An investigation of the terminal decline hypothesis: results from a population-based UK study of ageing

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August 2009

Outline

- Introduction
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  - previous methods of analysis
- Description of model and study
- Results
- Conclusions and further work

Definition

- 'factors related to the death of the individual cause a decline in intellectual performance. The onset of this decline may be detected in some instances several years prior to the death of the person' (*Kleemeier, 1962*)
- 'years to live' may be better indicator of cognitive performance than chronological age (*Riegel and Riegel,1972*)

Previous examinations of the T.D. hypothesis include:

- different versions of random effects models (e.g. constant rate of decline)
- time-to-death better indicator of change than age in the proximity to death (*Thordvalsson et al., 2006*)
- crude versions of change point models (e.g. all individuals experience a change in their rate of decline at the same point in time; no cross sectional differences accounted for). This is unlikely to happen in population-based samples.

Our proposal

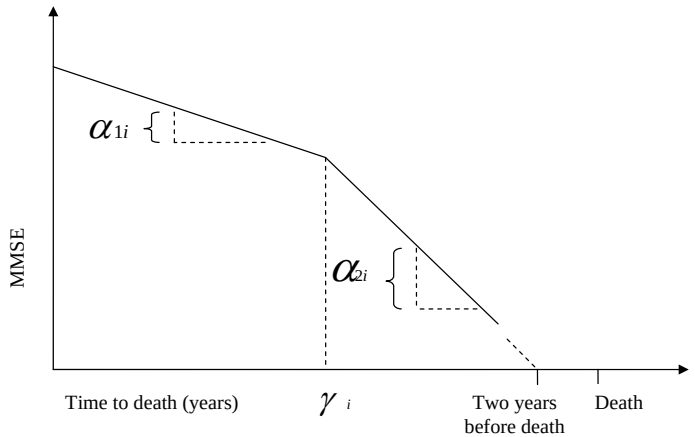
We propose to examine the T.D. hypothesis fitting a:

- time-to-death piecewise linear random change point model (*Kiuchi et al., 1995*)
- adjusting random effects (cognitive status before death, rate of change before and after change point) for possible cross sectional differences in age at death, education, gender and disability status at study entry.

Mathematical formulation (level 1)

$$
\begin{aligned}
Y_{it} &= f(T_{it}, \alpha_i, \gamma_i), \quad i = 1 \ldots, N \\
&= (\alpha_{0i} + \alpha_{1i} T_{it})\, \mathbf{1}(T_{it} < \gamma_i) \\
&+ (\alpha_{0i} + \alpha_{1i}\gamma_i + \alpha_{2i}\,(T_{it} - \gamma_i))\, \mathbf{1}(T_{it} \geq \gamma_i) + \epsilon_{it},
\end{aligned}
$$

where $\epsilon_{it} \sim N(0, \sigma^2), \forall i, t$



Mathematical formulation (level 2)

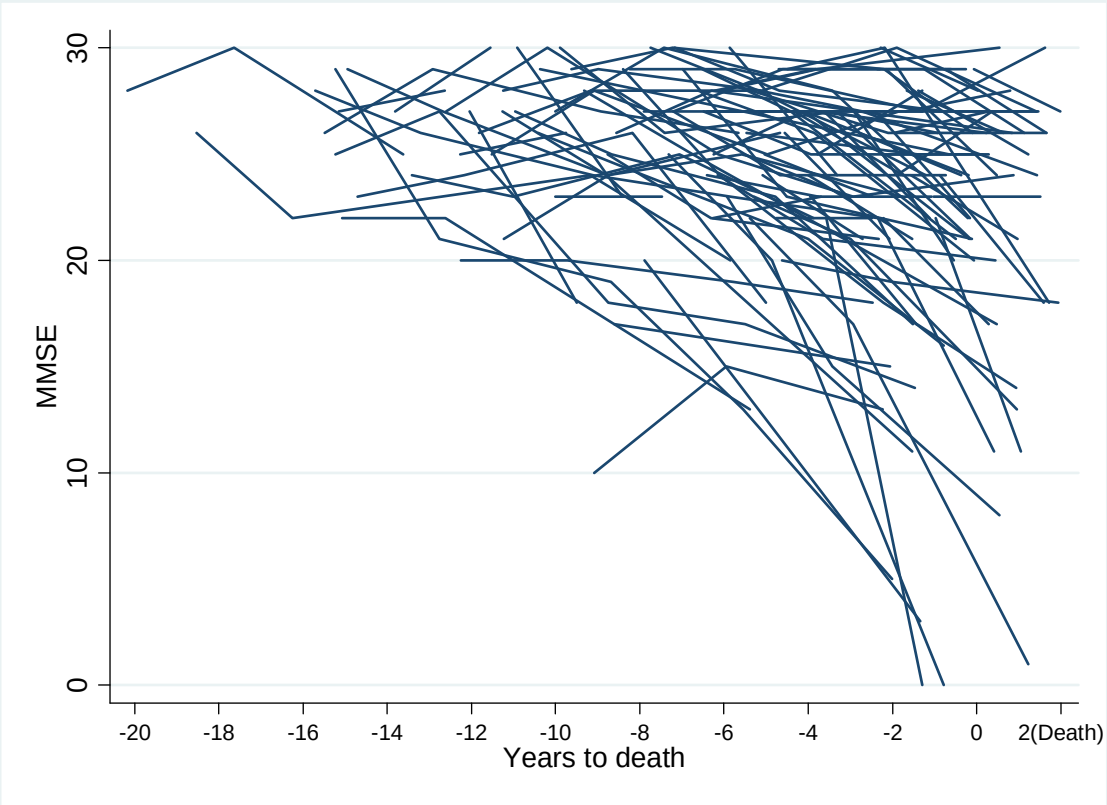
$$\text{level 2:} \begin{cases} \alpha_{0i} &= \alpha_{00} + \boldsymbol{\beta}_{\mathbf{0}}^{\mathbf{t}} \mathbf{Z}_i + u_{0i}, \\ \alpha_{1i} &= \alpha_{11} + \boldsymbol{\beta}_{\mathbf{1}}^{\mathbf{t}} \mathbf{Z}_i + u_{1i}, \\ \alpha_{2i} &= \alpha_{22} + \boldsymbol{\beta}_{\mathbf{1}}^{\mathbf{t}} \mathbf{Z}_i + u_{2i}, \end{cases}$$

