## STRATOS Survival Analysis Subgroup

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Current survival analysis group

- Michal Abrahamowicz
- Per Kragh Andersen
- Richard Cook
- Pierre Joly
- Torben Martinussen
- Maja Pohar-Perme

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... beyond the Kaplan-Meier, log-rank, and Cox regression model ...

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There is obvious overlap with the initial STRATOS topic groups:

- TG1: missing data
- ► TG2: selection of variables and functional form
- TG3: descriptive and initial data analysis
- ► TG4: measurement error and misclassification
- TG5: study design
- ► TG6: evaluating diagnostic tests and prediction models

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- TG1: missing data
- TG2: selection of variables and functional form
  - time-dependence and non-linear effects
- ► TG3: descriptive and initial data analysis
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- TG1: missing data
- TG2: selection of variables and functional form
- TG3: descriptive and initial data analysis
  - survival curves
  - event rates and person-years
- TG4: measurement error and misclassification
- TG5: study design
  - sample size for survival studies
  - special designs
- ► TG6: evaluating diagnostic tests and prediction models

- TG1: missing data
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- ► TG7: causal models
  - ipw and marginal-structural models

# Specific topics

- Time dependent covariates: usage and pitfalls
- Time-dependent effects and flexible modeling
- Multiple events
  - competing risks and multi-state models
  - recurrent events
  - joint models of survival and longitudinal markers
- Particular models
  - Cox proportional hazards
  - additive
  - accelerated failure time, parametric and non-parametric

- restricted mean life
- Penalized models and random effects
- Relative survival
- Interval censoring
- Causal/cumulative effects
- Validation



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- Time dependent covariates
  - survival by treatment response, immortal time bias
    - Gail 1972, Does cardiac transplantation prolong life? A reassessment, Ann Int Med.
    - Anderson, Cain and Gelber 1983. Analysis of survival by tumor repsonse, J Clin Onc.
    - Redmond, Fisher and Wieand 1983. The methodologic dilemma in retrospectively correlating the amount of chemotherapy, received in adjuvant therapy protocols with disease-free survival, Cancer Treatment Reports.
    - Buyse and Piedbois, The relationship between response to treatment and survival time, Stat in Medicine.
    - Suissa 2008. Immortal time bias in pharmacoepidemiology. Am J Epi.

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- Time dependent effects
  - $\beta(t) \times \text{NOT } \beta x(t)$

- Multiple events
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  - competing risks and multi-state

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- repeated events
- joint modeling

- Particular models
  - Cox model

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- Particular models
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#### Particular models

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- Accelerated failure time
- Residual life

- $\lambda_0(t)e^{X\beta+Zb}$  $Db \sim G(0,s)$
- Classic mixed effects: D = I, G = Gaussian, general s

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- Relative survival
- Interval censoring
- Causal modeling

- Software validation
- Many of these are complex methods
- I no longer trust unvalidated survival software

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- R survival
  - > 29K code, 12K test, (7 + 7 + 4) documentation
  - formal validation set
  - any untested code has a 1 in 5 chance of containing an error

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What is a sufficient test suite?

'When I use a word, 'Humpty Dumpty said, in rather a scornful tone, 'it means just what I choose it to mean neither more nor less.'

'The question is,' said Alice, 'whether you can make words mean so many different things.'

'The question is,' said Humpty Dumpty, 'which is to be master that's all.'

Validation is a Humpty Dumpty word.

Hypothesis: Examples that are in the documentation for standard software get used a lot. Usage decreases with distance.

- Simple command, in the package help files.
- In the package vignettes.
- Textbook used in school
- Non-theoretical journal article with code
- Textbook published since graduation

## What to do?

Should I spend all my energy on the survival package?

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- How do we influence other software?
- Good tutorials with data?
- Formal validation suites?