A Simulation Study of the Performance of the Prescription Time-Distribution Matching Method to Address Immortal Time Bias

Presenter: Ehsan Karim
Department of Statistics
University of British Columbia
ehsan@stat.ubc.ca

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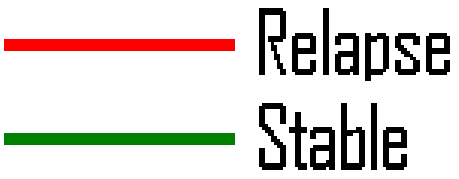
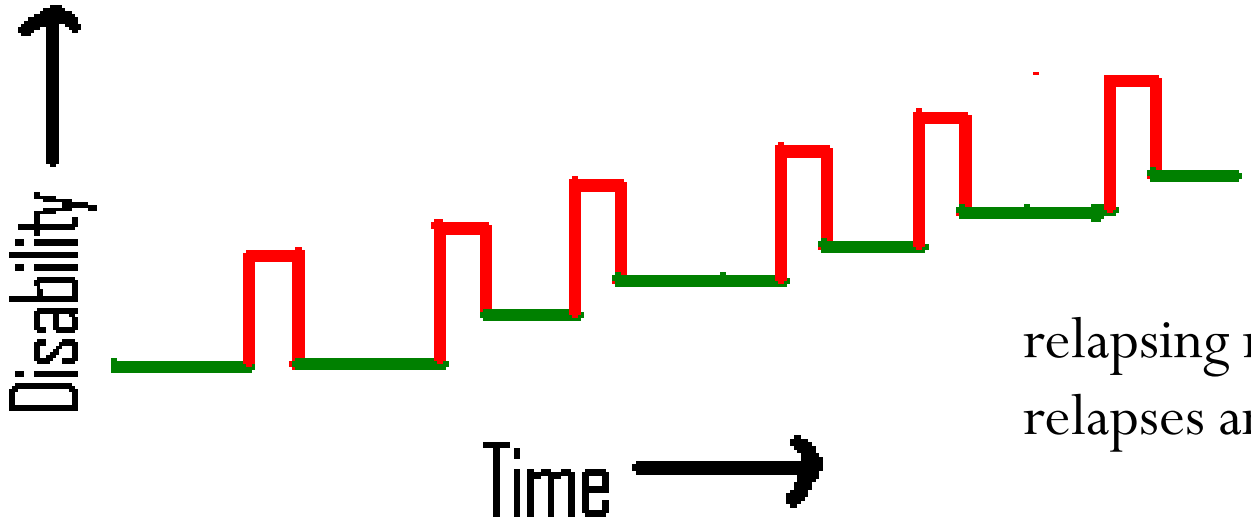
Outline >

- Motivation
- Immortal time bias
- Method
  - Time Distribution Matching (TDM)
  - Causal extension of TDM
- Simulation
- Results
  - Simulation
  - Data analysis

