



McGill

Department of  
Epidemiology, Biostatistics  
and Occupational Health

## BIostatISTICS SEMINAR

Winter 2018

### Martin Wolkewitz, PhD

Mathematician

Institute of Medical Biometry and Statistics, Freiburg Germany

## Multi-State Approaches To Unmask and Repair Survival Biases In Epidemiology

Tuesday, 13 March 2018

3:30 pm – 4:30 pm – Purvis Hall – Room 24 - [ALL ARE WELCOME](#)

**Abstract:** Survival bias is a common threat in time-to-event analyses of epidemiological studies. They might appear in the analysis of observational studies (such as cohort, case-control or case-cohort) and randomized trials; but they might also be introduced by design in prevalence studies. We discuss following types of bias: competing risks bias, time-dependent (aka immortal-time) bias, length bias, bias due to 'conditioning on the future' and a so-called 'healthy-candidate' bias. Using multi-state methodology, we show that each type can easily lead to serious misleading conclusions. Further, we show that claimed effects in popular published examples disappear when correctly analyzed. Multi-state models are essential to study clinically important endpoints which dependent on multiple time-dependent events and are usually hidden in classical analyses. Recent interesting examples are discussed from hospital epidemiology (cohorts and prevalence studies of nosocomial infections), a randomized trial regarding recurrent *C. difficile* infections, an observational treatment study of influenza patients and a study about survival of heads of government.

#### References:

- Wolkewitz, M, Schumacher, M (2016). Neuraminidase Inhibitors and Hospital Mortality in British Patients with H1N1 Influenza A: A Re-Analysis of Observational Data. *PLoS ONE*, 11, 9:e0160430.
- Wolkewitz, M, Schumacher, M (2017). Survival biases lead to flawed conclusions in observational treatment studies of influenza patients. *J Clin Epidemiol*, 84:121-129.
- Sommer, H, Timsit, JF, Wolkewitz, M (2017). Bezlotoxumab and Recurrent *Clostridium difficile* Infection. *N. Engl. J. Med.*, 376, 16:1594.
- Wolkewitz, M, Cooper, BS, Bonten, MJ, Barnett, AG, Schumacher, M (2014). Interpreting and comparing risks in the presence of competing events. *BMJ*, 349:g5060.

**Bio:** Prof. **Martin Wolkewitz**, mathematician, is leading the division 'Methods in Clinical Epidemiology' which belongs to the Institute of Medical Biometry and Statistics, Freiburg, Germany. He is the group leader of seven mathematicians and two health economists.

The main research interests of our group include: statistical modelling in clinical epidemiology, bias evaluation, health-care cost evaluation, risk communication, advanced survival analysis (such as multistate models, competing risk models), study designs with applications in hospital-acquired infections, antimicrobial resistance, influenza, oncology and society.