Title
Stress resistance, heterogeneity, and mortality plateaus: A comment on Drapeau et al (multiple letters)

Permalink
https://escholarship.org/uc/item/8jx0k0s3

Journal
Experimental Gerontology, 35(8)

ISSN
0531-5565

Authors
Mueller, LD
Drapeau, MD
Rose, MR
et al.

Publication Date
2000-11-27

DOI
10.1016/S0531-5565(00)00132-7

License
CC BY 4.0

Peer reviewed
Letter to the Editor

Stress resistance, heterogeneity, and mortality plateaus: a comment on Drapeau et al.

Drapeau et al. (2000) argue that their results provide evidence against the idea that heterogeneity in individual frailty is responsible for mortality rate plateaus. They compared age-specific mortality rates of selected lines that had previously been shown to have different starvation resistance and mean life span. They stated that “populations that are greatly differentiated for stress resistance should show great differences in their late-life mortality schedules” (p. 72). In this letter, I will show that a commonly used heterogeneity mortality model predicts exactly the opposite: differences in mortality rates among the selected lines will tend to diminish at old ages.

Assume that age-specific mortality rates are described by a Gompertz hazard function. One effect of selection on stress resistance might be to modify the age-independent mortality parameter, $A_j$, that is characteristic of a selected line (Nusbaum et al., 1996). Then, the mortality rate at age $x$ of an “average” member (at birth) of selected line $j$ is

$$\mu_j(x) = A_j e^{bx}.$$  

$A_j$ is a measure of the average stress resistance of individuals in line $j$, and lines that are “greatly differentiated for stress resistance” will have large differences in $A_j$. Individual heterogeneity in frailty (or stress resistance) is easily incorporated into this model by the methods of Vaupel and Yashin (1985a):

$$\mu_{ij}(x) = z_i A_j e^{bx},$$

where $\mu_{ij}$ is the hazard rate of individual $i$ in line $j$ at age $x$, and $z_i$ is the frailty of individual $i$. The $A_j$ may be scaled so that the $z_i$ have a mean value of 1 at birth in each line. If $z_i$ is gamma-distributed with variance $\sigma_j^2$ in line $j$, then the average mortality rate at age $x$ of individuals in line $j$ will be

$$\bar{\mu}_j(x) = \frac{A_j e^{bx}}{1 + \frac{A_j}{b} (e^{bx} - 1)}$$

(Vaupel and Yashin, 1985a). As $x$ becomes large, $\bar{\mu}_j(x)$ approaches an asymptote equal to $b/\sigma_j^2$. That is, the plateau mortality rate is independent of the average “robustness” ($A_j$) of the population, and selected lines that do not differ in the Gompertz age-dependent mortality parameter, $b$, or in variance of frailty, $\sigma_j^2$, will converge to the same late-age mortality rate. Thus, this heterogeneity model predicts the opposite outcome to that asserted by Drapeau et al. An even more paradoxical result is possible: if selection for
greater stress resistance results in decreased variance of frailty, then the lines selected for greater stress resistance may have higher plateau mortality rates than the unselected lines (Vaupel and Yashin, 1985a,b). Interestingly, Drapeau et al. were able to demonstrate significant differences in mortality rate among the selected lines before age 30 days but not later. That result is entirely consistent with the heterogeneity model presented here.

As a numerical example, consider two populations, stress resistant (SR) and control (C). Both populations have the same age-dependent mortality parameter and the same variance in frailty: $b = 0.12$, and $\sigma^2 = 0.75$. Both values are typical of Drosophila melanogaster (Fukui et al., 1996). The populations are differentiated only with respect to the age-independent mortality parameter. For the SR population, $A_j = 2 \times 10^{-4}$, and for the C population, $A_j = 1 \times 10^{-3}$. Thus, at every age, an “average” (at birth) C individual has five times the hazard rate of an “average” SR individual. Eq. (1) was used to calculate the ratio of mortality rates of the two populations (C:SR) as a function of age. The ratio was maximal at birth and declined thereafter (Fig. 1). Unless extremely large cohorts were used, it would be difficult to demonstrate differences in late-age mortality rates, even between populations that differed five-fold in “robustness.”

In summary, the results presented by Drapeau et al. are consistent with a basic heterogeneity model. That does not prove that the model is correct. However, it does support the model and it does show that their experiments do not constitute a refutation of heterogeneity theory. Furthermore, two recent papers suggest that convergence of mortality rates at old ages is a general consequence of within-line variation in age-specific

Fig. 1. Age-specific mortality rate differences between the two populations differing five-fold in age-independent mortality parameter. Solid line represents the ratio of mortality rates (untransformed) of the two populations; dashed line represents the difference in log-transformed mortality rates.
mortality risk. Service (2000) simulated among and within-line variation in both Gompertz parameters. Among-line variance of log(mortality rate) was greatest at intermediate ages. Pletcher and Curtsinger (2000) found that among-line variance of log(mortality rate) decreased at old ages under a wide variety of assumptions about among and within-line variation in mortality parameters. Contrary to the arguments made by Drapeau et al., it would be the absence of convergence in mortality rates between the selected lines that might constitute evidence against heterogeneity as an important cause of mortality rate plateaus.

References


P.M. Service *

*Tel: +1-520-523-5216; fax: +1-520-523-7500.*