Motivation > MS



- Multiple Sclerosis: damage of nerve cells

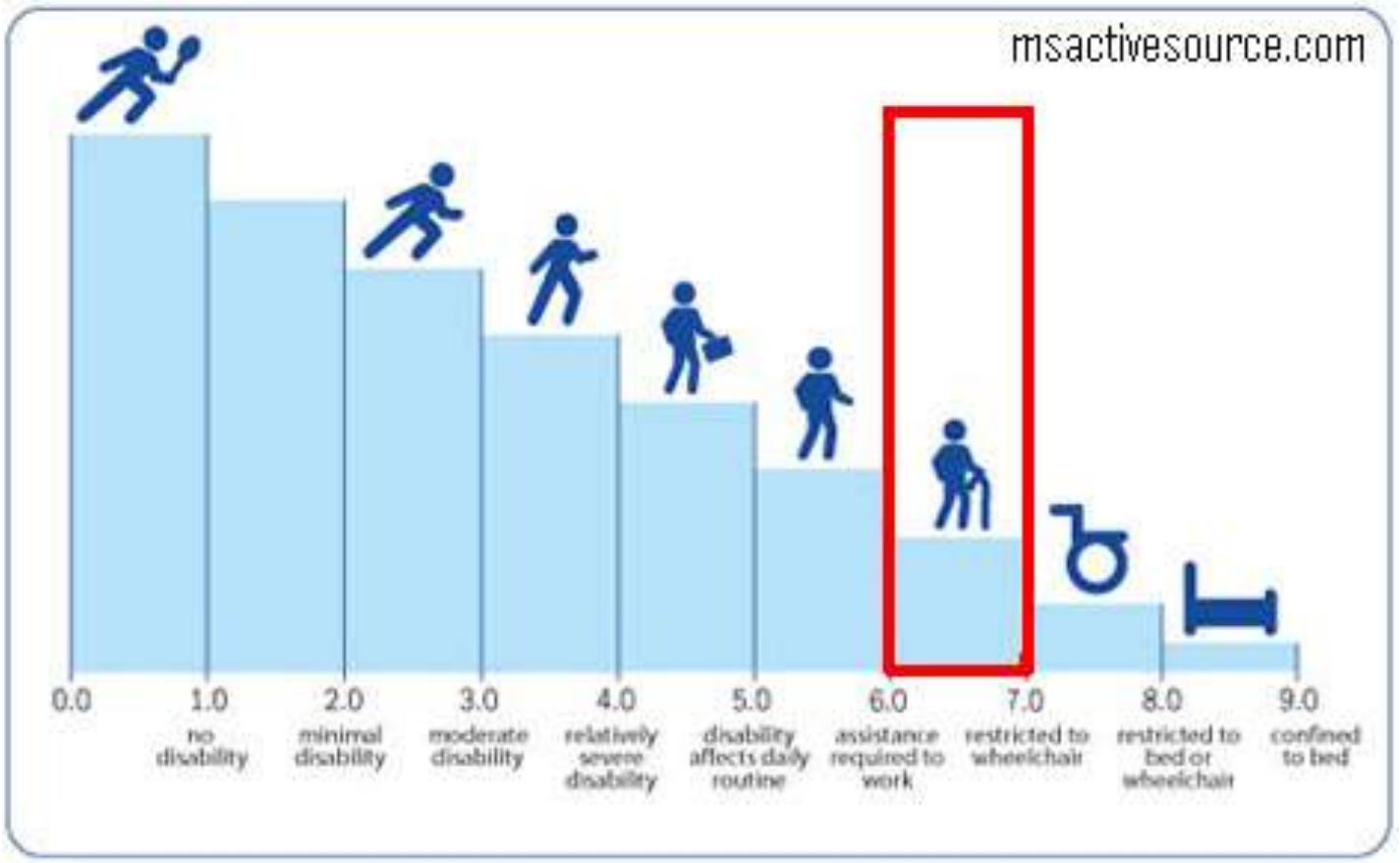


relapsing remitting:
relapses and remissions

- May lead to disability in the advanced stage

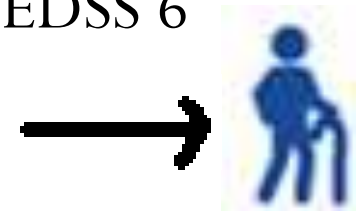
