

**Wiener Biometrische Sektion  
der Internationalen Biometrischen Gesellschaft  
Region Österreich – Schweiz**

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Einladung zum

**Biometrischen Kolloquium**

am Dienstag, den 29. Juni 2010 um 10:30 Uhr (s.t.)

in der Informatikbibliothek (Ebene 3, Raum 88.03.806) der  
Besonderen Einrichtung für Medizinische Statistik und Informatik  
(MSI) der Medizinischen Universität Wien  
Spitalgasse 23, 1090 Wien

Vortragender:

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**Flexible joint modeling of cumulative and non-linear  
effects of time-varying risk factors on the hazard**

Wir freuen uns auf zahlreichen Besuch.

Georg Heinze  
Präsident

Martin Posch  
Sekretär

# Flexible joint modelling of cumulative and non-linear effects of time-varying risk factors on the hazard

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Time-dependent covariates (TDC) are increasingly used in survival analysis to model the effects of prognostic and/or risk factors, as well as treatments, whose values change during the follow-up. Yet, an accurate modelling of the effects of TDC requires specifying the relationship between the hazard and the entire *vector* of its past values, rather than a scalar, and accounting for likely cumulative effects of the past values. This requires assigning differential weights to TDC values observed at different times in the past, but such weights are generally unknown and have to be estimated from the data at hand. Furthermore, the form of the dose-response relationship between the TDC value and the hazard is also typically unknown and has to be estimated. We extend our recent, simpler method [1] to model the cumulative effect of TDC, with simultaneous estimation of (i) weight function, as in [1], and (ii) possibly non-linear dose response curve. The weighed cumulative exposure (WCE) effect at time  $\tau$ , is a function of the time-dependent vector of past TDC  $x(t)$ , at  $0 < t < \tau$ :

$$WCE(\tau|x(t), t < \tau) = \sum w(\tau - t) * s[x(t)] \quad (1)$$

where  $w(\tau - t)$  is a weight function and  $s[x(t)]$  a dose-response function. Both  $w(\tau - t)$  and  $s[x(t)]$  are modeled using low-dimension cubic regression splines. The estimated WCE is then included as a TDC in the Cox's PH model. The model (1) is estimated using iterative 2-step alternating conditional estimation algorithm, which alternates between estimation of  $w(\tau - t)$  and  $s[x(t)]$ . The estimates of the two functions are evaluated in simulations. The model is then applied to re-assess the cumulative effects of blood pressure, measured at different times in the past, on cardiovascular risks.

[1] Sylvestre M.P. & Abrahamowicz M, Stat Med 2009; 28: 3437-3453].