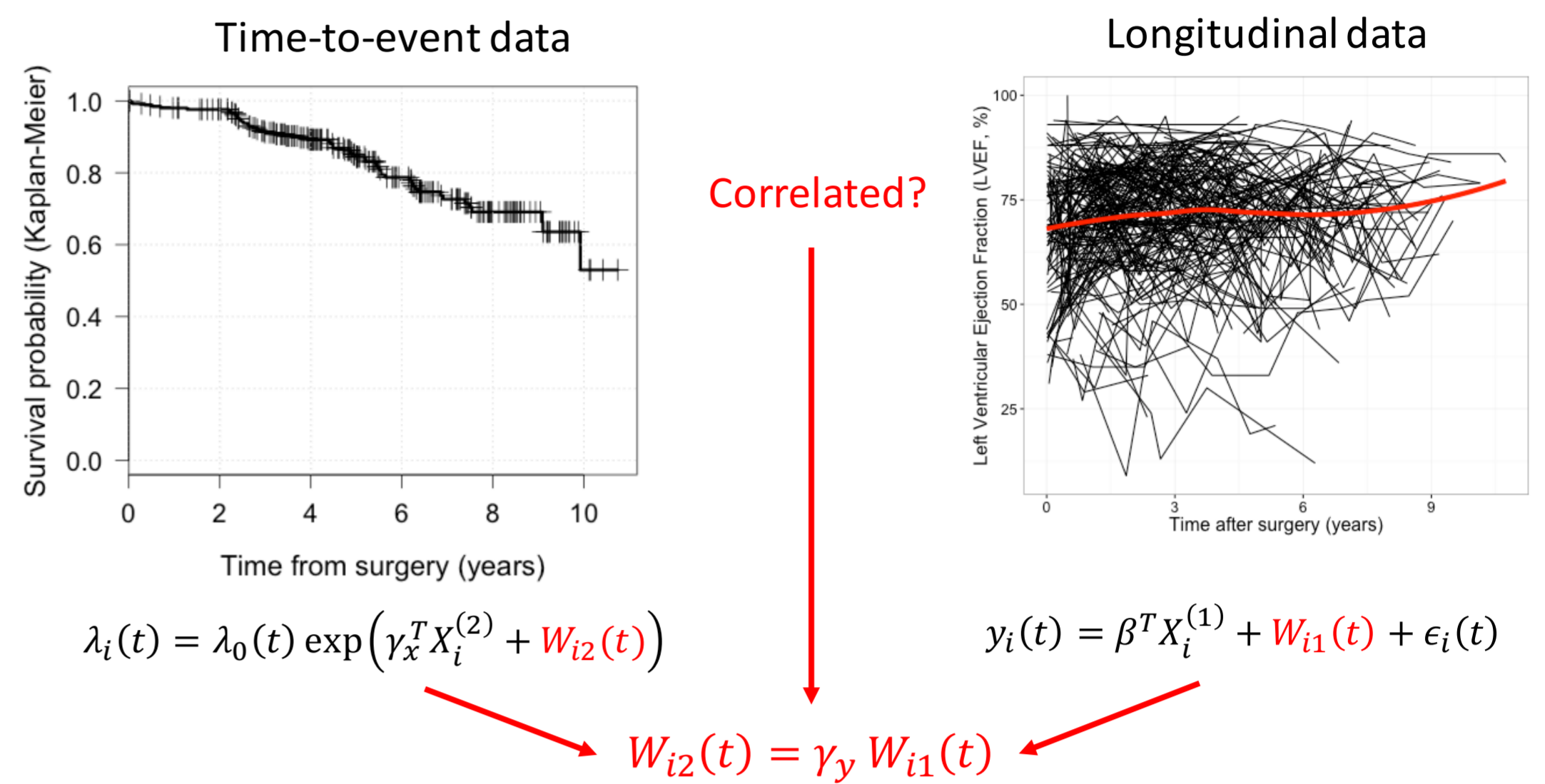


# Joint models of longitudinal and time-to-event data: extensions and recent developments

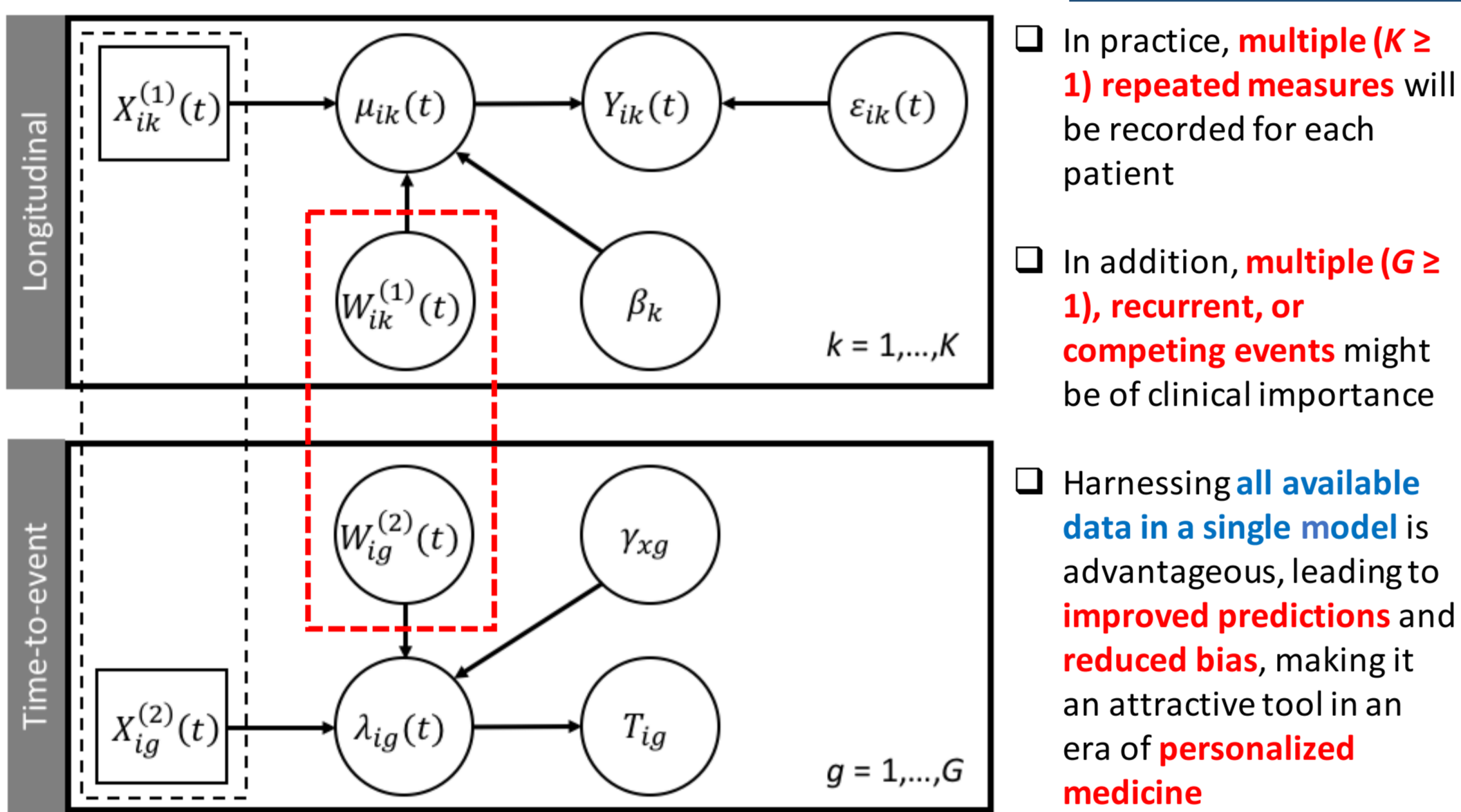
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## WHAT IS JOINT MODELLING?

- In clinical trials or cohort studies, measurements are repeatedly measured over time (e.g. cardiac ejection fraction), which we call **longitudinal data**
- In addition, the time to one or more clinical endpoints (e.g. death) is recorded, which we call **time-to-event data**
- Historically, these data have been **analysed separately**
- Problems with standard models?**
- Sickest patients more likely to drop out of study → **informative missingness**
- Repeated outcomes measured with error → **estimator attenuation**
- Time-varying covariates treated as constant between follow-up time in event-time model → **unrealistic**

