# STRATOS TG7: Causal inference

Bianca De Stavola (UCL, UK)
Els Goetghebeur (Gent, B)
Saskia Le Cessie (Leiden, NL)
Erica Moodie (Mc Gill, Ca)
Ingeborg Waernbaum (Uppsala,S)

Vanessa Didelez (Bremen, G)

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# Content - papers

The 'mother paper' - SIM 2020
**'Formulating causal questions and principled statistical answers'**

With on our website 'ofcaus.org'

- 'Simulation Learner' counterfactual outcome set simulator (point exposure and beyond)
- Various data analyses in SAS, Stata, R
- All code and synthetic data version on the website 'ofcaus.org'

Several (pre conferences) courses taught - yearly course in Paris

Several offspring papers published; e.g. 'Trial emulation and survival analysis for disease incidence registers: A case study on the causal effect of pre-emptive kidney transplantation' SIM, 2022.

Two follow-up papers in similar mode in the making:

- For survival outcomes (team 0 + Vanessa Didelez ) getting ready for course work on this
- For Longitudinal outcomes (Erica Moodie in the lead)


# Developing international standards in the analysis of patient reported outcomes in cancer clinical trials: methodological issues and STRATOS engagement in the European IMI-SISAQOL project

Saskia le Cessie, Limin Liu, Doranne Thomassen and Els Goetghebeur

S.le_Cessie@lumc.nl

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# SISAOL-IMI - guidelines for PROM analysis in oncology

Two papers currently accepted for Lancet Oncology:

- "Setting International Standards in Analysing Patient-Reported Outcomes and Quality of Life Endpoints in Cancer Clinical Trials - Innovative Medicines Initiative (SISAQOL-IMI): Stakeholder Views, Objectives, and Procedures".
- "Single-arm studies involving patient-reported outcome data in oncology: a literature review on current practice"

Input form STRATOS at ISCB22 meeting very helpful
In parallel surveys are run to develop consensus guidelines.

# "From single arm review to guidelines"

Case study developed with 'state of art treatment' inspired by Pfizer published study:

The PROFILE 1005 study, ESMO Open 2017;**2**:e000219. doi:10.1136/ esmoopen-2017-000219

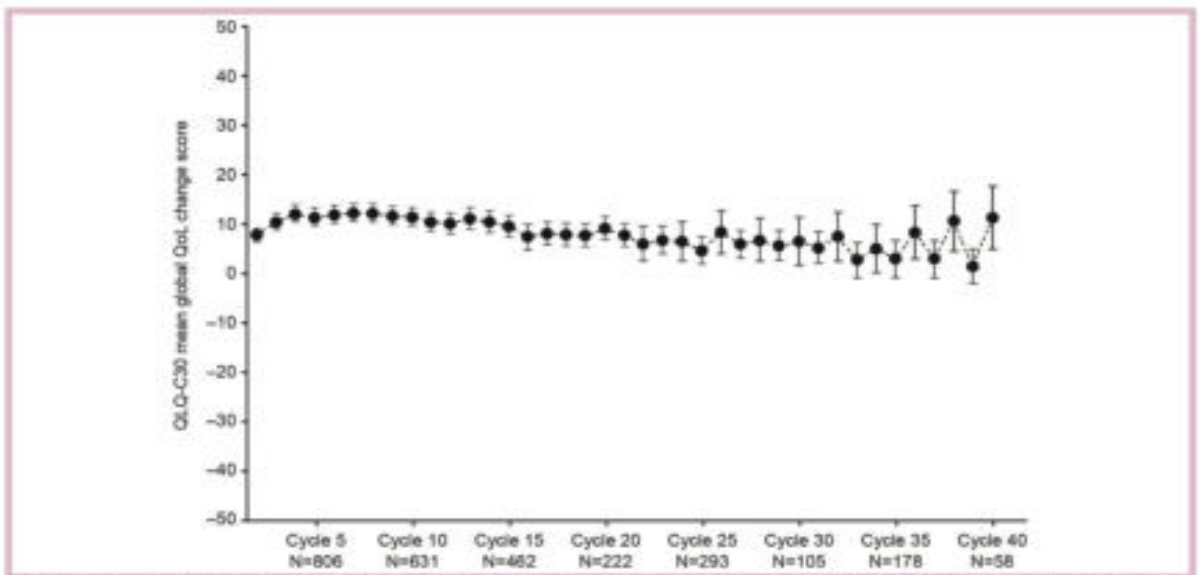


**Figure 2** Mean change from baseline in patient-reported European Organisation for the Research and Treatment of Cancer QLQ-C30 global quality of life (patient-reported outcome-evaluable population).

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# ‘Two more technical papers in the making

- Handling death and missing values (intercurrent events)
- Comparisons with external data

# 1. Handling death


PROs after death do not exist.

Ways to handle death (ICH-E9 addendum)

a. Describe PROs while alive (with % alive)

b. Incorporate death in PRO outcome (composite outcome
   - high PRO value versus low/death
   - assign particular value to death (e.g., 0 for QOL after death).

c. Extrapolate values after death (linear mixed models, imputation
   - Hypothetical strategy (what if death did not occur?)

What is an appropriate strategy, in which circumstances?

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# 2. Comparisons with external data


- Issues, using external historical data
  - Study populations
  - Type of PROs
  - Measurement timing and frequency
  - Within and between patient PRO variation
  - Follow-up time
  - Intercurrent events/death
  - Whether the setting is blinded or un-blinded
- …

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# Core set of variables


Our ideal:

- All studies (single-arm or RCT) in a disease domain should measure the same core set of baseline variables

Why?

To facilitate comparisons of PRO results of single arm studies to other data sources and to perform meta-analysis:

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# What else?

- Work on the glossary at several levels - a few years ago needs to be picked up
- Many talks were and are given
  at Biometrics conference, ISCB, RSS, JSM (23), Isaqol (23) ...
- Much more to do - also with other TGs
- Work with extra partners
- Collaboration is a source of much joy

# Questions?