Assessing the impact of COVID-19 on oncology clinical trials – application of the estimand framework

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PSI Conference Webinar: Impact of COVID-19 to estimands
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This talk

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Endpoint: **overall survival** in **superiority** trial.

How does COVID-19 change pre-pandemic clinical trial objective?

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It does not!

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   - Therapy available.

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- Trials started before pandemic: designed to inform clinical practice in a world without pandemic.

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Clinical trial objective pre-pandemic = post-pandemic.

Data collected and trial results useful for informing clinical practice in a world without COVID-19 pandemic?

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Estimate from initially planned analysis still provide answer to clinical trial objective?

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- Introduce **supplementary** estimands.

If you update estimand:

- Effect size?
- Sample size?
- Missing data handling?

ESTIMAND

COVID-19 IMPACT ASSESSMENT

VARIABLE

The variable (or endpoint) to be obtained for each patient.

Q: Does the current endpoint reflect the treatment effect in the original scientific objective?

POPULATION

The population of patients targeted by the clinical question.

Q: Are the enrolled patients representative of the target population?

INTERCURRENT EVENTS (ICEs)

Other ICEs not already addressed by treatment, population and variable, and how they are handled.

Q: Can the original clinical trial objective be addressed without defining new strategies for ICEs related to COVID-19? (e.g. apply pre-specified rules for discontinuations to discontinuations due to COVID-19)

TREATMENT

The treatment condition of interest.

Q: Are the treatment conditions (e.g. non-compliance, drug discontinuation, subsequent therapy) representative of what would have been administered pre-COVID-19?

SUMMARY

A population-level summary for the variable which provides a basis for treatment comparison.

Q: Is the summary measure still interpretable?

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Indirect:

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Indirect:

- Overwhelmed healthcare system.
- Lock-down.

Direct vs. indirect impact of pandemic

Direct:

- Treatment interruption or discontinuation due to **infection**.
- Additional therapies to treat COVID-19.
- Death due to COVID-19.

Indirect:

- Overwhelmed healthcare system.
- Lock-down.
- Treatment interruption or discontinuation due to **logistic reasons, patient or physician decision**.

Death due to COVID-19

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Direct impact

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- **Composite**: count as death.

Death due to COVID-19

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- **Hypothetical**: do not expect COVID-19 related deaths in a post-pandemic world.

Discontinuation from treatment not related to COVID-19 infection

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Indirect impact

Non-related discontinuation

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Hypothetical strategy.

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  - Estimate via **principal stratification**.

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- **Non-inferiority**: usual considerations apply, nothing specific to pandemic situation.

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Paper illustrates power of purpose-built networks.

Joint EFSPI / BBS Seminar: Estimands addendum is final: Anything new for oncology?

Basel Biometrics Section webinar
Basel, 29th June 2020

Kaspar Rufibach (Roche, member of BBS board)
Welcome and scene setting

Regulator's view (Anja Schiel, Norwegian Medicines Agency)
Experience with the estimand framework in oncology

Renaud Capdeville (Novartis), Tina Nielsen (Roche)
Challenges and open questions in hematology: RATIFY and GALLIUM

Break

Hannes Buchner (Staburo) & Ingolf Griebsch (Boehringer Ingelheim)
Treatment switching: challenges, estimands, and estimators

Stefan Englert (AbbVie)
Commentary on previous talks taking COVID-19 into account

Break

Panel discussion
(all speakers + Rob Hemmings from Consilium, Michael Wenger from Novartis)
Estimands – after first experiences anything new for oncology? If at all, what does it add?

Industry working group on estimands in oncology:

- Founded February 2018.
- European special interest group “Estimands in oncology”, sponsored by PSI and EFSPI.
- ASA scientific working group of ASA biopharmaceutical section.
- **38** members representing **22** companies.
- Regularly interacts with **7 health authorities**.

www.oncoestimand.org

Thank you for your attention.

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References I

- Degtyarev, E., Rufibach, K., Shentu, Y., Yung, G., Casey, M., Liu, F., Liu, Y., Sailer, O., Siegel, J., Sun, S., Tang, R. and Zhou, J. (2020). Assessing the impact of covid-19 on the objective and analysis of oncology clinical trials – application of the estimand framework (2020). Tech. rep., Industry working group "estimands in oncology". `https://oncoestimand.github.io/home/docs/onco_estimand_COVID-19_paper_v1.pdf`
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Doing now what patients need next

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Base packages: stats / graphics / grDevices / utils / datasets / methods / base
Other packages:

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