponsored by PSI and EFSPI

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BACKGROUND

With the release of the initial draft ICH E9 (R1) addendum in 2017, it was anticipated that the estimand framework will have a major impact on formulation of clinical trial objectives, trial design, sample size, conduct, data collection, and analysis. For time-to-event endpoints which are of key interest in oncology (such as progression-free or overall survival), many open questions concerning estimand definition, data collection, analysis methodology, and interpretation remained.

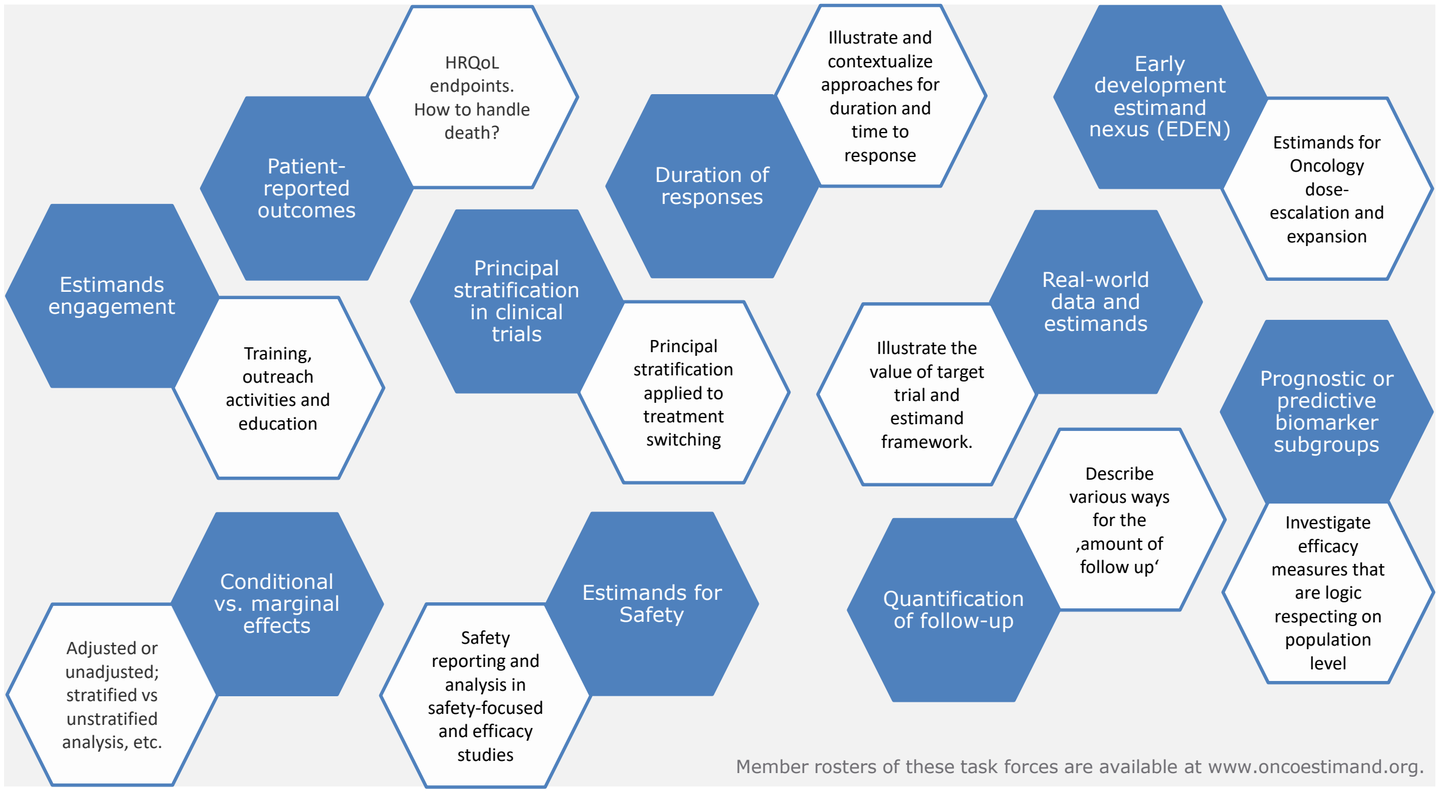
HISTORY and SCOPE

In February 2018, a cross-industry international working group (www.oncoestimand.org) was founded bringing together statisticians from industry, regulators, and academia to share experience and ensure common understanding and consistent definitions for key estimands, strategies for intercurrent events, and corresponding analysis in oncology.
In November 2018, the working group was established by EFSPI as European special interest group ‘Estimands in oncology’, sponsored by PSI and EFSPI. It became an ASA scientific working group in June 2019.

