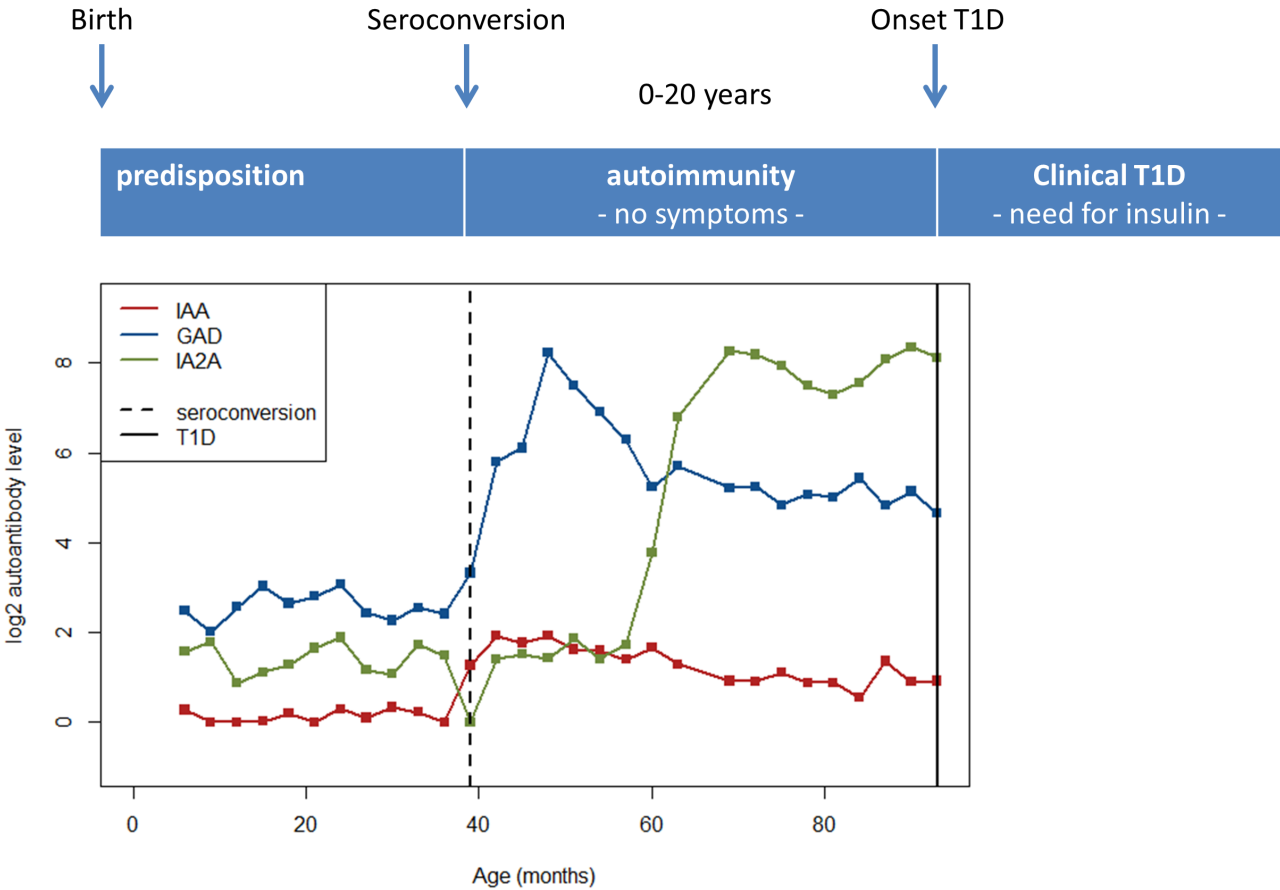


Joint Modeling of longitudinal and survival data

Meike Köhler
Institute of Diabetes Research
Helmholtz Zentrum München
meike.koehler@helmholtz-muenchen.de

15.07.2015

Development of Type 1 diabetes (T1D)



Challenges in modeling this type of data

The longitudinal marker $y_i(t_{ij})$ for subject $i = 1, \dots, n$ is

- measured at varying time points t_{ij}
- measured with error
- subject to informative dropout (no measurements after T1D onset)

Aim: Estimating the relationship between marker and time to event T_i

Joint models

1. submodel for the true trajectories $m_i(u)$, e.g. a mixed model

$$\begin{aligned}y_i(t_{ij}) &= m_i(t_{ij}) + \epsilon_i(t_{ij}) \\ &= \mathbf{x}_i(t_{ij})^\top \boldsymbol{\beta} + \mathbf{z}_i(t_{ij})^\top \mathbf{b}_i + \epsilon_i(t_{ij})\end{aligned}$$

