A comparative assessment of univariate longevity measures using zoological animal records

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Summary

Comparative biogerontology evaluates cellular, molecular, physiological, and genomic properties that distinguish short-lived from long-lived species. These studies typically use maximum reported lifespan (MRLS) as the index against which to compare traits, but there is a general awareness that MRLS is not ideal due to statistical shortcomings that include bias resulting from small sample sizes. Nevertheless, MRLS has enough species-specific information to show strong associations with many other species-specific traits, such as body mass, stress resistance, and codon usage. The major goal of this study was to see if we could identify surrogate measures with better statistical properties than MRLS but that still capture inter-species differences in extreme lifespan. Using zoological records of 181 bird and mammal species, we evaluated 16 univariate metrics of aging and longevity, including non-parametric quantile-based measures and parameters derived from demographic models of aging, for three desirable statistical properties. We wished to identify those measures that: 1) correlated well with MRLS when the biasing effects of sample size were removed; 2) correlated weakly with population size; and 3) are highly robust to the effects of sampling error. Non-parametric univariate descriptors of the distribution of lifespans clearly outperformed the measures derived from demographic analyses. Mean adult lifespan and quantile-based measures, and in particular the 90th quantile of longevity, performed particularly well, demonstrating far less sensitivity to small-sample size effects than MRLS while preserving much of the information contained in the maximum lifespan measure. These measures should take the place of MRLS in comparative studies of lifespan.

Keywords

aging; senescence; captive; maximum lifespan; demography; biogerontology

Introduction

Aging is a process that gradually impairs vigorous mature adults and renders them more susceptible to a wide range of diseases and disabilities, leading to a progressive increase in mortality risk. Maximum recorded lifespan (MRLS) is the standard comparative metric used in experimental and observational research into the causes of aging (Comfort 1979; Austad & Fischer 1991; Holmes & Austad 1995; Wilkinson & South 2002; Hulbert *et al.* 2007), and it is often taken as the key endpoint in comparisons among species, genotypes, or groups exposed to different environmental manipulations. Comparative biogerontologists have long made use of MRLS as a surrogate for species-specific aging rate, and much effort has gone into compiling tables of MRLS values for this purpose (Finch 1990; Carey & Judge 2000; de Magalhaes & Costa 2009).

It is widely appreciated, however, that MRLS is a problematic indicator for several reasons. First, MRLS is a downwardly biased indicator of extreme lifespan. As sample sizes increase, expected MRLS values are expected to increase as well. Second, the sample variance associated with estimates of population MRLS may be high, especially with small sample sizes. These two issues may present serious problems in comparative studies involving rare non-laboratory animals. Consequently, MRLS may differ across species owing to differences in the number of species records used to determine longevity as well as to inherent differences in the physiology and ecology of the species. Third, MRLS does not use data effectively in situations where records are incomplete, which is often the case in many observational studies where the terminal recorded event for an individual may not be death (i.e., right-censoring). Lastly, it reflects lifespan of a single individual per species, grossly overestimating the characteristics of other members of the species. Given the concern that some record-breaking lifespans may be exaggerated (Steven Austad, pers. comm.), such extreme dependence on single outliers is undesirable.

Other metrics have been introduced in attempts to improve upon MRLS by applying multivariate demographic models of aging, such as Gompertz or Weibull functions, to survival data (Promislow 1991; Wilson 1994; Ricklefs & Scheuerlein 2002). In some cases, these parameters have been assigned controversial biological interpretations, as, for example, when the slope of a Gompertz plot is interpreted as a measure of the rate at which aging occurs (Finch *et al.* 1990; Pletcher *et al.* 2000; Bronikowski *et al.* 2011), and the intercept of a Gompertz plot is interpreted as the inherent frailty of the members of the population (Spencer & Promislow 2005; Maklakov *et al.* 2006; Flatt & Kawecki 2007). In other cases, parameter estimates derived from these models are combined, for example by multiplication, to arrive at a univariate summary of aging rates (Ricklefs 1998; Ricklefs & Scheuerlein 2001). Non-parametric methods have also been proposed that summarize the lifespan distribution of an elite subset of the population into quantiles and/or means (Wang *et al.* 2004; Gao *et al.* 2008). One significant advantage of these alternative methods over MRLS is that their application is not limited to the empirical distributions of complete lifespans; they can benefit from the use of the Kaplan-Meier estimator, which allows the use of censored data. Each of these estimators, and their combinations, has only an indirect relationship to the underlying biological processes of aging, and it is unclear how well these longevity metrics perform compared to MRLS as an index of differences of the pace of age-related change among biologically interesting populations.