Key questions that are discussed are:

- How can time-to-event (T2E) endpoints be embedded in the addendum framework?
- What are key estimands and intercurrent events in Oncology?
- How do the five strategies to handle intercurrent events proposed in the ICH E9 addendum apply to T2E endpoints?
- How can established methods to answer questions in oncology be embedded in the estimand framework?
- Are there parts in the drug development lifecycle that require a causal interpretation of an estimand?
- What are estimands for T2E endpoints that are amenable to a causal interpretation?

TASK FORCES and CURRENT MAIN TOPICS



Member rosters of these task forces are available at www.oncoestimand.org.

BECOME A MEMBER

The general spirit of the working group is inclusive. If you’d like to contribute in one or the other way, we propose you first reach out to your company’s representative(s) (if applicable) and align within your company who is best placed to contribute to which task force.

PUBLICATIONS

- Lawrance, R., Degtyarev, E., Griffiths, P., Trask, P., Lau, H., D’Alessio, D., Griebsch, I., Wallenstein, G., Cocks, K., Rufibach, K. What is an estimand & how does it relate to quantifying the effect of treatment on patient-reported quality of life outcomes in clinical trials (2020). Journal of Patient-Reported Outcomes, 4(1), 68.
- Degtyarev, E., Rufibach, K., Shentu, Y., Yung, G., Casey, M., Englert, S., Liu, F., Liu, Y., Sailer, O., Siegel, J., Sun, S., Tang, R., Zhou, J. Assessing the impact of COVID-19 on the objective and analysis of oncology clinical trials – application of the estimand framework (2020). Statistics in Biopharmaceutical Research, 12(4), 427-437.
- Casey M., Degtyarev E., Lechuga M.J., Aimone P., Ravaud A., Motzer R., Liu F., Stalbovskaya V., Tang R., Butler E., Sailer O., Halabi S., George D. Estimand framework: Are we asking the right question? A case study in the solid tumor setting (2020). Pharmaceutical Statistics, 20, 324–334.
- Sun, S., Weber, J., Butler, E., Rufibach, K., Roychoudhury, S. Estimands in Hematology Trials (2021). Pharmaceutical Statistics, 20, 793-805.
- Bornkamp, B., Rufibach, K., Lin, J., Liu, Y., Mehrotra, D., Roychoudhury, S., Schmidli, H., Shentu, Y., Wolbers, M. Principal Stratum Strategy: Potential Role in Drug Development (2021). Pharmaceutical Statistics, 20, 737-751.
- Manitz, J., Kan-Dobrosky, N., Buchner, H., Casadebaig, M.L., Degtyarev, E., Dey, J., Haddad, V., Fei, J., Martin, E., Mo, M., Rufibach, K., Shentu, Y., Stalbovskaya, V., Tang, R., Yung, G., Zhu, J. Estimands for Overall Survival in Clinical Trials with Treatment Switching in Oncology (2021). Pharmaceutical Statistics, accepted.
- Hampson, L.V., Degtyarev, E., Tang, R., Lin, J., Rufibach, K., Zheng, C. Comment on Biostatistical considerations when using RWD and RWE in clinical studies for regulatory purposes: A landscape assessment (2021). Statistics in Biopharmaceutical Research, to appear.
- Siegel, J.M., Grinsted, L., Liu, F., Weber, J., Englert, S., Casey, M. Censoring and censoring mechanisms in oncology in light of the estimands framework (2022). Submitted.
- Siegel, J.M. Weber, J., Englert, S. The Role of Occlusion: Potential Extension of the ICH E9 (R1) Addendum on Estimands and Sensitivity Analysis for Time-to-Event Oncology Studies (2022). Submitted

Regularly updated list of Publications and Events with contributions from the working group are available on www.oncoestimand.org.

STATUS

As of 30 March 2022, the working group
- has 85 members (32 from Europe, 43 from US, and 10 from Asia) representing 43 companies / institutions,
- regularly interacts with eight Health Authorities globally,
- regularly organizes sessions and presents at conferences,
- has started to interact with academic colleagues.

After a first phase where five subteams have written several publication (see bottom panel), the working group operates now within 10 agile task forces to review and provide answers to key clinical trial issues in line with the estimand framework.

ACTIVITIES

Beyond work in the task forces, the aim of the working group is to provide answers to the above questions through a variety of activities. These will include:
- Collaborating with experts to refine and possibly extend available methods.
- Publishing reviews of the available methods, case studies, and white papers with recommendations, for statisticians and non-statisticians.
- Interacting with regulators and the broader clinical community to obtain a better understanding of their requirements. Work with them to agree on common definitions of estimands in oncology.
- Promoting good practice through templates for study protocols and statistical analysis plans.
- Providing trainings, workshops and talks. Example: Training for a general audience available on YouTube ‘Estimands in Oncology – How and Why’

WATCH HERE!

COLLABORATIONS

The working group closely collaborates with the EFSPI/EFPIA Estimands Implementation WG (EIWG) to implement estimands in drug development by collaborating with non-statistical partner functions. Stefan Englert is a member of both working groups and leads that collaboration.

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