

# TG7 MOVING FORWARD: EMBRACING JOINT DISAPPEARANCES

July 25, 2024

## TG7 – MEMBERS (@LORENTZ, \*SISAQOL)

Els Goetghebeur\* & Ingeborg Waernbaum (website)

Jack Bowden (launch) [**Michael Wallace**, Martin Wolkewitz]

Saskia le Cessie\*

Bianca De Stavola

Vanessa Didelez

Erica Moodie (excused)

Nan van Geloven (launch)

Young attendants @Lorentz workshop

Dries Reynders\*, Doranne Thomassen\*, Kelly Van Lancker

\*Setting International Standards in Analysing Patient-Reported Outcomes and Quality of Life Endpoints

# TABLE OF CONTENTS

I. So far

II. Now

III. What next

I. SO FAR

## THE 'MOTHER' PAPER

On '*principled* causal methods' (continuous outcome)

- ***Causal Estimands***
- Estimators
- Counterfactual **synthetic dataset**
- **Simulations** in real and counterfactual world

Analysis using R + SAS + Stata (SIM, 2020 & github)

# FOLLOW-UP FROM CONTINUOUS OUTCOME

- The **survival outcome** edition
  - Range of estimands (RD, HR, Acceleration Factors, SACE, ...)
  - Censoring
  
- IMI-SISA**QOL** with STRATOS:  
**repeated outcomes in mortal population**

*Limin et al., 2023*

## QOL COMPLICATIONS: LATE STAGE ONCO

- Single arm trial (+ external control)
- Two-dimensional outcome  
 $T_a$  and  $QOL_a(t)|T_a > t$
- Inter Current Events (Estimands)
- Missing Data (!)



## II. NOW



## INTER CURRENT EVENTS– THE STEPS



Which Estimand

What data is (not) missing?

# INTENSE COLLABORATION @ IMI- SISAQOL



**SISAQOL | IMI**

Setting International Standards in Analysing Patient-Reported  
Outcomes and Quality of Life Endpoints

WP3 involves STRATOS members:

Saskia le Cessie + Doranne Thomassen

Els Goetghebeur + Dries Reynders

Willi Sauerbrei

<https://eortchq.sharepoint.com/sites/SISAQOL/SitePages/Home.aspx>



**Clinical trial** in advanced lung cancer, single arm

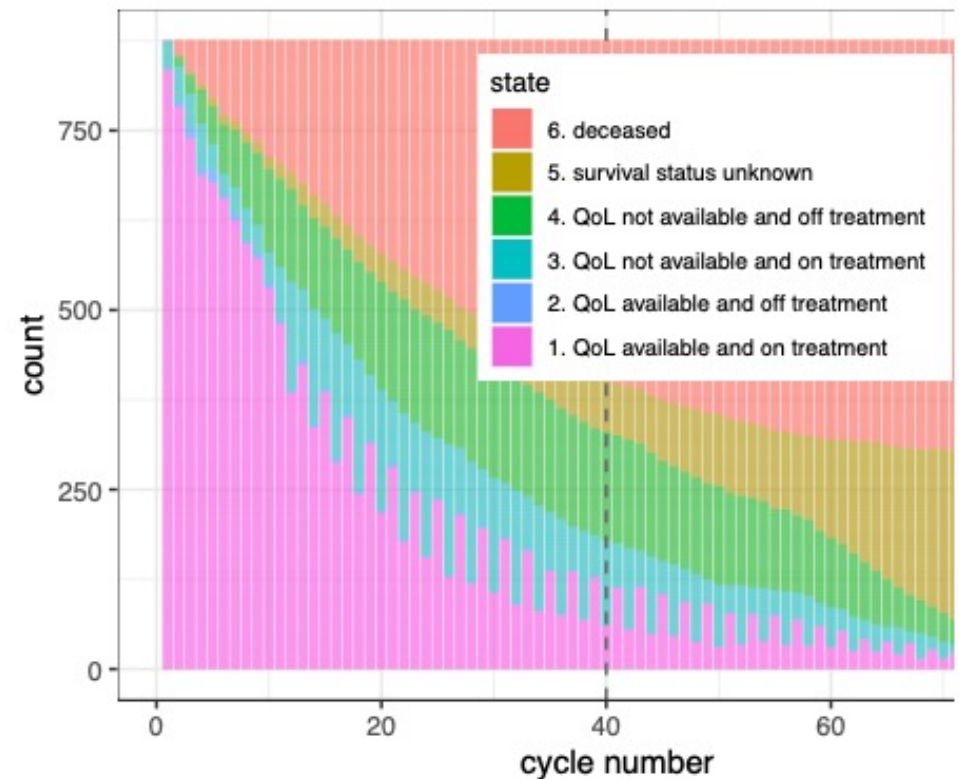


**Repeated PRO measurements** scheduled in 3 week cycles  
Global quality of life (**QoL, 0-100**)



**Intercurrent events**  
Progression of disease (**PD**)  
Treatment discontinuation (**TD**)  
**Death**

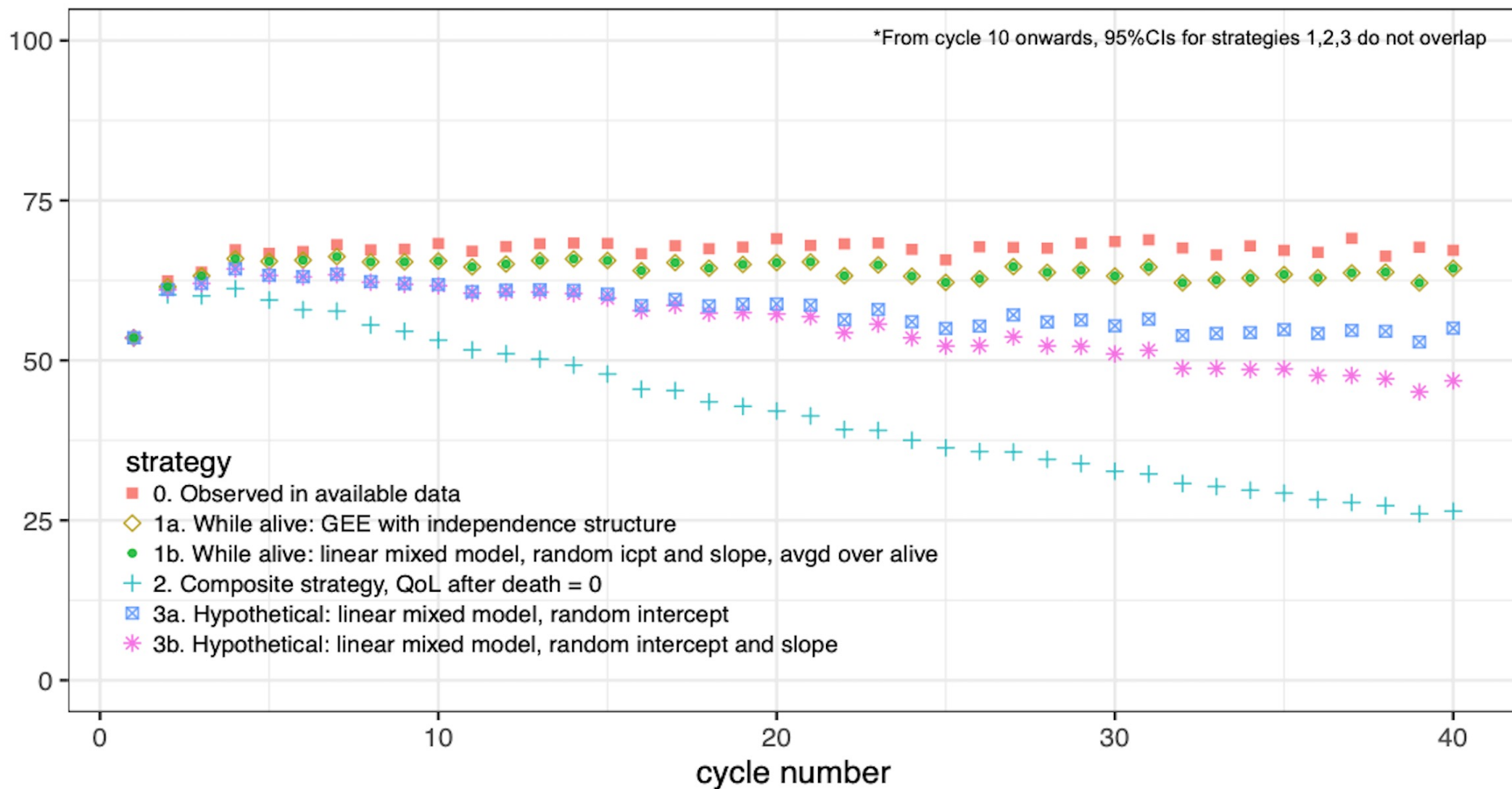
QoL outcome availability over time



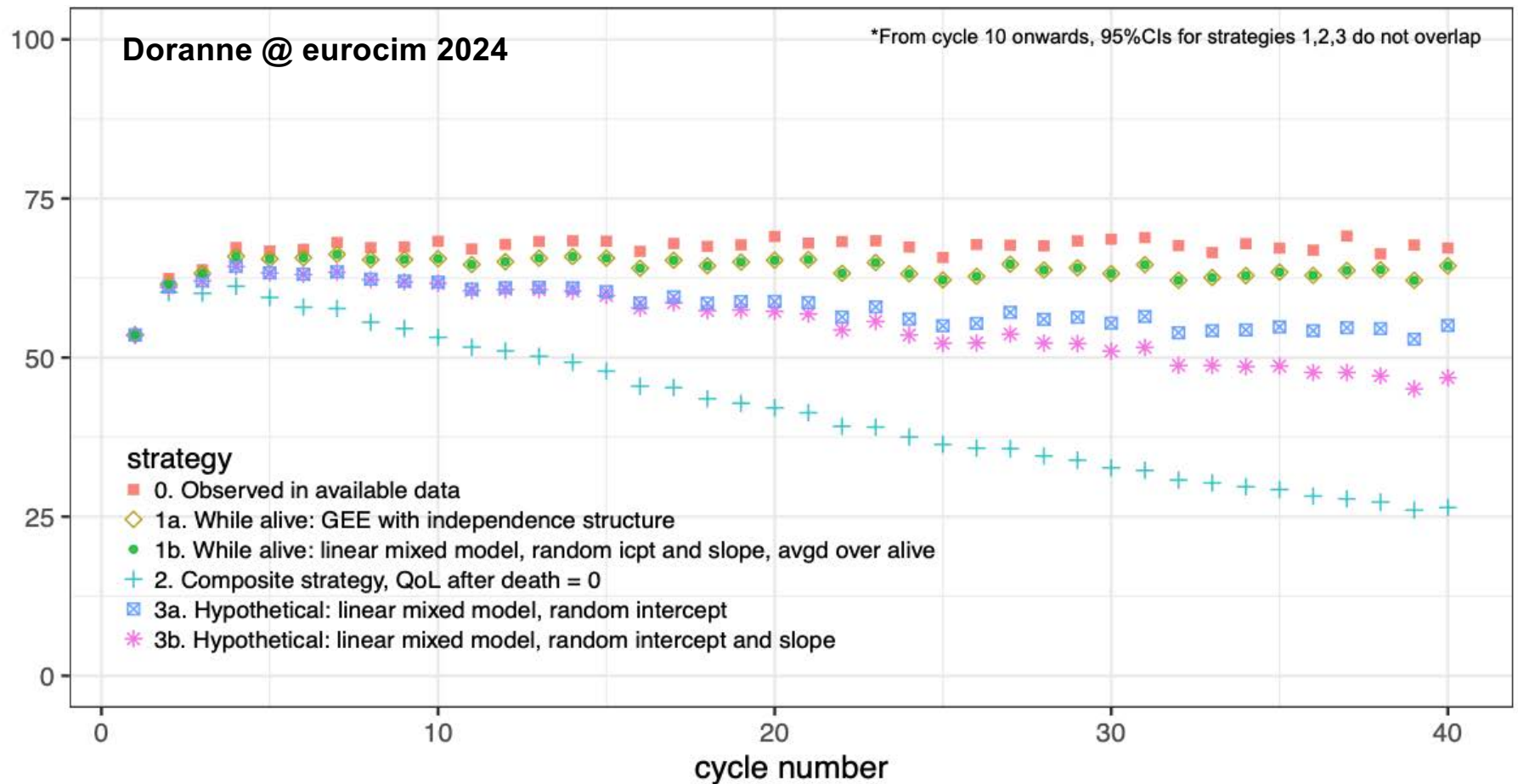
## Different strategies to handle death lead to diverging results

| INTERCURRENT EVENT STRATEGIES |           |              |                  | ANALYSIS   |   |
|-------------------------------|-----------|--------------|------------------|--|---|
| While no IE                   | Composite | Hypothetical | Treatment policy | QoL data included in the analysis (assuming missing data is handled separately)    | Estimation of mean QoL at each cycle (cycle number categorical in all analyses)   |
| Death                         |           |              | PD, TD           | All outcomes until death, including after TD/PD.                                   | Generalized estimating equations ( <b>GEE</b> ) + independence correlation structure<br><br>Linear mixed model ( <b>LMM</b> ), average predictions only over those alive, bootstrap SEs |
|                               | Death     |              | PD, TD           | All outcomes until death, including after TD/PD.<br><br>After death, QoL set to 0. | GEE with independence correlation structure<br><br>LMM also possible  |
|                               |           | Death        | PD, TD           | All outcomes until death, including after TD/PD.                                   | Marginal means from LMM   |
| Death                         |           | TD           | PD               | All outcomes before TD or death, including after PD.                               | LMM, average individual predictions only over those alive, bootstrap SEs  |

# Doranne @ eurocim 2024



Estimated mean global QoL



|                  |     |      |      |      |      |      |      |      |      |
|------------------|-----|------|------|------|------|------|------|------|------|
| survival         | 1   | 0.88 | 0.8  | 0.72 | 0.64 | 0.58 | 0.51 | 0.47 | 0.43 |
| progression-free | 1   | 0.8  | 0.59 | 0.47 | 0.36 | 0.29 | 0.23 | 0.18 | 0.16 |
| on treatment     | 1   | 0.78 | 0.63 | 0.53 | 0.42 | 0.36 | 0.29 | 0.24 | 0.2  |
| PROs avail.      | 834 | 694  | 538  | 390  | 221  | 238  | 107  | 140  | 61   |

# MISSING DATA

