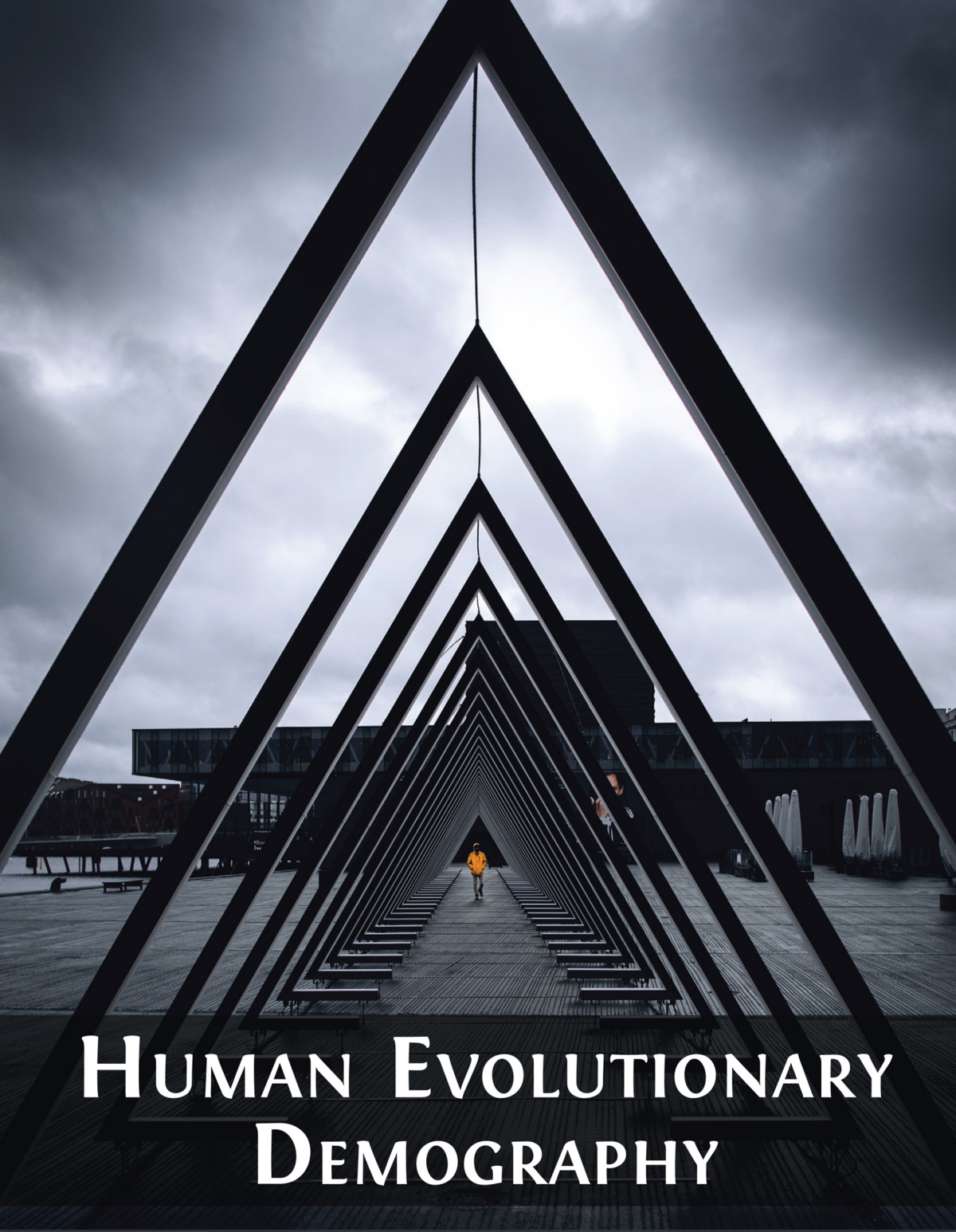

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17. Human Mortality from Beginning to End: What Does Natural Selection Have to Do with It?

Steven Hecht Orzack and Daniel Levitis

Evolutionary demographers who study human traits usually focus solely on natural selection as a cause of a trait's evolution. However, demographic stochasticity, genetic drift and phylogenetic inertia can also significantly influence trait evolution. We describe why accounting for these influences is necessary in order to correctly test hypotheses about the adaptive nature of human demographic traits. For example, "U"-shaped mortality from the beginning to the end of life is found in many vertebrates, which implies that phylogeny must be considered in understanding the evolution of this trait in humans. Even when these other evolutionary influences have negligible effects on a human demographic trait, it is incorrect to assume that the observed trait must be optimal. Current data and analyses are not sufficient to properly confirm the claim that "U"-shaped mortality rate in humans is the result of natural selection in humans or that it is optimal. We describe the additional data and analyses that are needed in order to properly test these claims.

