Covariates in the Illness-Death-Modell

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- Impact of covariates
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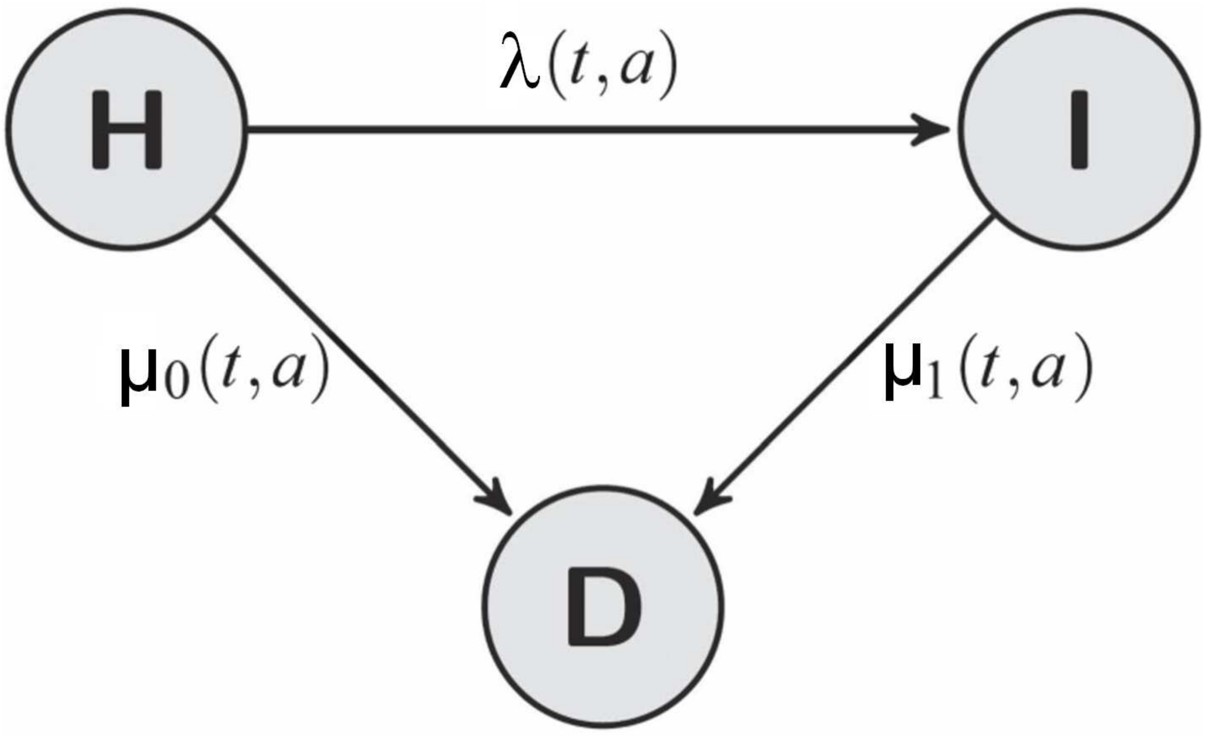
Illness-Death Modell 1/3

Only irreversible diseases (chronic, i.e. no remission)

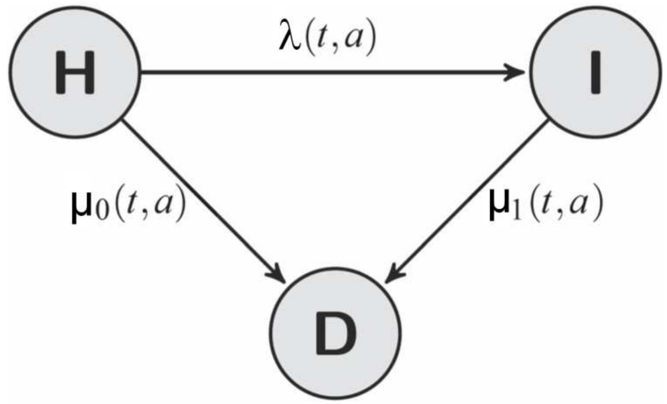


H Healthy
I Ill
D Dead

λ Incidence
μ_0, μ_1 Mortality

t Calendar time
a Age

Illness-Death Modell 2/3



Relevant events *for single subject*:

- Diagnosis (competing with death)
- Death

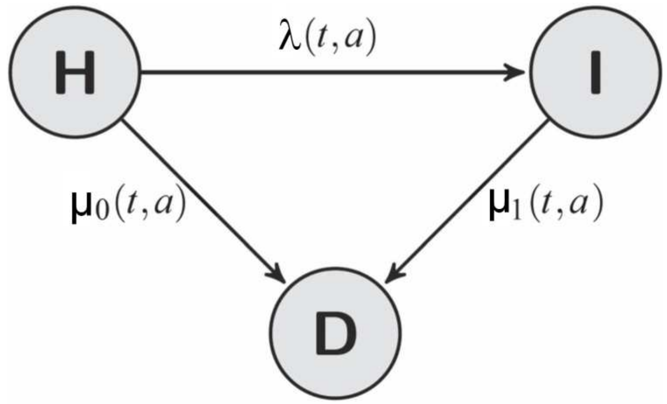
Simulation of events:

- First event: leaving state **H**
- If not dead → second event: death from **I**

} DES

Beyersmann et al. 2011

Illness-Death Modell 3/3



Age-specific prevalence

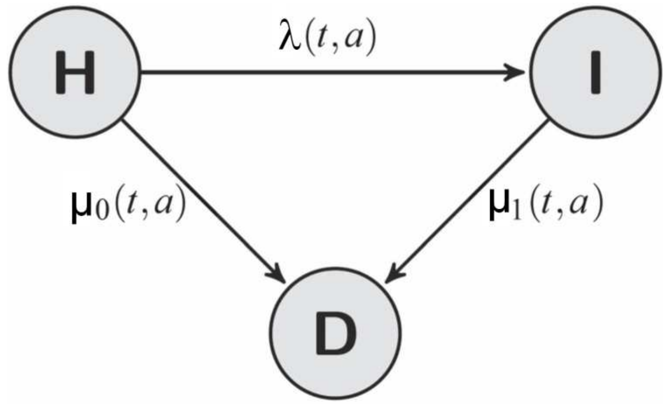
$$\pi(t, a) = \mathbf{I}(t, a) \,/\, \big(\mathbf{I}(t, a) + \mathbf{H}(t, a)\big)$$

solves PDE

$$(\partial_t + \partial_a)\, \pi = (1 - \pi)\, \big(\lambda - \pi\, (\mu_1 - \mu_0)\big)$$

Brinks & Landwehr 2014

Impact of covariates



How to deal with covariates *Z*?

$$\lambda = \lambda(t, a, Z)$$

$$\mu_0 = \mu_0(t, a, Z)$$

$$\mu_1 = \mu_1(t, a, Z)$$

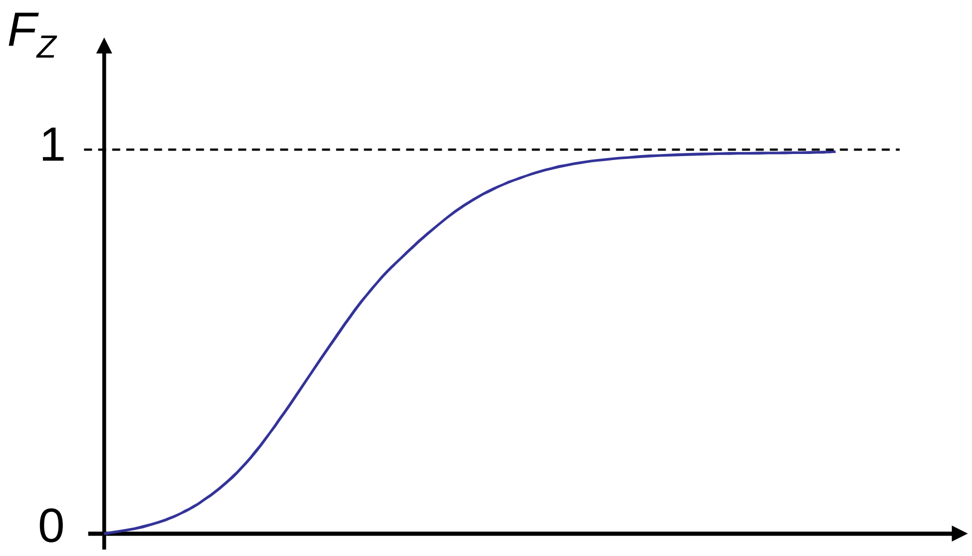
- Discrete event simulation (DES)
- PDE model $(\partial_t + \partial_a)\, \pi = (1 - \pi)\, \big(\lambda - \pi\, (\mu_1 - \mu_0)\big)$