Questions about the evolution of different aging rates and the cellular and molecular processes that can lead to striking differences in longevity among related species are the central arena for comparative biogerontology. Within orders of mammals, MRLS values among species of rodents or primates can vary 4- to 8-fold. Many evaluations of hypotheses about comparative aging among species have depended on MRLS as the index of inter-

species differences in aging rate, despite the measure's well-known defects. Our goal in this project was to make use of population data, obtained from zoo populations of nearly 200 bird and mammal species, to explore the sampling properties of various univariate aging and longevity metrics. Some of these metrics have been proposed by others, but some have not previously been applied to questions in the comparative biology of aging. We wished to understand how well each measure indicates extreme lifespan across a phylogenetically diverse range of species that differ in life history and data quality. In addition, we wanted to understand how robust each metric is to sampling effects, namely sampling variance and bias arising from small population sizes. A major goal of this study was to understand the limitations of MRLS as a comparative longevity metric and, if possible, identify an alternative measure for MRLS that minimizes the sampling issues and data-use restrictions associated with that measure.

The datasets available to test hypotheses in the comparative biology of aging differ in the proportion of missing values and in the extent of erroneous data. The data often combine records from wild and captive populations that differ in environmental factors (housing conditions, food availability, reproductive histories, predation and infection levels, etc.) that can have strong effects on mortality risks through both age-dependent and age-independent pathways. Although tables of MRLS values across species contain a good deal of information critical to testing ideas about the biology of aging, there is a pressing need to develop improved demographic endpoints for biogerontology.

Results

Onset of aging

Although it is not clear whether the aging process begins at any defined life history transition (birth, puberty, age at first reproduction), we assume here that deaths at the earliest ages, for example perinatal deaths and deaths of juveniles, are unlikely to be informative about inter-population variances in aging rates. We therefore used two methods to determine the age before which mortality should be ignored, and we report the results derived from both methods. We analyzed the subset of individuals from each species with events (deaths or last observations) that met or exceeded one of two species-specific truncation ages: 1) T_1, the age of reproductive maturity for that species, or 2) T_2, the age at which the mortality rate reaches a minimum (see Table S1 for species, relevant life history information, and T estimates). Across the 163 species that had at least 50 adults defined by both threshold definitions (T_1 and T_2), the truncation ages correlated reasonably well ($\rho = 0.53$, $p < 0.0001$, Spearman's rank correlation; see Figure 1). Nearly two-thirds of the species with both T_1 and T_2 estimates had an age at minimal mortality that exceeded the age at reproductive onset (108 of 163 species). This pattern is consistent with Promislow's (1991) earlier analysis of a much smaller set of species records in which he showed $T_1 < T_2$ in 75% (18 of 24) of cases where age at maturity and age at minimal mortality differed. More recent life history analyses also show that the onset of aging tends to follow the timing of reproductive maturity (Jones *et al.* 2008; Peron *et al.* 2010). The correlation between T_1 and T_2 estimates strengthened slightly when the collection of species was reduced to include only the 125 species with 150 or more adults ($\rho = 0.58$, $p < 0.0001$). While the positive correlation was encouraging, it seemed prudent to analyze the sampling properties of the various metrics using each T-definition independently. As we show below, however, the choice of T-definition had little effect on the sampling properties of the metrics.