Human life can be hazardous. For example, it is likely that 60% or so of conceptions die before birth, with most deaths occurring in the first month of pregnancy (see Léridon 1977; Macklon et al. 2002; Boklage 2005; Orzack et al. 2015; Jarvis 2016; Orzack and Zuckerman 2017 and references therein). The mortality rate during pregnancy declines rapidly thereafter and less than 1% of fetuses alive at the beginning of the third trimester die before birth.

This steep pre-birth decline precedes the beginning of what many demographers refer to as the "U"-shaped trajectory of age-specific mortality rate from birth onward (Gompertz 1825; Makeham 1860; Heligman and Pollard 1980; Gage and Mode 1993; Carnes et al. 1996; Levitis and Martínez 2013). This "law of mortality" is taken by many to describe the age-specific pattern of mortality from birth onward in all or most human populations. It is thought to have these features:

1. A decline in age-specific mortality rate to a low value "soon" after birth. This decline is the left limb of the "U".
2. A low age-specific mortality rate (the bottom of the "U") that often lasts well into adulthood. In some populations, there is a mortality increase and decrease around the time of the transition from juvenile to adult.

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3. An increase in age-specific mortality rate in later life. For example, in all populations in the Human Mortality Database (https://www.mortality.org), the mortality rate of 70-year-olds is higher than that for 60-year-olds and lower than that for 80-year-olds. This increase is the right limb of the "U".

From here on, we refer to the entire trajectory from conception onward as the "U"-shaped trajectory of age-specific mortality rate.

What Are the Possible Causes of the "U"-shaped Trajectory?

We begin by noting that many analyses seek to explain only the right limb of the "U", i.e. the later-age increase in age-specific mortality rate. Some investigators have sought a physiological explanation (e.g. Rubner 1908; Pearl 1928). More recently, many investigators have sought an adaptive explanation, i.e. one invoking natural selection as a cause. At first glance, such attempts would seem ill-conceived if not foolish. After all, senescence and death are things one would expect *not* to evolve. Isn't survival the consequence of the process of evolution via natural selection? In fact, senescence and death can be two consequences of this process (Bidder 1932; Williams 1957; Hamilton 1966; Kirkwood and Holliday 1979; Kirkwood and Austad 2000). All of these explanations involve the distinction between current evolutionary "fitness" (as determined by survival and reproduction) and future evolutionary fitness, but their causal details differ. For example, Williams (1957) proposed that senescence occurs because a "pleiotropic" mutation, one decreasing mortality rate earlier in life and increasing it later in life, can be favored by natural selection (see also Abrams 1993; Williams et al. 2006; Gaillard and Lemaître 2017). The reason is that a decrease in early mortality results in a greater number of descendants than would result from a later increase of the same magnitude, just as an earlier contribution to a savings account "outweighs" a later contribution of the same magnitude because of interest accrued. In contrast, Medawar (1946) and Hamilton (1966) proposed that late-age deleterious mutations potentially compromise future reproduction less as compared to early-age mutations. Accordingly, the intensity of natural selection against deleterious mutations decreases with age and so the age-specific mortality rate increases. See Charlesworth (2000) for details.

Despite these causal differences, William's hypothesis and the Medawar/Hamilton hypothesis are *adaptive* explanations. Natural selection is assumed to be the *only* evolutionary force acting on the trait. Given the constraint of either pleiotropy or of deleterious mutations, the population is expected to evolve to the predicted mortality rate trajectory, which is locally optimal, i.e. it results in a higher fitness than the alternative trajectories delineated by the model (see below). It is incorrect to refer to the Medawar/Hamilton explanation as "non-adaptive" (cf., Dańko et al. 2012).

What Are We to Make of Such Adaptive Explanations?

There is a two-part answer to this question. The first part is that the adaptive explanations provide important insights. For example, they demonstrate the necessity of considering the temporal expression of influences on survival and reproduction. They also illustrate how natural selection can cause the evolution of a partially-deleterious trait. The second part of the answer is that neither explanation is as illuminating as claimed by its original proponents. For

example, consider the prediction of Hamilton's (1966) model that the age-specific mortality rate increases monotonically after the age of first reproduction, which underlies his famous claim (p. 12) that "….senescence is an inevitable outcome of evolution". One can distinguish between a "strong" form of Hamilton's prediction, which is that age-specific mortality rate increases monotonically, and a "weak" form of his prediction, which is that age-specific mortality rate eventually increases. Evidence *for* the strong prediction necessarily supports the weak prediction but not vice-versa. Evidence *against* the strong prediction does not necessarily refute the weak prediction but evidence against the weak prediction necessarily refutes the strong prediction.

What Evidence Do We Have About the Age-specific Mortality Rate?