Impact of covariates: DES

For first event of subject *i*:

1) calculate: $F(t, a, Z_i) = 1 - \exp(-\int(\lambda + \mu_0)(t - a + \tau, \tau, Z_i)\, d\tau)$

2) Inverse sampling from *F* to obtain time of first event



Impact of covariates: PDE

1) Calculate „effective rates“

- $\bar{\lambda} = \int \lambda(Z)\, f(Z)\, dZ$
- $\bar{\mu}_0 = \int \mu_0(Z)\, f(Z)\, dZ$
- $\bar{\mu}_1 = \int \mu_1(Z)\, f(Z)\, dZ$

2) Feed effective rates into PDE

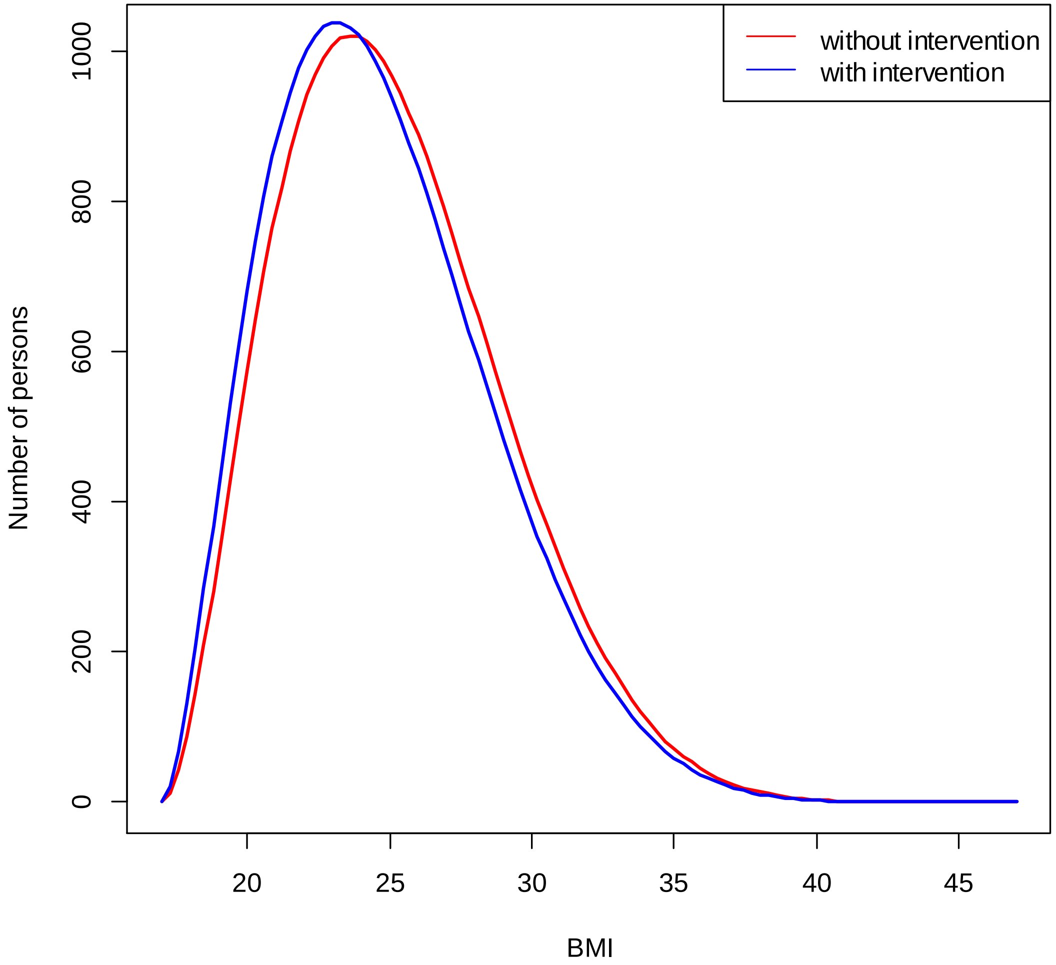
$$(\partial_t + \partial_a)\, \pi = (1 - \pi)\, \big(\, \bar{\lambda} - \pi\, (\, \bar{\mu}_1 - \bar{\mu}_0)\big)$$

