

## REPLY TO BREDBERG AND BREDBERG: **Do some individuals age more slowly than others?**

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Bredberg and Bredberg (1) suggest that some individuals age more slowly than others and that this accounts for the leveling off of death rates after age 100 y. They make this claim in a letter responding to Vaupel et al. (2).

Bredberg and Bredberg (1) vaguely describe their mathematical model without specifying formulas. Apparently, their model is based on

$$q(x-70, b) = ae^{b(x-70)}$$

where  $x \ge 70$  is age and q(x - 70, b) is the annual probability of death at ages 70+ y for an individual with aging rate b. Parameter a is a constant that the authors set at 0.021, and b is normally distributed at age 70 y with mean of 1.107 and SD of 0.0091. The risk of death among survivors to age x is then given by

$$\overline{q}(x-70) = \int_0^\infty q(x-70,b) \cdot \pi(x-70,b) db,$$

where  $\pi(x - 70, b)$  is the probability distribution of bat age  $x \ge 70$  y. At age 70 y, this is the normal distribution specified by Bredberg and Bredberg (1), but at higher ages the distribution is given by

$$\pi(x-70,b) = \frac{\pi(0,b) \cdot s(x-70,b)}{\int_0^\infty \pi(0,b) \cdot s(x-70,b)db},$$

where s(x - 70, b) is the chance of surviving from 70 y to age x > 70 y for individuals with rate of aging b.

This model has serious deficiencies.

Normal distributions can take on negative values, but a negative rate of aging is implausible. Because the mean of the distribution Bredberg and Bredberg (1) used is more than 11 SDs from zero, this fact is unlikely to have much impact, but it is a theoretical blemish. Perhaps the authors worked with a truncated normal distribution to only account for positive values.

In most cases, the so-called accelerated aging models—in which some individuals age more rapidly than others—lead to a decline in mortality at advanced ages, not a plateau (refs. 3–6, among others). In particular, in the model described above which Bredberg and Bredberg (1) may have used, the average annual risk of death reaches a maximum and then declines toward zero.

Furthermore, Bredberg and Bredberg (1) do not cite research that suggests variation among individuals in rates of aging is low and perhaps close to zero (7, 8). If individuals share the same rate of aging but differ in their initial mortality—parameter *a* in the model above then death rates can approach a plateau (9). Conversely, if a mortality plateau is approached at advanced ages, a plausible explanation is that individuals differ in their value of *a* but not *b* (10).

1 J. Bredberg, A. Bredberg, Centenarians may hold a key to continued rise of human longevity. Proc. Natl. Acad. Sci. U.S.A. 118, e2110032118 (2021).

2 J. W. Vaupel, F. Villavicencio, M.-P. Bergeron-Boucher, Demographic perspectives on the rise of longevity. Proc. Natl. Acad. Sci. U.S.A. 118, e2019536118 (2021).

5 M. Finkelstein, V. Esaulova, Asymptotic behavior of a general class of mixture failure rates. Adv. Appl. Probab. 38, 244–262 (2006).

6 D. R. Steinsaltz, K. W. Wachter, Understanding mortality rate deceleration and heterogeneity. Math. Popul. Stud. 13, 19–37 (2006).

7 J. W. Vaupel, Biodemography of human ageing. Nature 464, 536–542 (2010).

8 F. Colchero et al., The long lives of primates and the 'invariant rate of ageing' hypothesis. Nat. Commun. 12, 3666 (2021).

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The authors declare no competing interest.

PNAS 2021 Vol. 118 No. 32 e2110693118

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Published August 5, 2021.

https://doi.org/10.1073/pnas.2110693118 | 1 of 2

<sup>3</sup> J. W. Vaupel, A. I. Yashin, Heterogeneity's ruses: Some surprising effects of selection on population dynamics. Am. Stat. 39, 176–185 (1985).

<sup>4</sup> J. S. Weitz, H. B. Fraser, Explaining mortality rate plateaus. Proc. Natl. Acad. Sci. U.S.A. 98, 15383–15386 (2001).

**9** J. W. Vaupel, K. G. Manton, E. Stallard, The impact of heterogeneity in individual frailty on the dynamics of mortality. *Demography* **16**, 439–454 (1979). **10** T. I. Missov, J. W. Vaupel, Mortality implications of mortality plateaus. *SIAM Rev.* **57**, 61–70 (2015).