Some of the diversity of the trajectories of the age-specific mortality rate is depicted in Figure 1 in Jones et al. (2014) (see also Vaupel et al. 2004; Cohen 2017; Jones and Vaupel 2017). For some species, the age-specific mortality rate increases monotonically, which supports the strong and weak predictions. For others, the mortality rate eventually increases after the age of first reproduction, which contradicts the strong prediction and supports the weak prediction. Other studies not compiled by Jones et al. also reveal this result. For example, Orzack et al. (2011) reported for a long-lived seabird that the age-specific mortality rate of reproductive individuals first decreases and then increases. (The age-specific probability of successful reproduction also decreases but then increases.)

Even when aggregated data from individuals of a species reveal a monotonically-increasing age-specific mortality rate, there can be individuals who live well past most others, thereby demonstrating that the length of an individual life can depend upon fixed and/or random differences among individuals (Tuljapurkar et al. 2009). This demonstrates that mortality need not be a unitary phenomenon within a species (see also Zuo et al. 2018). Such heterogeneity may indicate that there is no fixed length of life. Even if there is a fixed limit to lifespan, longer life may be accessible to most individuals. Determining the influences that govern extremes of the age-specific mortality rate trajectory is the goal of studies of human centenarians (Yashin et al. 2000; Andersen et al. 2012; Barbi et al. 2018) and of organisms that can live much longer than humans (de Magalhães et al. 2007; Keane et al. 2015).

Figure 1 of Jones et al. (2014) indicates that the age-specific mortality rate decreases at some time during life in twenty-four of forty-six species depicted. Of these, seventeen exhibit a decrease and an increase (inconsistent with the strong form of Hamilton's prediction but consistent with the weak form). Seven others reveal only a decrease. In addition, there are two species that appear to be "non-senescent", i.e. to have a constant age-specific mortality rate.

Do these nine species constitute evidence *against* the weak prediction (and therefore against the strong prediction)? If so, they might indicate that an increase of the mortality rate with age could be avoided altogether. These data suggest that the weak prediction is false but they are *not* sufficient to demonstrate that such an increase can be avoided. Why? One reason is that demonstrating the absence of an increase in the mortality rate means demonstrating that an effect does not exist. Accordingly, it is essential to assess whether a study could detect the presence of an effect. Typically, one does this by estimating the statistical power to detect a trend (see Petrascheck and Miller 2017). Such an estimate of the statistical power to detect a given (small) increase in the mortality rate is lacking for the nine species.

Another reason why these data do not falsify the weak prediction is that the absence (or presence) of an increase in the age-specific mortality rate is a claim about the entire lifetime. The implication of this can be illustrated by considering the analysis of the small aquatic invertebrate, *Hydra magnipapillata*, which is one of the two "nonsenescent" species depicted by Jones et al. The mortality rate trajectory they present is based upon the data collected by Schaible et al. (2015), who also present data consistent with a constant age-specific mortality rate for a second species, *H. vulgaris*. The latter species was previously studied by Martínez (1998) who also reported a "lack of senescence" of age-specific mortality rate. These important and well-done studies of laboratory cohorts (some tracked for up to eight years or so) reported constant age-specific mortality rates that are so small that they would imply, if maintained, that 5% of the individuals in a cohort would be alive after hundreds if not thousands of years (see Table 1 of Schaible et al. and also Figure 1 of Jones et al.). The constancy of the age-specific mortality rate is impressive given that an individual is just a few millimeters long.

However, these data do not underwrite the claim of Schaible et al. (2015, p. 15701) that *Hydra* has a "non-senescent life history" or the claim of Archer and Hosken (2016, p. R202) that *Hydra* "escapes senescence". The reason is seemingly contradictory: there are too few deaths. Doesn't this confirm the claim of non-senescence? No. The reason is that the weak prediction about the age-specific mortality rate is a prediction about the entire life. To this extent, *entire* lives (or nearly so) must be measured in order to make a claim that the age-specific mortality rate does *not* eventually increase. (The converse is not true in that one could base a claim *for* such an increase on a small interval of the lifetime.) What *would* support the claim for no eventual increase is a *high* constant age-specific mortality rate, such that we observe the death of all or most all individuals. Instead, in the case of *Hydra*, we have a "censored" data set (because of the low constant mortality rate) and it is the censored portion of the lives (the end) that is needed to support a claim as to the absence of an increase in the age-specific mortality rate. In contrast, assessments of the age-specific mortality rate in, say, humans are not censored in the sense described here because they are based on observations of completed lives. If human data were censored so as to include mostly uncompleted lives, one could also infer that humans have a 5% chance of living for hundreds of years. For example, the National Center for Health Statistics (2018) report (p. 52) that the annual mortality rate in the United States for children less than one year old was 0.0059 in 2015. If this rate were to remain constant as the cohort gets older, it implies that approximately 5% of the cohort would be alive at age 500.