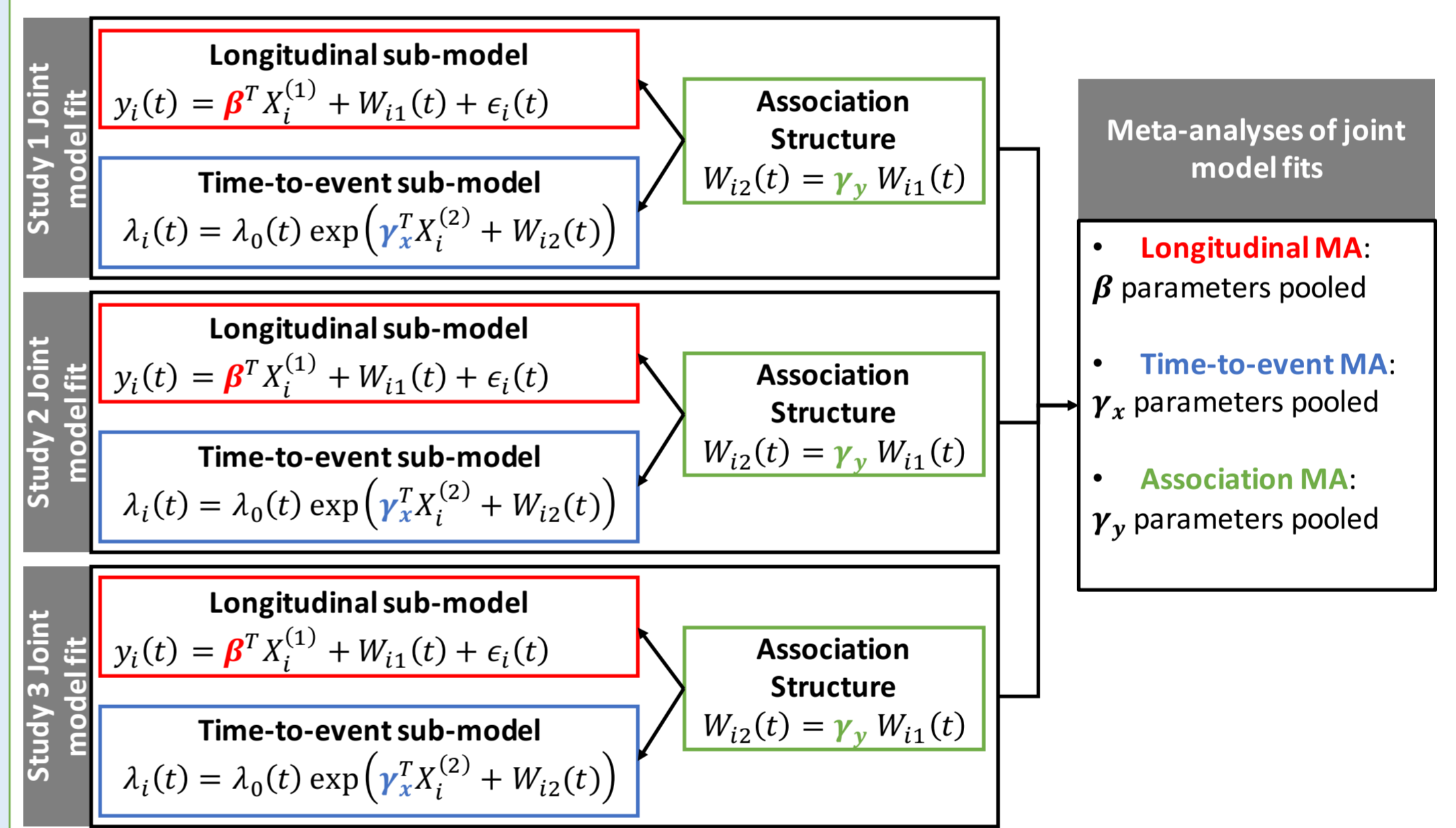


## EXTENSION TO MULTIVARIATE DATA



## META-ANALYSIS (MA) OF JOINT OUTCOMES

- Investigation to examine the benefits of **joint models in a multi study case**
- Considering **two stage MA** where models are fitted to each study then study coefficients pooled using standard MA methods



## RECENT METHODOLOGICAL DEVELOPMENTS

- Research has **predominantly focused on univariate data**, but a review identified a growing methodological literature on multivariate data
- Majority of articles only considered **either** multivariate longitudinal or time-to-event data, not both
- Numerous innovations** in models, distributional assumptions, estimation methodologies
- Diverse range of **association structures** (red box in model graph above) linking sub-models
- Limited clinical applications**, with methodological papers concentrating mostly on cardiovascular, neurodegenerative, lung, cancer, and HIV/AIDs diseases

## SOFTWARE

- Currently **no statistical software available** to fit joint models to **multivariate longitudinal data**
- A number of software options for fitting joint models to **competing risks data**, each incorporating different sub-models and association structures
- Multivariate data increases number of random effects in model, leading to exponential **increase in computational time**
- joiner package** freely available for installation in R software for fitting joint models to univariate data
- Development of joiner to incorporate **multivariate outcomes** is on-going

## JOINT OUTCOME MA – SIMULATION STUDY