Metric estimates

Using both threshold definitions, we estimated sixteen univariate longevity values (defined in Table 1) for each of the 175 (T_1) and 165 (T_2) species, respectively, that had at least 50

adult individuals (as defined by each *T*-definition) with recorded events (Supplement Tables S2A and S2B). For a few cases of the T_1 treatment, the Weibull function failed to converge. This may have resulted from too few adult deaths in the dataset (Ricklefs 1998) or from inclusion of part of the early age range typified by elevated mortality (by definition, this would not be a problem using the T_1 criterion).

Correlations among metrics

We correlated estimates across species using both truncation methods (Table 2) holding population size constant (a full correlation matrix, in which sample size is not corrected for, is presented in Table S3 of the Supplemental Information). In general, the nonparametric measures of lifespan were highly correlated among each other (0.869 or better). Except for the mean (e_0) and median lifespan (Q_{50}), the lowest partial correlations among non-parametric estimators were between MRLS and Q_{90} (0.950 for T_1 and 0.941 for T_2). The partial correlation between MRLS and Q_{95} was also 0.950 using the T_1 criterion but higher (.957) for T_2. With the exception of the Weibull intercept, W_A, and Ω (a function of the slope and intercept of the Weibull model), parametric measures of mortality correlated negatively with MRLS and the other nonparametric measures of longevity. This is to be expected, because these are aging parameters, and aging and longevity are negatively associated. Of these, only the Gompertz and Weibull intercepts (G_A and W_A) correlated reasonably well with MRLS (-0.789 and -0.698 for G_A and -0.928 and -0.938 for W_A). Slopes and intercepts were poorly correlated for both the Gompertz and Weibull models. Independence between G_A and G_B estimates has been previously recently reported across eight primate species (Bronikowski *et al.* 2011).

Correlations between metrics and population sizes

We correlated metric estimates with population sizes (*n*) using both T_1 and T_2 criteria (Figure 2). In most cases, metrics that were estimated using T_1 were less strongly associated with *n* than those estimated using T_2. As expected, we found positive correlations between *n* and MRLS (+0.105 and +0.162). Positive correlations increased with increasing *x* in M*x*LS (the mean lifespan of the *x* longest-lived individuals), reaching +0.276 and +0.312 with M32LS. For these metrics, the T_2 treatment yielded slightly greater correlations that the T_1 treatment. With the exception of W_A, parametric measures were very sensitive to the choice of *T*. The Weibull and Gompertz slopes, as well as the Weibull omega measure, yielded moderately negative correlations with *n* in the T_2 treatment (-0.358, -0.480, and -0.480, respectively). Using T_1, however, these correlations remained negative but markedly decreased in magnitude (-0.039, -0.127, and -0.089). The Weibull and Gompertz intercepts were weakly and positively correlated with population size, except for G_A estimated with T_2, which was the highest correlation that we observed (+0.313). Promislow et al (1999) also report little association between Gompertz parameters and population size in simulated populations using a defined age of onset (similar to our T_1 treatment). The more extreme quantile-based measures (Q_{90}, Q_{95}, e_{90}, and e_{95}) showed the weakest associations with sample size (correlations ranged between -0.037 and +0.018). The measures of central tendency (Q_{50} and e_0) correlated weakly and negatively with *n* using T_1 (-0.066 for both) and correlated more strongly with T_2 (-0.174 and -0.147). Correlations involving these measures, and using either T_1 or T_2, most closely resembled those generated from the extreme quantile-based measures.

Rank persistence

We next asked how finite population size affected the ranking of lifespan metrics across all study species. Every population (for our purposes, a population was considered the worldwide collection of animals of the same species, and we use species and population interchangeably) was re-sampled n_i times with replacement, where n_i was each species'

