

# Topic Group 5 (Study Design) Update in Leiden

September 20, 2024

**Co-Chairs:** Mitch Gail, Suzanne Cadarette\*

**Members:** Gary Collins, Susan Halabi, Rima Izem, Thomas Lumley,  
Paola Rebora, Peggy Sekula, Neus Valveny

**Guest:** Nicholas Bakewell\*

*\*attended meetings / workshops in Leiden*

# Website

## Aim

To provide accessible and accurate guidance in the design of observational studies.

## Key Principles

There already exist several guidelines for **reporting** the findings of observational research, notably the STROBE Statement and various extensions, e.g. when using routinely collected data (RECORD), or when examining genetic associations (STREGA).

TG5 focus is on developing guidance for **planning** observational studies. Key steps are: 1) define study objectives, 2) select the best design that minimizes threats to validity while acknowledging practical constraints, and 3) outline the main analytical approaches to ensure analyses are in accord with study aims.



Topic group 5 is a member of the [STRATOS Initiative](#) (STREngthening Analytical Thinking for Observational Studies) which is a large collaboration of experts in many different areas of biostatistical research. Ongoing research, discussions and activities within STRATOS are conducted in nine [topic groups](#) and several cross-cutting [panels](#).

# Agenda

- **Update from Activities in Leiden**

- **Brief Response to Questions**

1. Why is it important that this TG/Panel exists?
2. What have you done in the past 10 years?
3. What are the relevant methodological issues?
4. What do you still plan to do in the next three years?
5. What have been/continue to be the main challenges?
6. Does this TG/Panel still need to exist?



# Update from Activities in Leiden



- Arrived with **NO** TG / panel collaborations
- Leaving with 5 (just a start!)

## 1. Glossary Panel

- Study design figures and terminology with variety of examples
- Specific to osteoporosis, target *Osteoporosis International*

## 2. TG4 (measurement error & misclassification)

- Large healthcare utilization (claims) data and validation
- Fracture examples, external data

# Update from Activities in Leiden



## 3. TG8 (survival analysis)

- Immortal time and other time related biases
- TG5 proposed new immortal time issue related to drug discontinuation

## 4. TG3 (IDA)

- Leverage IDA and SAPI and translate to osteoporosis field

## 5. Theme: Estimands and survival analysis

- Overview: ICH-E9, Causal Roadmap & Target Trial Emulation
  - Pull-in other TG5 members (e.g., Rima Izem)
- Translate with examples in osteoporosis field

# 1. Why is it important that this TG/Panel exists?

- Strength in analytical thinking beings with study design!
- TG5



3. What are the relevant methodological issues?

Thinking / Planning



## 2. What have you done in the past 10 years?

1. Gail MH, Altman DG, Cadarette SM, Collins G, Evans SJW, Sekula P, Williamson E, Woodward M for the STRATOS initiative (STREngthening Analytical Thinking for Observational Studies). [Design choices for observational studies of the effect of exposure on disease incidence.](#) *BMJ Open* 2019;9(12):e031031.

*The purpose of this paper is to help readers choose an appropriate observational study design for measuring an association between an exposure and disease incidence. We discuss cohort studies, sub-samples from cohorts (case-cohort and nested case-control designs), population-based case-control studies and hospital-based case-control studies. Although these designs are well described in textbooks on epidemiology, our purpose is to introduce a broad readership to these designs and their strengths and weaknesses.*



## 2. What have you done in the past 10 years?

2. Gail M, Cadarette S on behalf of TG5. STREngthening Analytical Thinking for Observational Studies (STRATOS): Introducing the Study Design Topic Group (TG5). *Biometric Bulletin* 2019; 36(2): 12-13.

- Website
- Some conference presentations



# 5. What have been/continue to be the main challenges?

- Member engagement – pandemic did not help!
- Largely: Mitch, Peggy
- Suzanne needed to finish self-controlled designs paper (outside STRATOS)
- 2024: new members!!

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## REVIEW

## ACKNOWLEDGMENTS

## KEY

## Control yourself: self-controlled stu

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# Ongoing TG5 Projects

## 1. Prognostic studies

- **Lead(s):** Peggy Sekula
- **Status:** under review by Publication Panel

## 2. Long-term dynamic therapy [DM] on outcome [hip fracture]

- **Lead(s):** Suzanne & Nicholas
- **Status:** full draft near ready for review by co-authors

## 3. Sample size: rare diseases, new considerations, e.g., hybrid designs

- **Leads:** Neus, Susan, Paola
- **Status:** planning stage



# TG5 Ongoing Projects

Ideas (early discussions)

## 4. Challenges with ML/AI & How to Overcome Them

- **Lead:** Susan Halabi
- **Status:** idea stage

## 5. Hybrid Designs

- **Lead(s):** Rima and Paola
- **Status:** idea stage

- Rima Izem: recently presented on target trial/estimands:
  - EMA/HMA RWE methods meeting in Amsterdam ([Joint HMA/EMA Big Data Steering Group workshop on real-world evidence \(RWE\) methods | European Medicines Agency \(europa.eu\)](#))

**4. What do you plan to do in the next three years?** Covered earlier 😊



**6. Does this TG still need to exist?**



**2026**