Motivation >

- Disability scores: EDSS



Motivation >

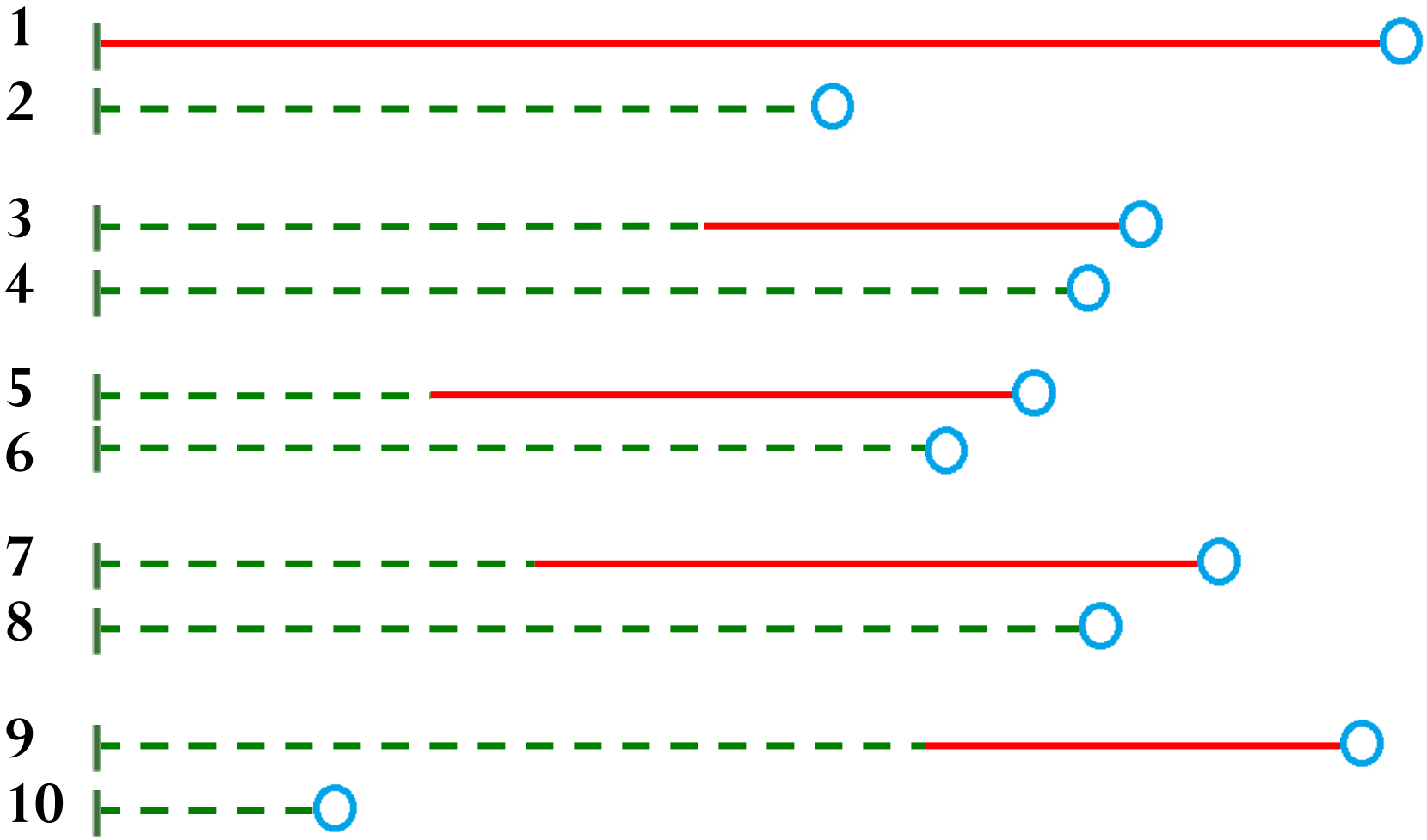
- Treatment: beta-interferon (INFB)
- Baseline: Eligibility to INFB (reimbursement scheme)
- Survival outcome: time to EDSS 6