We also note that current analyses do not support the claims by Martínez (1998, p. 217) that there is no "[age-specific] decline in reproductive rates" and by Schaible et al. (2015, p. 15701) that there are "constant age-specific…reproduction rates". One reason is the censoring mentioned above; most lives are uncompleted. Even given such censoring, the data suggest either a decline in age-specific reproductive rate (as later acknowledged by Martínez, see his Figure 2 and p. 220) or an increase that is sometimes followed by a decrease for some cohorts (see Schaible et al. Figure 3). Their claim (p. 15703) that the age-specific reproductive rate "eventually reached a cohort-specific constant level" conflicts with visual impression of a lack of constancy and the statistical basis for the claim about eventual constancy is not presented (see also Estep 2010).

Despite ambiguity about the eventual trend of age-specific mortality rate, the Martinez and Schaible et al. data do not support the strong prediction that the rate increases monotonically.

This is weaker than a conclusion that there is no increase (and no senescence) but it is important. There are many possible reasons for the discrepancies between observed trajectories of the age-specific mortality rate and those predicted by the adaptive models outlined above. For example, the evolution of age-specific mortality rate could be influenced by mutations and natural selection in ways not assumed by Hamilton (Cichoń 2001; Baudisch 2005; Dańko et al. 2012).

What Should We Conclude About the Causes of the "U"-shaped Mortality Rate Trajectory in Humans?

We start by recalling that what needs to be explained is the *entire* "U"-shaped trajectory of mortality rate. The mortality rate is likely high just after conception but declines rapidly during pregnancy. After birth, it is relatively low and possibly constant for several decades. It then increases rapidly for several decades and becomes high. The age-specific mortality rate may even become constant but high at very old ages (Barbi et al. 2018; Newman 2018a, b; Wachter 2018). Do these "phases" of mortality each have a different evolutionary explanation, or are they best understood as having one explanation? The answer to this question is unknown. The separation of the pre-birth and post-birth trajectories arose mainly because the former trajectory was poorly characterized until recently. It still remains much less well characterized than the latter trajectory. Hence, the separation of the two arose because of a lack of data, instead of from empirical results indicating that the two trajectories must have distinct evolutionary causes. However, some investigators do believe that these trajectories need different evolutionary explanations (e.g., Medawar 1952; Hamilton 1966).

Most research has focused on only one part of the post-birth trajectory: the increase in age-specific mortality rate later in life. This is when most people die and so there are huge amounts of data available (e.g., Oeppen and Vaupel 2002; Colchero et al. 2016). Abundant data attracts investigators. In contrast, much of early pre-birth mortality is hidden from view and relatively few people attain the age of 100.

The evolutionary process described by Hamilton (1966) does not predict a downward age-trend in pre-reproductive mortality. To explain this discrepancy, Hamilton posited that it is selectively advantageous for parents to eliminate likely-inviable offspring as early as possible so that the saved energy can be invested into later likely-viable offspring. He may be correct to assume that pre-birth mortality and later mortality require different adaptive explanations. In order to assess whether his explanation is correct, it is important to reconcile the apparent contradiction between the high level of pre-reproductive mortality and the assumption that natural selection is powerful enough to result in an optimal age-specific mortality rate trajectory. All other things being equal, if natural selection is this powerful, it should also be powerful enough that all offspring be viable until they reproduce or at least that mortality of offspring occur immediately after conception so that minimal energy is wasted.

Hamilton's model also predicts death at the end of reproduction because survival thereafter cannot increase offspring number and thereby increase evolutionary fitness. Post-reproductive survival is anecdotally observed in many but not all animal species. There are conflicting claims about its frequency and extent in natural populations because of methodological and empirical challenges (Cohen 2004; Reznick et al. 2006; Levitis et al. 2013; Croft et al. 2015; Lemaître and Gaillard 2017; Ellis et al. 2018; Johnstone and Cant 2019). Sometimes even determining the end of reproduction is difficult. However, one can distinguish between the many species in

which a minority of individuals live past the end of reproduction and the many fewer species in which many individuals survive well past the end of reproduction. Both patterns contradict Hamilton's prediction but the evolutionary implications of the contradictions differ. The first pattern suggests that natural selection acted in the way Hamilton posited but that it is not the sole important influence on the mortality rate trajectory. In contrast, the second pattern suggests that the selective process he described does not capture an important aspect of the evolution of the mortality rate trajectory. Hamilton (p. 37) argued (following Williams 1957) that the second pattern ("typical" post-reproductive survival) is an adaptation that evolved so that a mother avoids the hazards of further reproduction and is thereby alive to provide care, energy and knowledge to her extant offspring. This would imply that there has been natural selection to end reproduction before the expected end of life. Another possibility is that post-reproductive individuals survive because they provide such resources to grand-offspring. This would imply that there has been natural selection to extend survival past the expected end of reproduction. These hypotheses involve the inter-generational transfer of resources, the potential evolutionary influences of which have been analyzed theoretically (Lee 2003, 2008; Chu and Lee 2006; Chu et al. 2008; Gurven et al. 2012). As explored elsewhere in this volume, current data for humans better support the hypothesis that post-reproductive survival of human females is due in part to the evolutionary advantage of transfers of resources from grandmothers to grand-offspring (Hawkes and Blurton Jones 2005; Hawkes 2010; Lahdenperä et al. 2011; Chapman et al. 2019).