sample size, and each species was ranked in order of each longevity value (resulting in 16 metric-specific ranking vectors). For example, a MRLS vector may be ordered species A > species B > species C > species D and a W_A vector may rank species B > D > A > C. This procedure was repeated, and each pair of metric-specific ranking vectors was analyzed for stability. Rank persistence, as inferred by a low Spearman's Footrule Distance D and a high Spearman's ranked correlation coefficient ρ, quantified how robust each measure was to sampling variation. We investigated four population size treatments. The $n \geq 50$ treatment included all species populations with at least 50 observed adult deaths ($n_{T1,50} = 175$, $n_{T2,50} = 165$). We performed three other rank persistence analyses using the same resampling approach, except that we made the minimal sample size requirement more stringent each time. We considered species with $n \geq 150$ ($n_{T1,150} = 147$, $n_{T2,150} = 126$), $n \geq 500$ ($n_{T1,500} = 66$, $n_{T2,500} = 56$), and $n \geq 1500$ ($n_{T1,1500} = 15$, $n_{T2,1500} = 13$). Note that the treatments differed only in the choice of which species to use; any species chosen for a treatment had all of its individuals included in the analysis. Rank persistence averaged over 1000 resampled population pairs is described in Table 3. For each treatment, robustness measure, and T-definition, the five most persistent metrics are indicated in boldface and the five least persistent metrics are shaded.

In general, the non-parametric estimators outperformed the parametric estimators in nearly every treatment. The sole exception was that the Weibull intercept W_A was a frequent top-five performer. The Gompertz intercept G_A performed well at the highest population size treatment using the T_2 definition. G_B, W_B, and Ω were always among the least persistent metrics. Of the nonparametric estimators, the quantile-based approaches demonstrated the most persistence. This was especially evident in the metrics that described central tendency (e_0 and, to a lesser degree, Q_{50}). More extreme values of longevity, Q_{90} and e_{90}, also performed very well across all treatments. The M32LS method performed very well at low sample sizes but less so at the $n \geq 500$ and $n \geq 1500$ treatments.

All of the metrics under consideration are subject to sample size bias. For this reason, we reasoned that the species rankings reflected both inherent differences in the biology of species as well as variation in the size of the pooled zoo animal population datasets provided by ISIS. We note that datasets available for testing hypotheses about species differences in aging and longevity are also likely to contain a preponderance of small populations, similar in this way to the datasets available through ISIS. We attempted to remove the latter source of variation from our rank persistence analysis by randomizing sample size. As before, a rank persistence analysis was performed using populations with adult numbers of at least 50, 150, 500, and 1500 individuals. In this treatment, however, the resampling procedure was changed. Instead of taking n_i samples from each species i, the number of samples was randomized; the exponential of some uniformly distributed number of samples x_i were drawn with replacement over the interval $\ln(50) \leq \ln(x_i) \leq \ln(n_i)$ (this sets the range at between 50 and n_i with most samples near the low end of the range). As before, adults were those individuals with terminal events (deaths or last observations) defined by T_1 or T_2 and rank persistence was quantified by D and ρ. Mean persistence values are shown in Table 4.

The randomized treatments demonstrated weaker rank persistence. This is what we would expect if randomizing sample size eliminated that component of the fixed species rank determined by population size. This was consistent with our goal of removing sample size as predictor of longevity. In general, the quantile-based nonparametric estimators appeared to preserve rank best, although the Weibull intercept W_A again showed relatively high rank persistence. Interestingly, the relative advantage of these nonparametric estimators over the alternatives appeared to be greater with randomized population sizes. This finding suggests that sample size variation has a greater effect on parametric measures of longevity than on non-parametric measures. As before, W_A and the more intermediate quantile measures, Q_{50}

and e_0, performed best and Q_{90} and e_{90} performed next best. As a group, parametric methods continued to appear to be the worst performers (excepting W_A). At high sample sizes, however, the Gompertz intercept G_A performed relatively well, providing species ranks that were roughly as persistent as the quantile-based measures. The largest change in relative performance involved nonparametric measures M16LS and M32LS; these were middling-to-good performers with fixed populations sizes but very poor performers when sample sizes are randomized. It appeared that for metrics MxLS, increasing x made for better metrics when samples sizes were fixed but worse metrics when sample sizes varied. This makes sense when we consider that, in terms of population lifespan quantiles, MxLS has different meanings as population size changes. Using unrealistically low population sizes to illustrate this point, MRLS is Q_{95} in a population of 20 but equal to Q_{50} (the longevity median) in a population of two.