- Covariates: gender, relapse, EDSS, age, disease duration

Motivation >

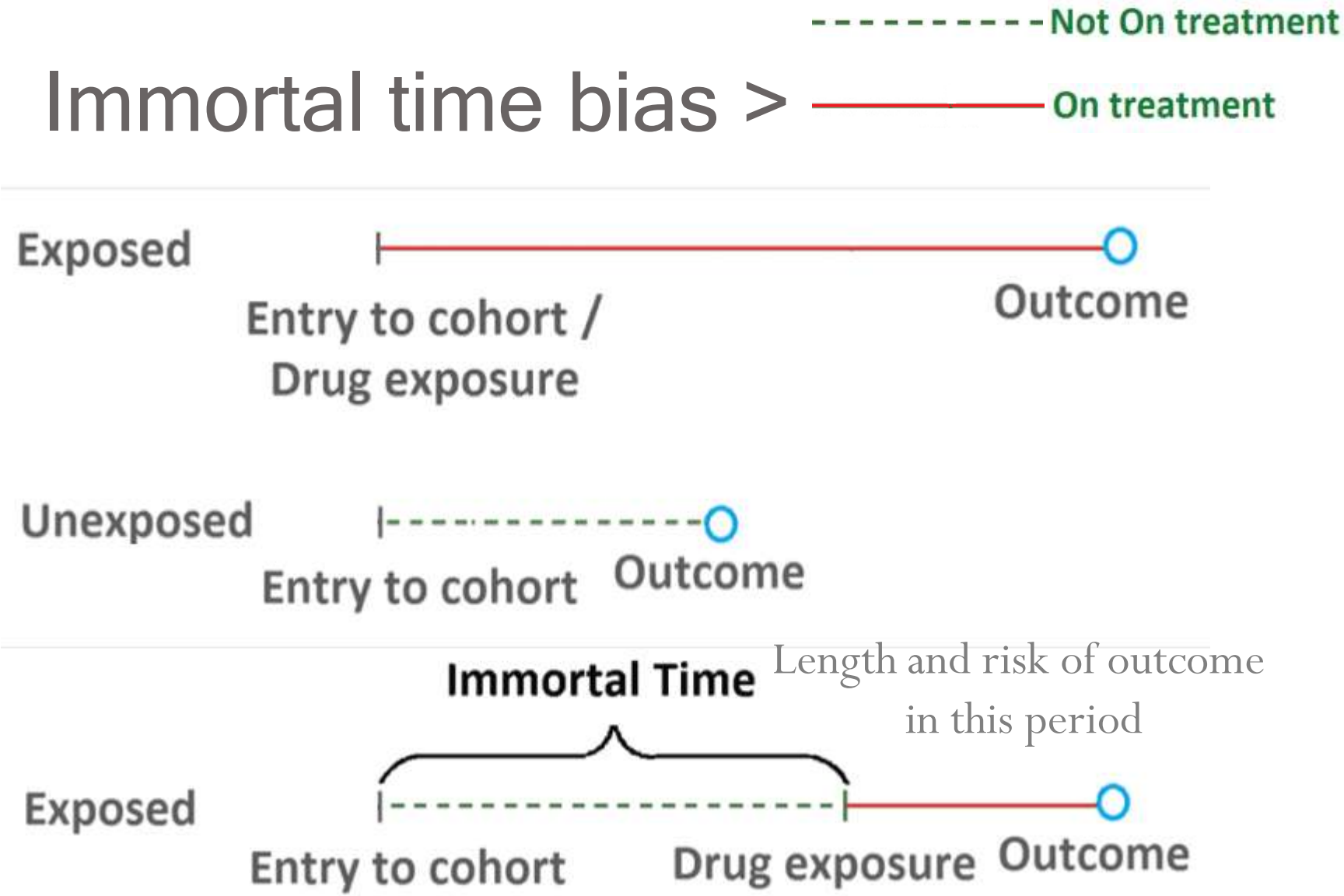
- Observational Multiple Sclerosis data



Motivation >

- Analysis strategies:
  - Time-dependent Cox
  - Nested Case control
  - Pooled Logistic regression
  - Marginal Structural model
  - Or something simpler …?