Whatever the ultimate explanation of post-reproductive survival in humans proves to be, it is clear that Hamilton's 1966 model does not provide a complete causal explanation of the entire "U"-shaped mortality rate trajectory in our species. The weak prediction that age-specific mortality rate eventually increases is correct. However, the strong prediction arising from his model is incorrect. As Hamilton acknowledged, his model also does not provide an explanation for the pre-birth decline of age-specific mortality rate or for post-reproductive survival. In addition, it does not predict a possible late-age transition between increasing and constant age-specific mortality rates.

How Can We Develop Better Causal Understanding of Mortality Rate Evolution?

In order to answer this question, we describe the causal scheme contained in Hamilton's and Williams' models. They assumed that the trajectory of age-specific mortality rate is optimal, that is, it has evolved because it results in a greater number of descendants as compared to plausible alternatives. In addition, those investigators who have focused specifically on the human-mortality-rate trajectory have assumed it to be the result of natural selection acting either in our species or in our recent ancestors. There are two reasons why these assumptions can lead to incorrect understanding:

The first reason is that it privileges natural selection as a causal explanation. Since Darwin and Wallace's discovery of natural selection in the nineteenth century, evolutionary biologists have debated a variety of claims about the influence of natural selection on trait evolution as compared to the influence of other processes. Two such processes, genetic drift and demographic stochasticity (Parsons et al. 2010; Der et al. 2011), cause traits to evolve without the influence of natural selection. In all real populations, only a finite number of individuals reproduce and the number of offspring each produces is finite. Accordingly, the distribution of

traits among the parents is different from the distribution among their offspring. Genetic drift and demographic stochasticity necessarily influence "micro-evolution", the process of short-term evolution within species, to a small or large extent. They can also contribute to the process of long-term evolution (Wright 1931, 1932, Kimura 1968, 1983; King and Jukes 1969).

Another potential influence on a current trait is evolution in a past environment (Felsenstein 1985; Orzack and Sober 2001; Hansen and Orzack 2005). The influence of this "phylogenetic inertia" has been studied extensively in recent decades, with an important focus being how to control for it when testing hypotheses about adaptation in the current environment. If a trait is present in, say, two related species or populations, it is conceivable that it evolved once in a common ancestor, instead of evolving twice independently. Phylogenetic inertia and current natural selection can jointly contribute to a trait's evolution (Orzack and Sober 2001; Hansen and Orzack 2005). These considerations underscore the need for assessment of the nature of *evidence* about natural selection in the past and current environments. Methods for doing so are reviewed in Hansen et al. (2008) and O'Meara (2012). Ignoring common ancestry among species or populations can falsely increase the apparent amount of independent data one has to test an adaptive hypothesis.

For example, Wilson (2005) claimed that religious belief is a group adaptation because it increases cooperation and reduces exploitation among adherents. He based this conclusion on his assessment of data on thirty-five religions. Each is assumed to provide independent evidence. Each religion has distinctive features (see pp. 426–27) but it is unclear that they each provide independent evidence for (or against) his hypothesis. For example, the religions listed include "Tibetan Buddhism, tenth century", "Tibetan Buddhism, general", and "Tibetan Buddhism, fifteenth century" (not to mention various forms of Buddhism in India, Japan and Korea). The Tibetan forms are not identical. But this does not mean that whatever group benefit each may provide arose independently within each group. If instead, a group benefit arose in the "ancestral" form of Buddhism that gave rise to these three religions, they provide just one independent piece of evidence for the hypothesis. It is even possible that a group benefit to religious belief arose in a religion ancestral to *all* of these religions. If so, there would be only one possible evolutionary event in the sample, instead of thirty-five. An analysis in which the potential dependencies among the data are accounted for is required to assess whether the group-benefit hypothesis is true.

Such an accounting is also necessary in the context of assessing hypotheses about the evolution of the human-mortality-rate trajectory. A "U"-shaped mortality trajectory occurs in a variety of mammals, including other primates (e.g. Caughley 1966; Gage 1998, and references therein). Barring evidence that the most recent species from which *Homo sapiens* evolved did not have a "U"-shaped mortality trajectory, we must account for the possibility that humans have this trait because it evolved in our ancestral lineage prior to the evolution of our species. It may or may not have been adaptive when it evolved. If it were adaptive, it may or may not have been optimal. It cannot be taken to be self-evident that the "U"-shaped mortality trajectory in humans is adaptive (much less optimal) either in the current environment or in the environment inhabited by *Homo sapiens* prior to the "modern" environment of the last few thousand years (see below).