where $\mathbf{u_i} \sim MVN(\mathbf{0}, \Omega), \quad k = 0, 1, 2; \quad i = 1, \ldots, N$

Cambridge City over 75 Cohort Study (CC75C)

- population-based study of individuals aged $\geq$75 yrs. old in 1985 (N=2106; 99% now deceased; long follow-up).
- cognitive function measured using the Mini Mental State Examination (MMSE)-integer scores in [0-30] interval with high scores indicating good cognition.
- subsample examined consisted of 1079 individuals who were last seen $\leq$ 7 years before death and at least twice.

- 69% left school aged $\leq$ 15 yrs. old, 43% disabled, 64% women, 81 yrs. old=mean initial age, 88 yrs. old=mean death age;



Results (1)

Table: Posterior mean, st. dev. and 95 % credible interval of estimates of fixed effects

Parameter	**Estimate**	**St.dev**	**95 % Cr.Int.**
Intercept (α_{00})	26.8	0.3	[26.15,27.40]
Slope before C.P.(α_{11})	-0.1	0.04	[-0.20,-0.01]
Slope after C.P. (α_{22})	-0.8	0.08	[-0.9,-0.6]
Change point (μ_γ)	-6.6	0.2	[-7.07,-6.23]

Distribution of random change points

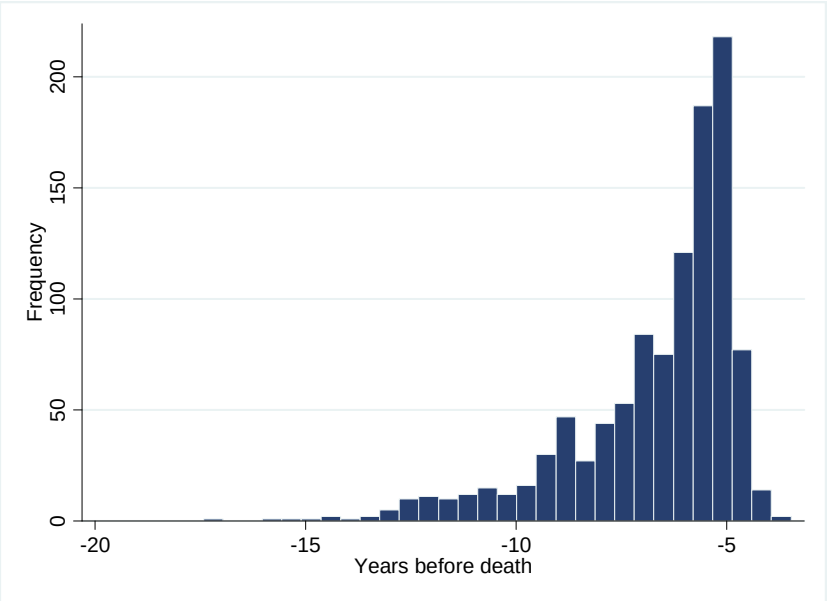


Figure: Distribution of the random change points

Results (2)

Table: Posterior mean and st.dev. of estimates of risk factors

Risk factor	**C.status 2 years before death**	**Rate of change before change point**	**Rate of change after change point**
Women	*-0.8 (0.30)*	-0.06 (0.04)	*-0.3 (0.09)*
Disability	0.6 (0.30)	0.02 (0.04)	*-0.3 (0.06)*
Education	*0.3 (0.06)*	0.006 (0.007)	0.02 (0.01)
Age at death	*-0.2 (0.02)*	0.001 (0.01)	*-0.02 (0.01)*

Conclusions

Our model permitted the identification of:

- the onset of T.D for each individual in the sample
- a phase of slow decline and a terminal phase for each individual
- risk factors that are relevant for each phase of the process

Further work

- mixture model allowing some individuals not to have a change point
- investigation of whether the onset of T.D. varies by measures of cognitive ability
- investigation of effect of risk factors on onset of T.D.

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We thank CC75C participants and their relatives