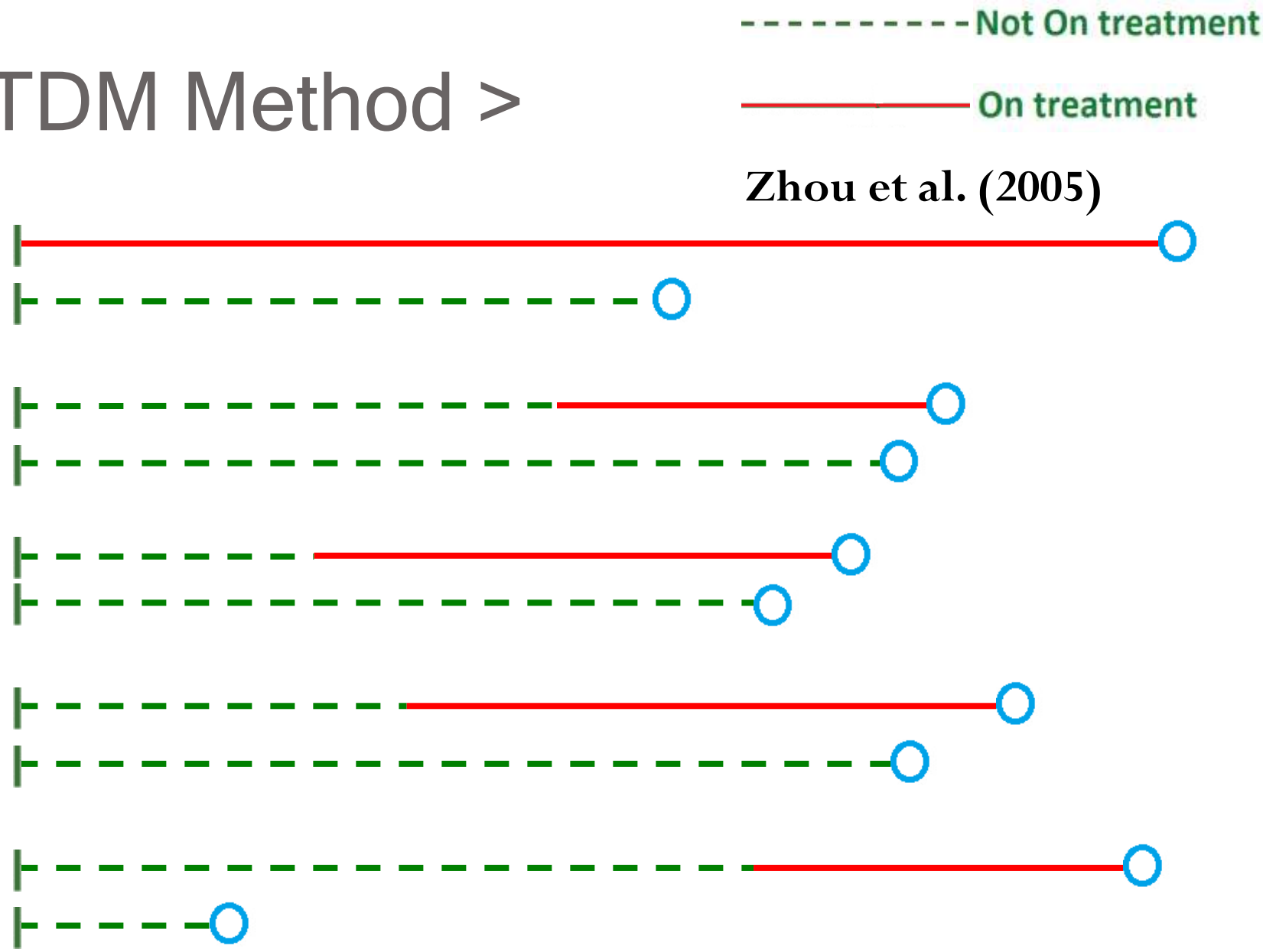
Immortal time bias >



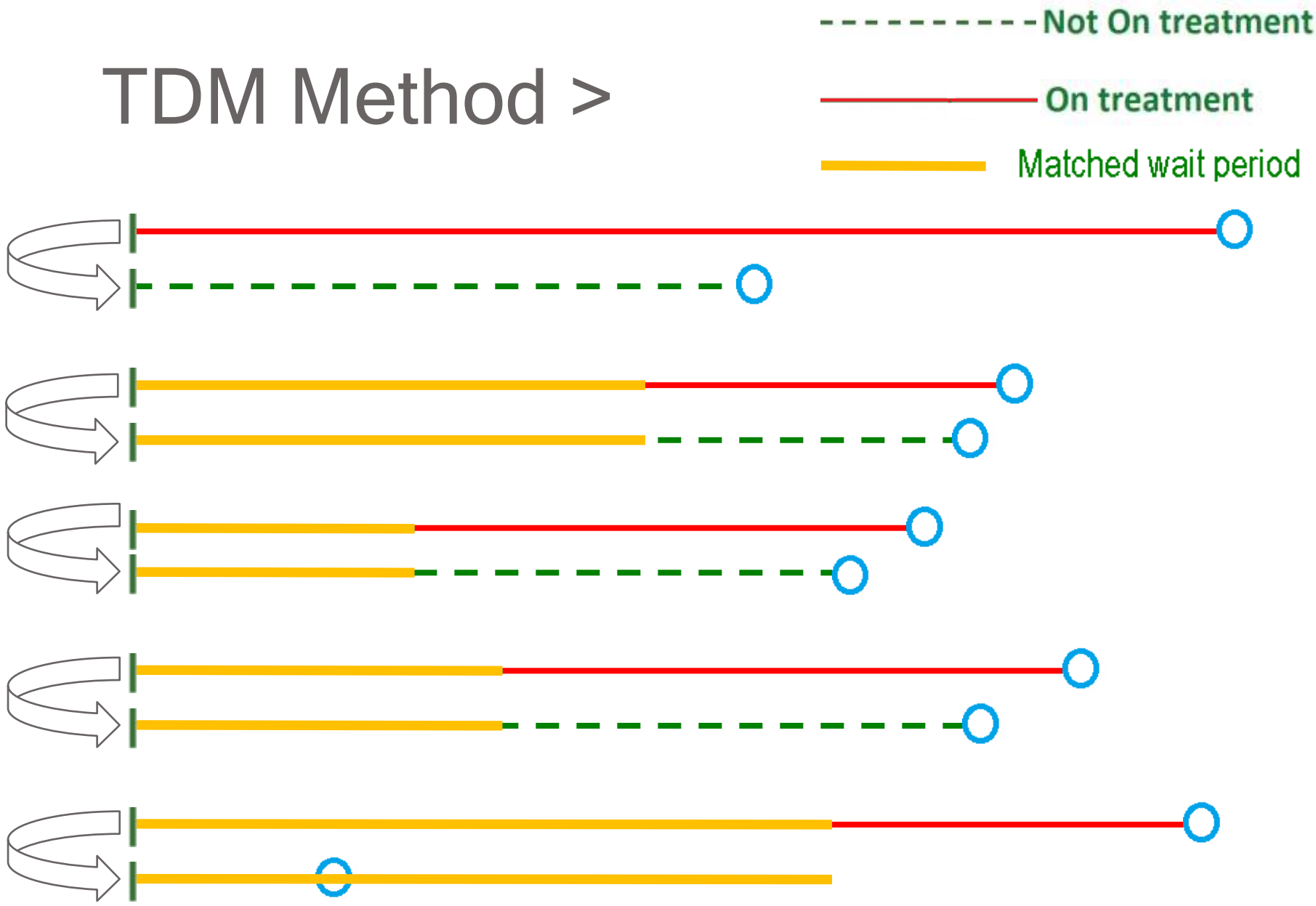
Immortal time bias >

- Simpler analysis strategies:
  - Simple Cox with ever versus never treated (?)
  - Simple Cox with baseline shifted forward (?)
  - Simple Cox excluding wait times (?)
  - Time distribution matching and then simple Cox (?)