The second reason why a focus on optimality and natural selection can lead to an incorrect understanding is that optimality does not have necessary priority as an explanation for any

trait even if natural selection is an important influence on its evolution. This is true even for mortality and reproduction, which are the "stuff" of evolutionary fitness. These traits and others defined with respect to numbers of individuals can evolve via neutral evolution, i.e. in the absence of natural selection (e.g. see Kolman 1960; Poethke 1988; Orzack and Tuljapurkar 1989; Orzack and Hines 2005; Proulx and Adler 2010). In addition, natural selection need not cause even the average trait in the population to evolve to match the optimal trait, much less cause the trait of an individual to be the optimal trait (see Birch 2016 and references therein). One possible reason is that the optimal trait does not breed true.

The common focus in human evolutionary demography on optimality appears to be in part due to the use by practitioners of the common assumption in economics that individuals (or businesses) possess optimal consumption and production behaviors (see examples and discussion in Friedman 1953; Winter 1964; Ursprung 1988; Schoemaker 1991; Hodgson 1994; Rogers 1994). Other concepts in economics that may provide insights to evolutionary biology and evolutionary demography (e.g., Ward 1992; Nonacs and Dill 1993; Hammerstein and Hagen 2005; Bendor et al. 2009) have been much less used by biologists and demographers. Why this is so is unclear; see Samuelson (1985).

A Claim that the Age-specific Mortality Rate Trajectory in Humans is Optimal

Chu et al. (2008) derived a model that predicts that the optimal age-specific mortality rate trajectory from birth onward (not from conception) is "U"-shaped. Their important model predicts that the age-specific mortality rate declines after birth because the selective advantage of a reduction in mortality increases with age. This increase occurs because the amount of energy invested in the offspring increases with age. Their model also predicts that individuals survive past the end of reproduction because surviving individuals can still transfer resources such as knowledge and resources to offspring. The authors state correctly (p. 171) that "Age-specific mortality is U-shaped for many species…". Their title, *Explaining the Optimality of U-Shaped Age-Specific Mortality*, reflects the authors' beliefs that 1) these observed U-shaped trajectories are optimal and 2) that the apparent qualitative match of the shape of observed trajectories and the U-shaped trajectory predicted by the optimality model reveals *why* it is optimal. The notion appears to be that the model correctly represents the biology that has led to the evolution of an optimal trajectory.

What should we make of Chu et al.'s claim about the "U"-shaped mortality rate trajectory in humans? Their claim that the trajectory is optimal could be true. However, this is a conclusion that needs to be substantiated by evidence; it cannot be assumed to be true or even likely true.

In order to illustrate the analyses needed to assess the adaptive significance of the trait, we focus on the high pre-birth mortality (although Chu et al.'s model does not strictly apply to this period of development). The analyses that we use to assess this hypothesis are similar to those needed to assess the rest of the mortality rate trajectory.

As noted above, perhaps up to 60% of conceptions die within the first month or two of pregnancy. The proximate cause of much of this mortality is thought to be aneuploidy (the absence of one of two copies of a chromosome or the presence of an extra copy) caused mostly by errors during meiosis, the process by which haploid gametes are produced, see Guerneri et al. 1987; Hassold and Hunt 2001; Plachot 2001; Menasha et al. 2005). Most aneuploidies appear to

be fatal because the genetic information needed for normal development is unbalanced (Torres et al. 2008). The high frequency of aneuploidies in human ova has often been attributed to the long duration of female meiosis (Shuttleworth 1909; Jenkins 1933; Penrose 1933, 1934). The production of an ovum begins before a woman is born and pauses until sexual maturation (De Felici et al. 2005). After that time, usually a single ovum matures each month until menopause occurs. Accordingly, at least ten years and as many as fifty or so years could elapse between the time an ovum's precursor cell arises and the time the ovum is mature. It is possible that the length of this process is a cause of aneuploidy. There could be other causes (Brook et al. 1984; Nagaoka et al. 2012). For example, the incidence of aneuploidy of chromosome 21 among newborns appears to decline with maternal age before it increases (Erickson 1978) suggesting that hormonal imbalance may be an influence.

The production of a single mature ovum each month implies that at most 600 or so of the hundreds of thousands of primary oocytes in a woman's ovaries become fertilizable. The consequence of this sampling process is stochastic variation in the frequencies of genetic variants (generated by mutation and by the process of genetic recombination during development of the oocyte; see Hou et al. 2013). This sampling is expected to result in the loss of rare mutations (Ewens 2012). The mutations lost could include those that change the mortality rate trajectory in such a way that it results in higher fitness, as even advantageous mutations are most likely lost due to genetic drift. A quantitative calculation might reveal that the influence of natural selection and the influence of genetic drift are comparable in magnitude. This would imply that the trajectory is relatively immutable across species and that the potential for adaptive evolution is reduced. This reinforces the need for the investigator to provide evidence for the influence of natural selection on the trajectory. In the end, consideration of other evolutionary influences may not alter our conclusions about the power of natural selection. However, whatever the outcome, this kind of analysis is essential.