2. submodel for time-to-event T_i , e.g. proportional hazards

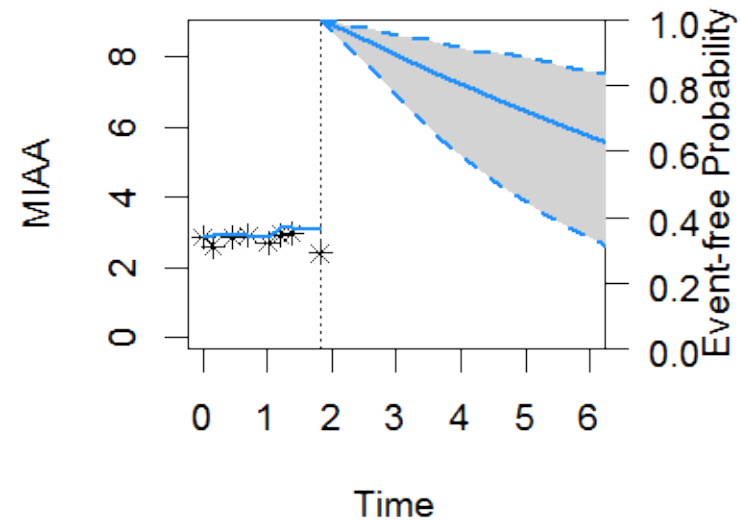
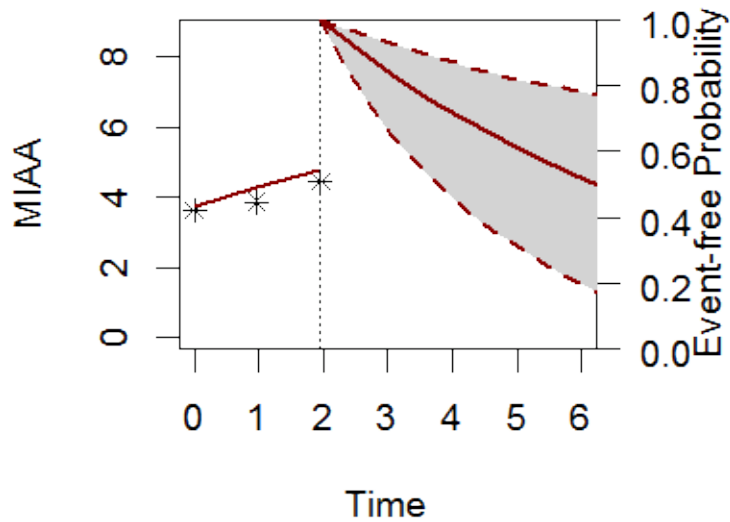
$$\lambda_i(u) = \lambda_0(u) \exp \{ \boldsymbol{\alpha} \cdot m_i(u) \}$$

3. combined into a *joint* likelihood

$$f(T_i, y_i(t_{ij})) = \int f(T_i | b_i) f(y_i(t_{ij}) | b_i) f(b_i) db_i$$

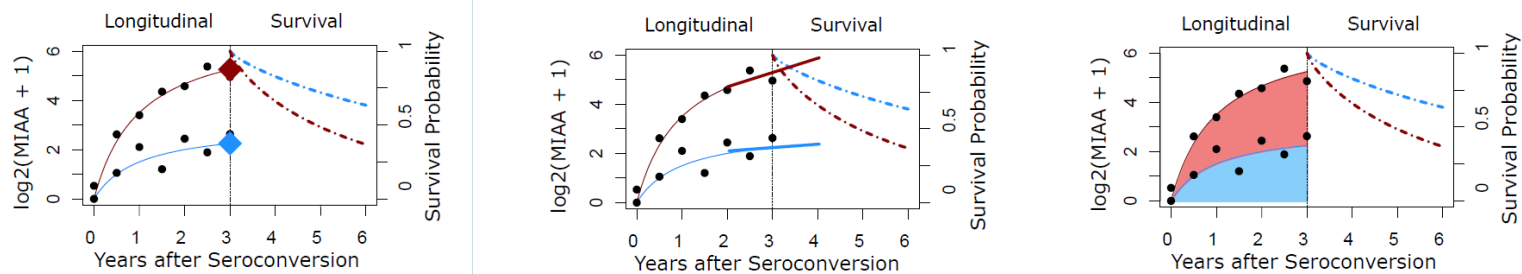
Dynamic prediction

Observed trajectories < 2 years and predicted time-to-diabetes for 2 subjects (matched for covariates).



Further information

- Inference is based on the EM-algorithm or on Bayesian approaches
- Joint models are a broad class of different models, e.g. different specifications of the link between longitudinal and survival.



- Joint models are implemented in different R-packages, e.g. JM, JMbayes, and `lcmm` (latent class model)

Further readings

- Article on the JM-package (Section 1 and 2 give a clear and short overview)
Rizopoulos, D.(2010). JM: An R package for the joint modelling of longitudinal and time-to-event data. *Journal of Statistical Software*, 35(9): 1-33.
- Standard review paper on the class of Joint Models
Tsiatis, A.A., and Davidian, M. (2004). Joint modeling of longitudinal and time-to-event data: an overview. *Statistica Sinica* 14: 809-834.
- Overview of latent class approaches
Proust-Lima, C., Sene, M., Taylor, J.M., and Jacqmin-Gadda, H. (2014). Joint latent class models for longitudinal and time-to-event data: A review. *Statistical Methods of Medical Research*, 23: 74-90.