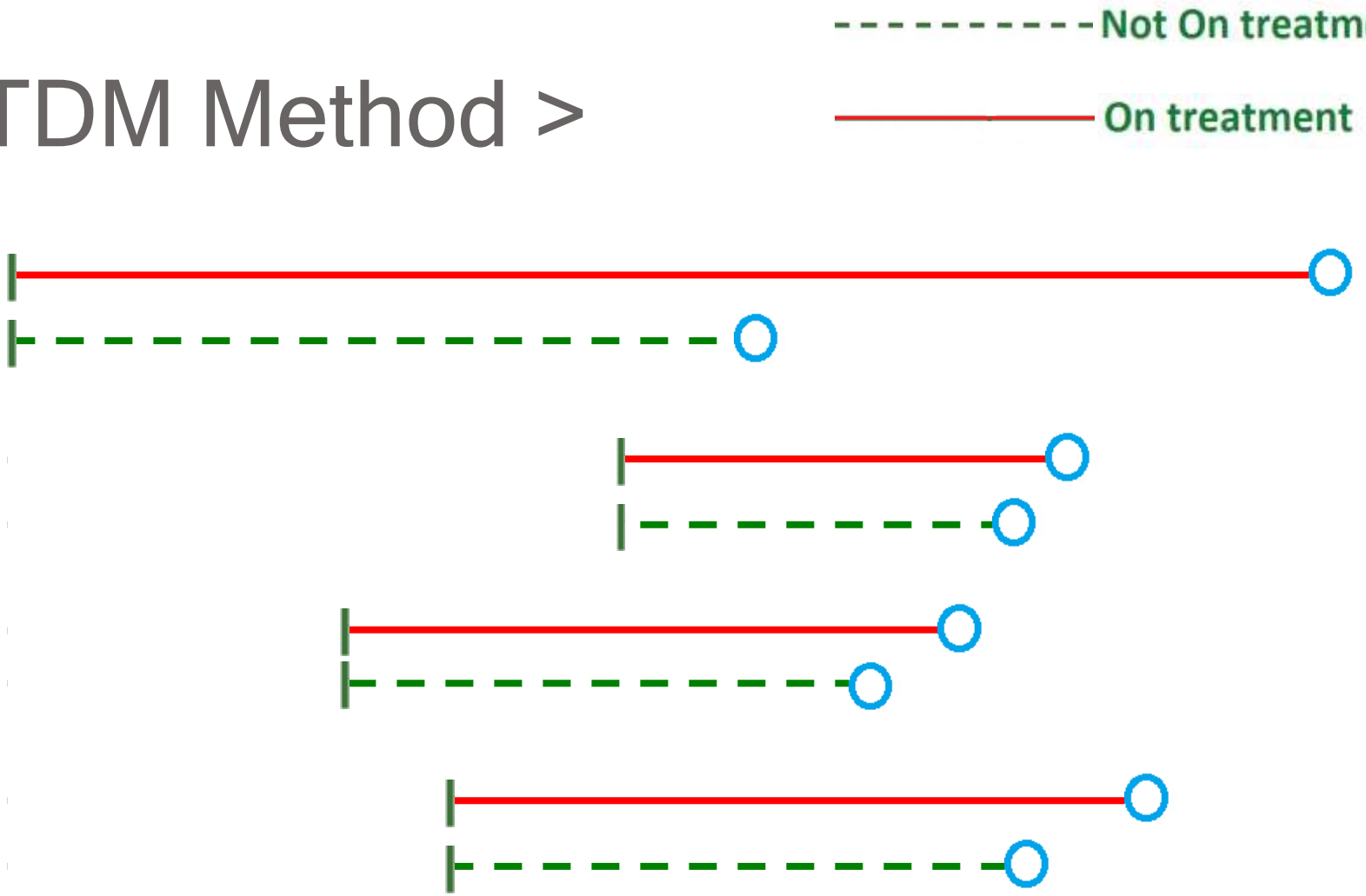
TDM Method >



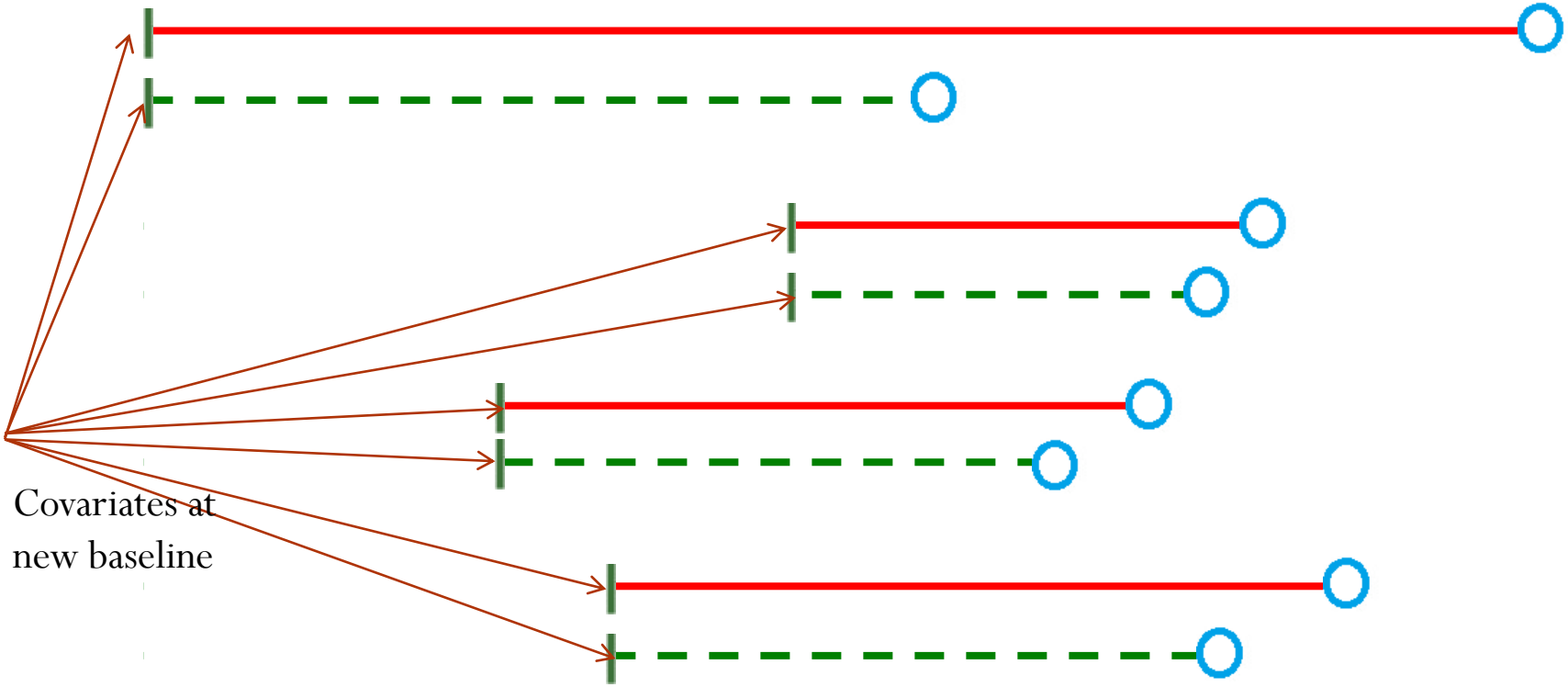
TDM Method >



TDM Method >



Causal extension of TDM >



Simulation >

Sylvestre et al. (2008)

- Generate survival population data using **permutation algorithm**

- 1,000 subjects from the population with
  - Follow-up is 5 years
  - Event time generated from exponential
  - Censoring and wait time generated from uniform
  - Covariates include a fixed and a time-dependent
  - Exposure is binary and time dependent