We next consider the influence of phylogenetic inertia on pre-birth mortality in humans. There is evidence that some degree of fetal wastage is widespread among vertebrates, invertebrates, and even plants and fungi (Levitis 2011; Levitis et al. 2017). It occurs in a variety of placental mammals (Brambell 1942, 1948; Casida 1953) including primates (Turner et al. 1987; Harley 1988; Palombit 1995; Knapp et al. 1996; Takeshita et al. 2016).

This suggests that an evolutionary explanation that relies solely upon human-specific biology may be incorrect. To resolve this, we need better comparative data on the amount of fetal wastage in at minimum our closer primate relatives, including chimpanzees, gorillas, and orangutans. If there is a significant difference in the amount in fetal wastage in humans as compared to the amount in these and other primates, it is circumstantial evidence that the amount in humans has evolved after our lineage split from those leading to these other species. We can then look to specific aspects of human biology in order to explain this difference. There is some evidence that the amount of fetal wastage in humans is higher than that of other primates (Corner and Bartelmez 1953) but we lack adequate comparative data and this is an unresolved issue. This analysis again illustrates how consideration of other evolutionary influences can alter our conclusions about the power of natural selection.

How Does One Test the Hypothesis of Optimality?

Let's imagine that our "U"-shaped age-specific mortality rate trajectory has in fact evolved entirely via natural selection in our species. Proving optimality requires evidence that it results in higher fitness than plausible alternatives. Would it be reasonable to conclude from the qualitative match between the "U"-shapes of the observed and optimal trajectories that Chu et al.'s claim of optimality is optimal?

The notion of optimality embodies the Darwinian idea that natural selection occurs when the trait of *an* individual outperforms other traits that an individual might possess. All other things being equal, this superior performance by the individual implies that the population should evolve to consist entirely (or nearly so) of individuals with that trait. Accordingly, assessment of whether a trait is optimal *requires* assessment of whether individuals are identical in the trait they express; this need not mean that individuals are identical at any given time, as the comparison is made over the entire time over which trait expression influences fitness. Assessment of optimality also *requires* a quantitative test of the optimality model's prediction. Orzack and Sober (1994a, b) describe why these analyses are necessary to support a claim of optimality.

In order to assess whether the observed mortality rate trajectory is optimal, we must determine whether individuals differ with respect to the mortality trajectory they would express if each had multiple lives to live. If such data were available for a reasonably large set of randomly-chosen individuals, one could compare the trajectories with a log-rank test (Harrington and Fleming 1982). A significant test statistic would suggest that there are differences among individual trajectories and imply that natural selection has not been powerful enough to cause the optimal trait to be fixed in the population. If there is no evidence for such heterogeneity (as determined by standard statistical criteria, such as a change in the Akaike Information Criterion), the observed and optimal distribution of lifespans can be compared quantitatively, say, with a goodness-of-fit test. If there is no evidence for a discrepancy between them (as determined by standard interpretation of the observed test statistic), one can conclude that current evidence supports the claim that the age-specific mortality rate trajectory is optimal (as compared to the non-optimal alternatives delineated in the optimality model). Orzack and Sober (1994a, b) explain how various combinations of qualitative and quantitative test outcomes support different inferences about the power of natural selection to influence a trait's evolution.

Of course, any heterogeneity among individuals in a real population with respect to their potential mortality rate trajectories is unobserved because each individual dies once. The observed age-specific mortality rate trajectory is aggregated over individuals and so it can by itself *never* underwrite a claim for optimality at the level of the individual. Accordingly, by itself even a quantitative match of the observed and optimal trajectories underwrites at most the claim that natural selection has had an important influence on the evolution of the mortality trajectory. This is not a trivial accomplishment but it leaves unresolved whether the trajectory is optimal. In contrast, a discrepancy between the observed and optimal trajectories can underwrite a claim *against* optimality.