Example: BMI and diabetes

- Incidence of diabetes increases by 10% per 1 unit increase in BMI
- Mortality increases by 2% per 1 unit (absolute) deviation from 23 in BMI
- DES: n = 10.000, birth cohort (*1970) of German males
- Cohort mortality from DESTATIS

Two simulations

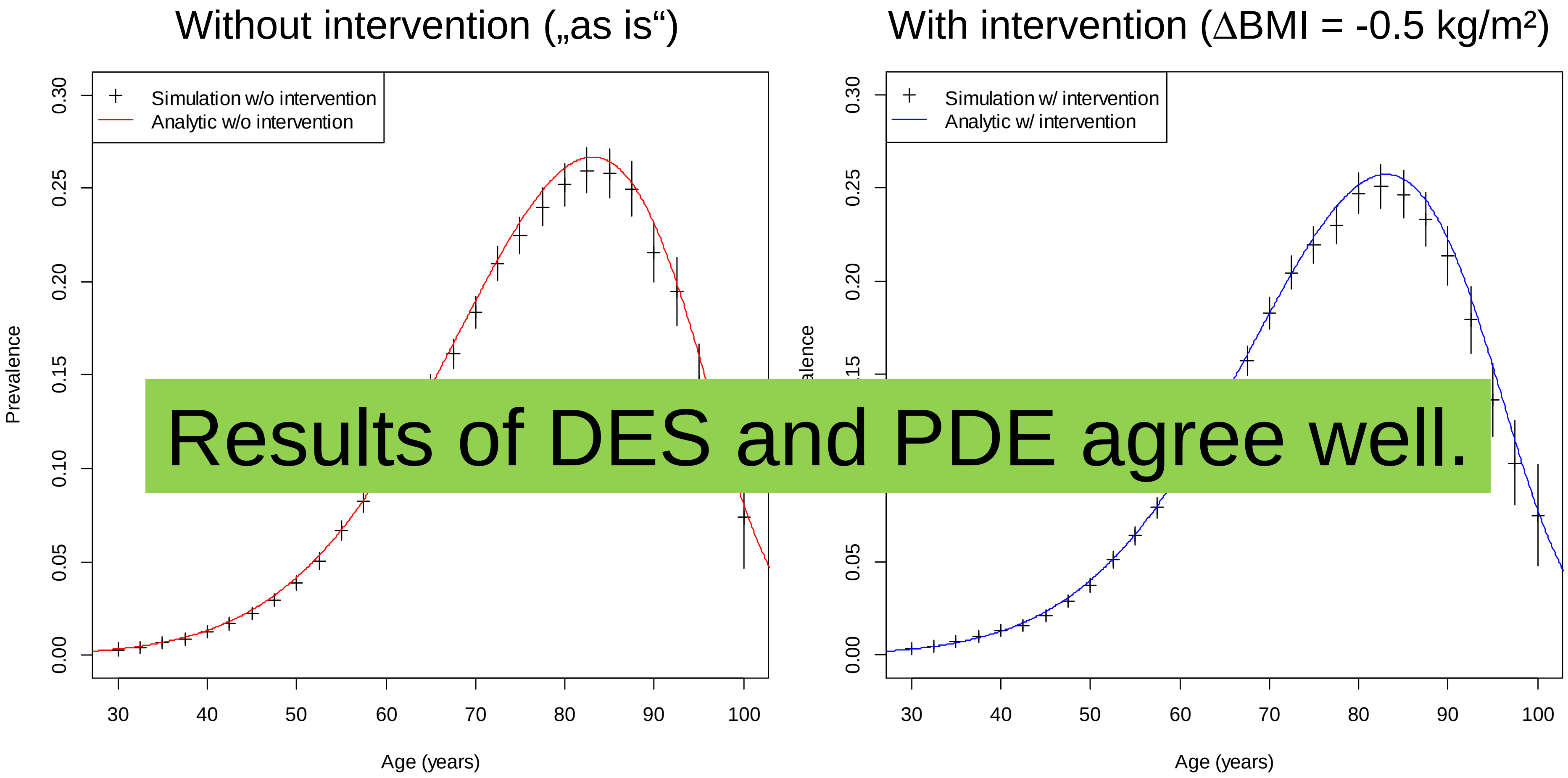
BMI distribution as in German males (DEGS) approximated by β(3,8) distribution and β(2.8,8) distribution



Results

+ DES

— — PDE with ERM



Conclusions

- Results of DES and ERM agree
- ERM much faster than DES
- Estimation of important epidemiological / public-health figures possible