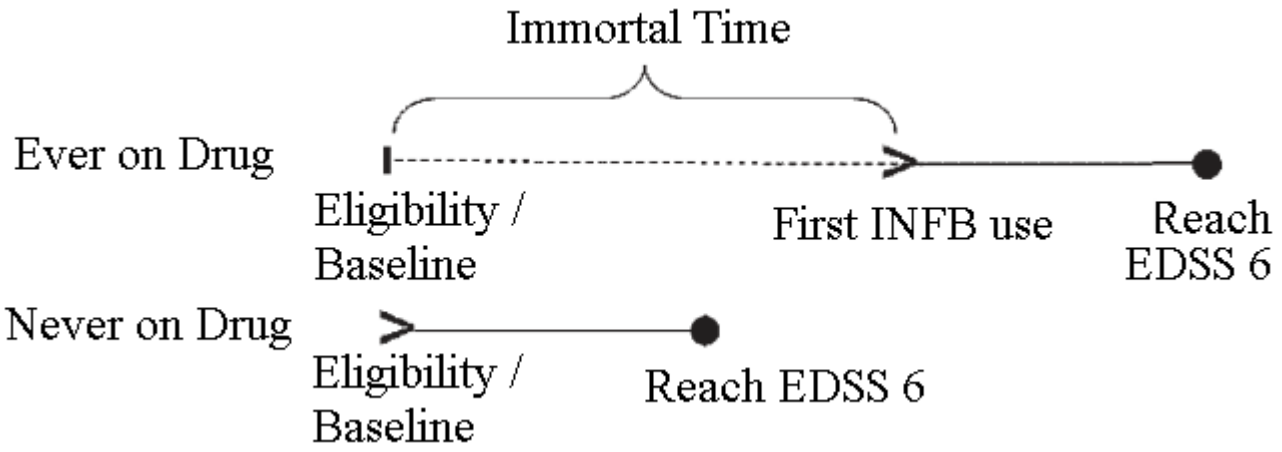
Simulation >

- Calibration and sensitivity:
  - Immortal time distribution
  - Censoring
  - Sample size
  - exposed/unexposed ratio

Multiple sclerosis data >

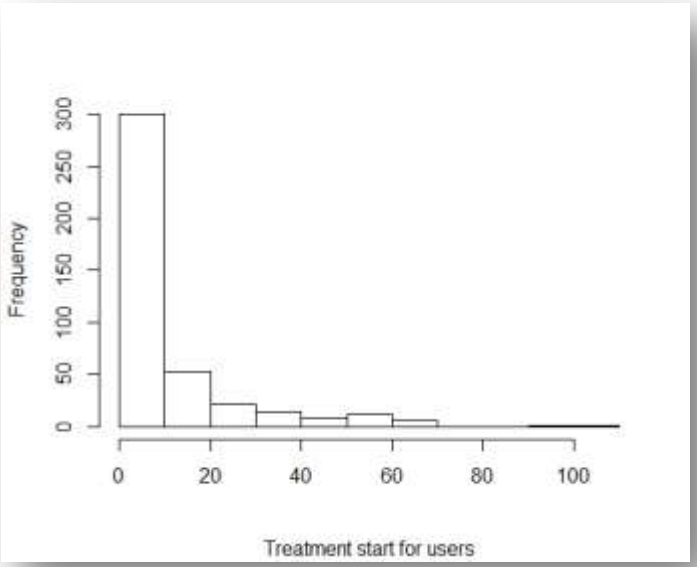
- 747 eligible patients
- Maximum 13 years of follow-up

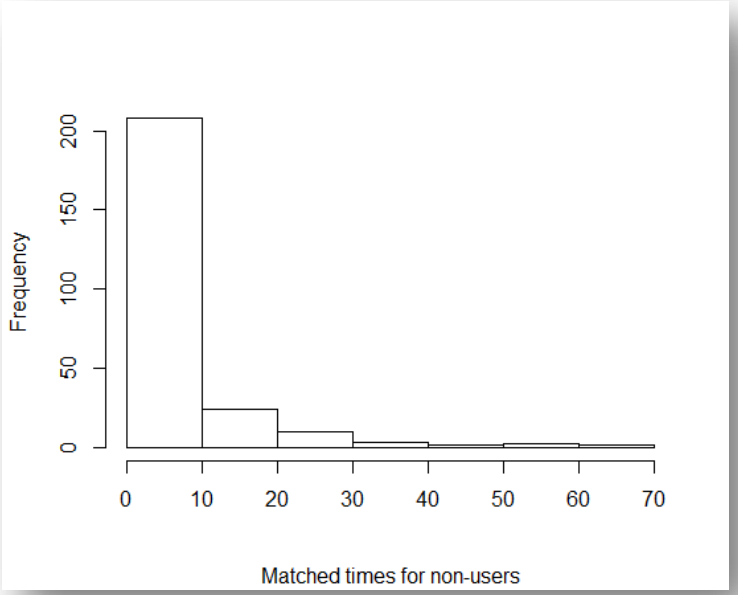
- 3029 person-years of follow-up
- 1461 person-years under beta-interferon



Multiple sclerosis data >

- Wait periods are matched





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endMS Research and Training Network

CIHR IRSC Canadian Institutes of Health Research / Instituts de recherche en santé du Canada

MS Multiple Sclerosis Society of Canada

References >

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send comments to

ehsan@stat.ubc.ca

Thank You!

send comments to
ehsan@stat.ubc.ca