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• We are all going to die...

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This results in different survival trajectories.

At a population level this creates heterogeneity.

## How can we model this?

Two random variables:

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#### **Survival function**

$$s(x|z) = e^{-\int_0^x \mu(t|z)dt},$$
  

$$\mu(x|z) = -\frac{d \ln s(x|z)}{dx}.$$

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Given that  $\mu(x|z) = z\mu(x)$ 

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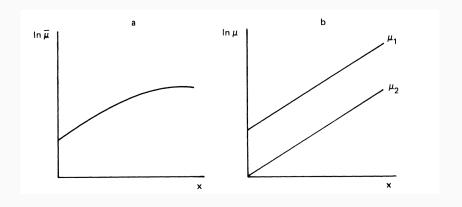
$$\bar{\mu}(\mathbf{x}) = \bar{\mathbf{z}}(\mathbf{x})\mu(\mathbf{x})$$

where  $\bar{z}(x) = \int_0^\infty z \pi(z) dz$  at any age x.

The population hazard at any age x is a function of the baseline  $\mu(x)$  and the average frailty  $\bar{z}(x)$  among survivors to this age.

individuals ≠ POPULATION

#### **INDIVIDUALS VS POPULATION HAZARDS**



Vaupel and Yashin (1985)

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- · It is a model for cohort mortality,
- · Frailty acts multiplicatively on the baseline hazard,
- Frailty does not change with age. It remains the same for all ages. It is
  often called fixed-frailty model.

## Continuous frailty

#### **CONTINOUS FRAILTY**

X: continous r.v.

Z > 0: continous r.v. with density  $\pi(z)$ .

Hazard and survival functions for populations

• 
$$\bar{\mu}(x) = \int_0^\infty \mu(x|z)\pi(z)dz = \bar{z}(x)\mu(x)$$

• 
$$\bar{s}(x) = \int_0^\infty s(x|z)\pi(z)dz$$

#### A NOTE ABOUT THE LAPLACE TRANSFORM

## A function of functions It helps us to transform a function f(t) to another function f(s).

The Laplace transform of a function f(t),  $t \ge 0$  is

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In probability:

$$\mathcal{L}_f(s) = \mathbb{E}(e^{-sX})$$

and

$$\mathbb{E}(x) = -\mathcal{L}_f'(0)$$

$$\mathbb{V}(x) = \mathcal{L}_f^{\prime\prime}(0) - [\mathcal{L}_f^{\prime}(0)]^2$$

#### LAPLACE TRANSFORM IN FRAILTY MODELS

The survival function for the total population is the Laplace transform of the frailty distribution at x = 0, calculated for the cumulative baseline hazard H(x)

$$\bar{s}(x) = \int_0^\infty s(x|z)\pi(z)dz = \int_0^\infty e^{-H(x)z}\pi(z)dz = \mathbb{E}(e^{-H(x)z}) = \mathcal{L}_Z(H(x)).$$

An extremely useful tool in modelling unobserved heterogeneity:

$$\bar{s}(x) = \mathcal{L}_Z(H(x))$$

## \_\_\_\_

What are the distributions of X and Z?

#### A PARAMETRIC APPROACH

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The gamma distribution has a flexible shape and converges to a normal distribution,

It has a simple Laplace transform.

Gamma frailty model

$$Z \sim \Gamma(k, \lambda)$$
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# Density function of Z

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Laplace transform of Z and survival function of the population

$$\mathcal{L}_Z(H(x))=\bar{s}(x)=(\frac{1}{1+\frac{1}{k}H(x)})^k$$

## Average frailty of the population

If  $\bar{z}(0) = 1$  and  $k = \lambda = 1/\gamma$ , where  $\gamma$  can be interpreted as the squared root of the coefficient of variation of Z at any age.

$$\bar{z}(x) = \frac{1}{1 + \gamma H(x)} = [\bar{s}(x)]^{\gamma}$$

Mortality hazard for populations

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Thus  $\gamma$  tell us the amount of frailty in a population.

**Gamma-Gompertz** 

## **GAMMA-GOMPERTZ**

 $X \sim Gompertz(a,b)$ 

### **Individual hazard**

$$\mu(x) = ae^{bx}$$

$$H(x) = \frac{a}{b}(e^{bx} - 1)$$

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a: initial level of mortality,

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 $\gamma$ : amount of frailty in the population.

Gamma-Gompertz via the Mode

# **GAMMA-GOMPERTZ VIA THE MODE**

 $X \sim Gompertz(b, M)$ 

### **Individual hazard**

$$\mu(x) = b \mathrm{e}^{b(x-M)}$$

$$H(x) = e^{-bM}(e^{bx} - 1)$$

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b: individual rate of ageing,

M: modal age at death,

 $\gamma$ : amount of frailty in the population.



## **GAMMA-GOMPERTZ-MAKEHAM**

 $X \sim Gompertz - Makeham(a, b, c)$ 

### **Individual hazard**

$$\mu(x) = ae^{bx} + c$$

$$H(x) = \frac{a}{b}(e^{bx} - 1)$$

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a: initial level of mortality,

b: individual rate of ageing, c: external mortality,

 $\gamma$ : amount of frailty in the population.



**Fitting Gamma-Gompertz** 

#### Maximize likelihood

$$L(\theta,\beta,\gamma) = \left( \prod_{i=1}^{n} \frac{\mu(x_i;\theta) e^{y_i} \beta}{1 + \gamma H(x_i;\theta) e^{y_i \beta}} \right)^{\delta_i} \left( 1 + \gamma H(x_i;\theta) e^{y_i \beta} \right)^{-\gamma}$$

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where  $\theta = a, b, M$ .

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  - · other frailty distributions: log-Normal, Beta, etc.

### FITTING GAMMA-GOMPERTZ - AGGREGATED DATA

When having aggregated data (i.e. death counts and exposures from the HMD)

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$$\ln L(\theta, \gamma) = \sum_{x} (D(x) \ln \bar{\mu}(x; \theta, \gamma) - E(x) \bar{\mu}(x; \theta, \gamma))$$

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  - · based on GLM models
  - other distributions: Kannisto, Gompertz, Weibull, etc.

When and why to use frailty model?

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 shared frailty: effect of genetics in twins (Yashin and Iachine, 1997; Wienke, 2001) and long-lived families,

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- stochastic vitality: changes in frailty over age (Manton and Yashin, 1997)

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- Variance of frailty determines the degree of unobserved heterogeneity.

#### **FURTHER READING**

- Vaupel, Manton and Stallard. The Impact of Heterogeneity in Individual Frailty on the Dynamics of Mortality. Demography, 1979.
- Vaupel and Yashin. Heterogeneity's ruses: Some surprising effects of selection on population dynamics. American Statistician, 1985.
- Vaupel and Missov. Unobserved population heterogeneity: A review of formal relationships. Demographic Research, 2014.
- Steinsaltz and Wachter. Understanding mortality rate deceleration and heterogeneity. Mathematical Population Studies, 2006.
- Horiuchi and Wilmoth. Deceleration in the age pattern of mortality at olderages. Demography, 1998.
- Wienke. Frailty models in survival analysis, 2016.

# **Questions?**