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# **Software Implementation for Wulfsohn-Tsiatis**

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# Outline

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- Longitudinal data

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- Longitudinal data
- Survival data

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- Joint model

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- Longitudinal data
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- Joint model
- Computational implementation

# Longitudinal data

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- Random effects model

$$Y_{ij} = \boldsymbol{x}_{1i}(t_{ij})^T \boldsymbol{\beta}_1 + U_{0i} + U_{1i}t_{ij} + \epsilon_{ij}$$

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- where

$$\begin{pmatrix} U_{0i} \\ U_{1i} \end{pmatrix} \sim \left( N\begin{pmatrix} 0 \\ 0 \end{pmatrix}, \begin{pmatrix} \sigma_{00} & \sigma_{01} \\ \sigma_{10} & \sigma_{11} \end{pmatrix} \right),$$

or, alternatively,

$$\mathbf{U}_i \sim N(\mathbf{0}, \mathbf{V}).$$

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or, alternatively,

$$\mathbf{U}_i \sim N(\mathbf{0}, \mathbf{V}).$$

- Also,

$$\epsilon_{ij} \sim N(0, \sigma_\epsilon^2).$$

# Survival data

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- Survival data with hazard

$$\alpha(t; \boldsymbol{x}_{2i}, \boldsymbol{U}_i) = \alpha_0(t) \exp\{\boldsymbol{x}_{2i}(t)^T \boldsymbol{\beta}_2 + \gamma(U_{0i} + U_{1i}t) + \textcolor{red}{U}_{2i}\}$$

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- Observe time  $s_i$  with associated failure indicator

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- Joint model - idea is to combine longitudinal and survival elements in a larger meta-model, see Wulfsohn and Tsiatis (1997)

# Joint model I

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- Observed data likelihood

$$\prod_{i=1}^m \left[ \int_{-\infty}^{\infty} \left\{ \prod_{j=1}^{n_i} f(y_{ij} | \cdot) \right\} f(s_i, \Delta_i | \cdot) f(\mathbf{U}_i | \mathbf{V}) d\mathbf{U}_i \right]$$

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- EM algorithm
- Maximisation (M) step
  - score equations

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  - maximum likelihood estimates

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- Maximisation (M) step
  - score equations
  - maximum likelihood estimates
  - Newton-Raphson iterative algorithm

# Joint model II

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  - conditional expectations of the form

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where

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- Implementation...

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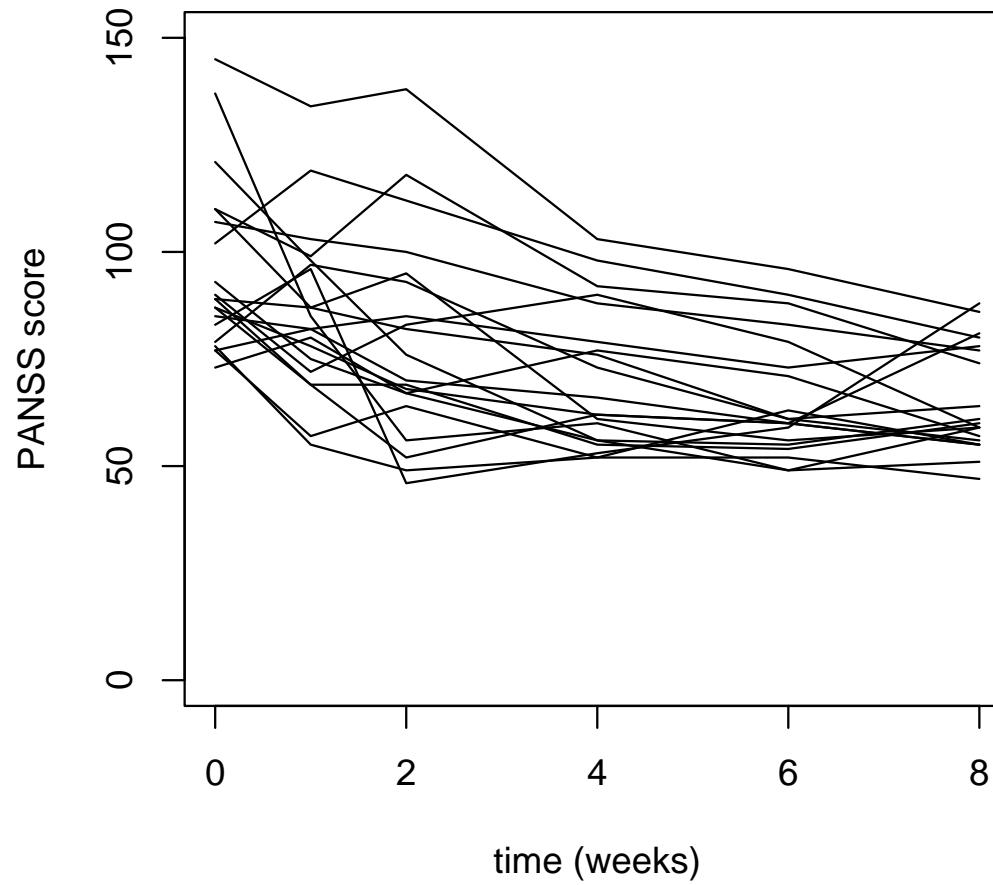
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- Flexibility in choice of latent association, frailty etc.
- Running C from R
- Comprehensive R Archive Network (CRAN)

# PANSS data

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# Bibliography

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Wulfsohn, M. S. and Tsiatis, A. A. (1997). A Joint Model for Survival and Longitudinal Data Measured with Error.  
*Biometrics*, **53**, 330-339.