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 $\bullet \ \ \text{We are all going to die}...$

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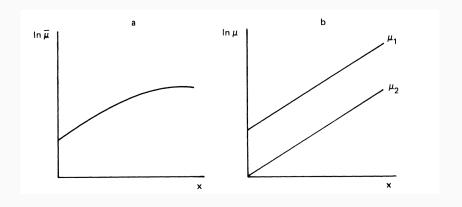
$$\bar{\mu}(\mathbf{x}) = \bar{\mathbf{z}}(\mathbf{x})\mu(\mathbf{x})$$

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,
- Individual hazards are proportional to the baseline hazard,
- Individual frailty does not change with age. It remains the same for all
 ages. It is often called fixed-frailty model.

Continuous frailty

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X: continous r.v.

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

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Hazard and survival functions for populations

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

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

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Can we get a closed form for $\bar{s}(x)$?

A note on the Laplace transform

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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)

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

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An extremely useful tool in modelling unobserved heterogeneity:

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

What are the distributions of X and Z?

 $X\sim$ Gompertz or Gompertz-Makeham,

 $extit{X} \sim ext{Gompertz-Makeham,}$

What about Z?

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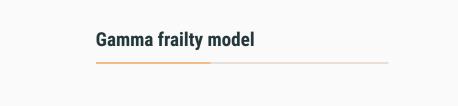
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Frailty distributions with closed-form Laplace transforms are the most convenient to work with

 $Z\sim$ Gamma, Inverse Gaussian, Log-Normal, etc.

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

It has a simple Laplace transform.



$$Z \sim \Gamma(k, \lambda)$$
 such that $k, \lambda > 0$

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Density function of Z

$$\pi(0,z) = \frac{\lambda^k}{\Gamma(k)} z^{k-1} e^{-\lambda z}$$

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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 γ can be interpreted as the squared root of the coefficient of variation of Z at any age.

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

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Thus γ tell us the amount of frailty in a population.

Gamma-Gompertz

 $X \sim Gompertz(a, b)$

Individual hazard

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

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

If
$$Z\sim \mathsf{Gamma}(\gamma)$$

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$$\bar{\mu}(x) = \frac{ae^{bx}}{1 + (\frac{a\gamma}{b})(e^{bx} - 1)}.$$

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Life expectancy: see Castellares, Patricio and Lemonte (2020)

Gamma-Gompertz via the Mode

GAMMA-GOMPERTZ VIA THE MODE

 $X \sim Gompertz(b, M)$

Individual hazard

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

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

If
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b: individual rate of ageing,

M: modal age at death,

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Gamma-Gompertz-Makeham

GAMMA-GOMPERTZ-MAKEHAM

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

Individual hazard

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

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

If
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a: initial level of mortality,

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

 γ : 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 $\theta = a, b, M$.

In R:

manually, using optim()

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- manually, using optim()
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 - · include covariates
 - · other frailty distributions: log-Normal, Beta, etc.

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Maximize Poisson log-likelihood

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

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- manually, using optim()
- R-Package:MortalityLaws
 - · based on GLM models
 - other distributions: Kannisto, Gompertz, Weibull, etc.

FITTING GAMMA-GOMPERTZ - EXAMPLE

My GitHub: github.com/jssalvrz

Directory: EDSD/UnobsHeter

- GGFun.R: Functions to fit the Gamma-Gompertz model (with and without the Mode) using aggregate data.
- Dat.RData: Data from the Human Mortality Database.
- UnobserHeterFit.R: Run the analysis.

When and why to use frailty model?

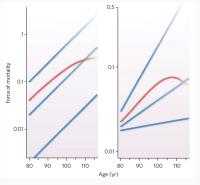
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Vaupel (2010)

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 - Be extremely careful when adding covariates!! (Wrigley-Field, 2020)

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Other applications in genetics, biostatistics, biodemography, evolutionary demography

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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.

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 - Model "old-age" mortality, where does "old-age" start?

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.
- Castellares, Patricio, and Lemonte. On gamma-Gompertz life expectancy.
 Statistics and Probability Letters, 2020.

Questions?