The Importance of Understanding Evolutionary Causation

Any endeavor to assess the influence of natural selection must attend to consistency between causation in the observed biology and assumed causation in the adaptive model being investigated. This imperative can be illustrated by considering the cause of the pre-birth mortality in humans. As noted above, the rate of this mortality appears to decrease dramatically during pregnancy. Could this trend be explained by extrapolation of the causal framework in Chu et al.'s (2008) model? Much of the earliest mortality is likely the death of embryos and fetuses that are incapable of normal development and could not eventually reproduce if they did not die. Accordingly, the mortality rate declines because after these deaths occur most but not all of the remaining individuals are capable of normal development and most will be born alive. In contrast, in Chu et al.'s model, the decline of early mortality after birth arises from the increase in the selective advantage to a parent of protecting energetic investment in current offspring. This benefit increases as the offspring gets older. This explanation for the post-birth attenuation of the mortality rate cannot provide a causal account for most of the pre-birth decline of the "U"-shaped trajectory because the latter arises from the elimination of inviable offspring. Energetic investment in the inviable offspring is not being protected. We emphasize that Chu et al. make no claim that their model explains pre-birth mortality in humans.

At present we lack an adaptive explanation of the age-specific mortality-rate trajectory from conception onward. Such an explanation must account for the apparently distinct causes of the pre-birth and post-birth declines in the trajectory. It has been claimed that a mother can "suppress" offspring if the present environment is less suitable for those offspring than is the future environment for future offspring (Wasser and Barash 1983; Wasser and Isenberg 1986). Proponents assert that this explanation is in keeping with the adaptive explanation for such mortality in other mammals. There is evidence that pregnancy failure is associated with stress (see Table 1 in Wasser and Isenberg 1986), but this is not sufficient by itself to demonstrate that failure is adaptive, much less optimal. Further assessment of this claim will require analysis of an optimality model that includes the indirect transfer of energy from current offspring (by their termination) to future offspring as well as the direct transfer of energy from parents to current offspring.

Going Forward in Human Evolutionary Demography

The important distinctions between the hypotheses that natural selection has had some influence or an important influence on a trait and the hypothesis that a trait is optimal usually go ignored by evolutionary demographers. The consequence has been inferential ambiguity about the power of natural selection to influence trait evolution. A resulting danger is that investigators may make contradictory conclusions about the occurrence of optimality given the same data in part because they use unspecified "private" criteria in their judgment of optimality (see examples from evolutionary biology in Orzack 2014).

Human evolutionary demographers would do well to avoid such inferential ambiguity by exercising care when testing hypotheses about the realized influence of natural selection on trait evolution. Human evolutionary demography will become a more meaningful endeavor if two changes occur. One is the adoption of higher standards for the evaluation and testing of hypotheses about optimality and adaptation, which depends in part on having data on current

trait function and on the history of trait evolution. Human evolutionary demographers do understand the potential of the latter influence on trait evolution in a narrow sense in as much as they often invoke the action of past natural selection. For example, Robson and Kaplan (2003, p. 150) claim that long human life expectancy (and high intelligence) evolved in response to life in the "hunter-gatherer societies that prevailed for the two million years of human history". Similarly, Kaplan and Lancaster (2003, p. 179) claim that human patterns of fertility, mating and parental investment are a "constellation" of traits that "derives from the hunter-gatherer way of life, which characterized the vast majority of human evolutionary history" and Volk and Atkinson (2013, p. 182) claim to "generate a reliable estimate of [infant mortality and child mortality] levels in the EEA". The EEA or "environment of evolutionary adaptedness" was defined by Bowlby (1969, p. 58) as

> [...] the environment in terms of which the adaptedness of man's instinctive equipment must be considered [...] [it] is the one that man inhabited for two million years until changes of the past few thousand years led to the extraordinary variety of habitats he occupies today.

Our point is not to agree or disagree with the specific claims made above. Instead, our point is that human evolutionary demographers already traffic in the notion that history matters. The notion is that only *human* history matters (although sometimes this is extended to include some of our nearest primate relatives, such as the chimpanzee). This may be true but it is not self-evidently true, despite how special the traits possessed by humans are (see also Irons 1998). Either way, this acknowledgement of the potential influence of past natural selection on current human demographic traits illustrates that the path forward towards improved practice in human evolutionary demography can be rooted in part on current conceptual understanding. When invoking the action of past natural selection, human evolutionary demographers need only extend the potentially relevant history of trait evolution to include other primates and probably other vertebrates.

The second change needed in order that human evolutionary demography continues to make progress is for practitioners to understand the potential of forces *other than natural selection* to influence trait evolution. Such an understanding has been instrumental in allowing evolutionary biologists to better understand the evolution of a myriad variety of non-demographic traits (e.g. Wright 1932; Lande 1976; Kimura 1983; Hartl et al. 1985; Lynch and Hill 1986; Lynch 1990; Proulx and Adler 2010; Koonin 2016; Šustar and Brzović 2016; Charlesworth and Charlesworth 2018) and demographic traits (e.g. Tuljapurkar et al. 2009; Steiner et al. 2010; Orzack et al. 2011; Steiner and Tuljapurkar 2012) in many organisms. Just as evolutionary biology needs demography in order to achieve its explanatory potential (cf. Metcalf and Pavard 2007), so too does human evolutionary demography need evolutionary biology.

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