Results were largely unaffected by our choice of T-definitions and persistence metric (D or ρ). In no case did altering these choices change a top-five performing metric (in terms of rank persistence) into a bottom-five performer. Ranked correlations between D and ρ values were very high in all population size treatments and using both T-definitions, with ranked correlation coefficients among persistence measures ranging between 0.941 and 0.988 (Table 5, "fixed" and "D and ρ" headings; "fixed" refers to the condition of this treatment where population sizes are preserved and not randomized, as in the following treatment). Likewise, persistence values were highly correlated across T-definitions. Ranked correlations ranged from 0.950 to 0.994 (Table 5, "fixed" and "T_1 and T_2" headings) in the three treatments with lowest population sizes. In the highest population size treatment, n 1500, the ranked correlations ranged somewhat lower, 0.721 and 0.812.

Discussion

A wide range of bird and mammal species have evolved that differ widely in life histories, including variation in the rate at which aging leads to increased risks of mortality due to disease and infirmity. This rich set of related species could, in principle, be used to generate and evaluate hypotheses about the cellular and physiological factors that time the aging process, factors that make it very unlikely that a particular mouse will survive 5 years, a dog survive 20 years, and a human survive 110 years. Lifespan is a convenient, if flawed, surrogate for addressing hypotheses about the biological basis for aging rates because many factors besides age change can lead to death, and because aging leads to many consequences in addition to changes in mortality risk. Ideally, hypotheses about the distribution of aging rates and age-dependent changes across species could be tested by a database in which multiple age-sensitive traits had been tested in hundreds of individuals across a wide range of diverse species. In practice, however, physiological data of this kind are available only for a handful of species, and for most species the only available data relevant to questions of comparative aging rate are in the form of survival tables. The obvious problem is to determine the best way to summarize these population–specific tables and provide a comparative metric that preserves relevant biological information relating to lifespan while disregarding the effects of extraneous or confounding factors, such as population size.

Despite the widespread appreciation of its statistical association with population size, the maximum recorded lifespan (MRLS) is favored by comparative biologists because it is believed to measure an individuals' intrinsic potential for long life. The degree to which the other metrics measured this maximum, without regard for the biasing effects of small sample size, is quantified by the partial correlations between candidate metrics and MRLS, holding population size constant. Population size bias is addressed more directly by the total correlation between sample size and metric value. Ideally, the best measures of extreme lifespan are those with the greatest magnitude of partial correlations with MRLS and the

least magnitude of the total correlation between the measure and sample size. By these criteria, the best are those that nonparametrically define some well-defined elite fraction of the population: Q_{90}, Q_{95}, e_{90}, and e_{95}. Given that adult lifespans are typically right-skewed, we expected that measures of central tendency should be affected least by sample size. Instead, we found negative correlations between these measures and n that were slightly stronger than those obtained from Q_{90}, Q_{95}, e_{90}, and e_{95}. Good evidence has been collected to suggest that animal size and lifespan are positively associated. If zoos favor larger collections of smaller animals (a feasible expectation given resource limitations), then these negative correlations between n and mean and median lifespans may reflect true associations between intrinsic aging and population size and not simply bias. Such associations would cause effects that act in opposition to the effects of sample size bias on MRLS estimates. Put differently, maximum recorded lifespan would be *more* sensitive to n than reflected by our correlation estimate. We note, however, that regardless of whether we choose the ideal correlation to be zero or slightly negative, Q_{90}, Q_{95}, e_{90}, and e_{95} still appear to best satisfy these criteria for best longevity metrics.

Because MRLS observations depend upon the identification of single individuals, it seemed reasonable to expect that estimates would suffer from high sampling error. Indeed, our re-sampling analysis indicated that MRLS had a larger sampling variance than the quantile-based measures at all sample sizes. The difference intensified when species were disassociated from population sizes, suggesting that small sample bias may contribute to the sampling error for MRLS. Most parametric estimates suffered from high sample variance. The quantile-based measures produced the most reliable estimates, especially when population sizes were allowed to vary. Excluding those that describe the central tendency, we see that the least extreme measures Q_{90} and e_{90} are the least variable.

The 90th quantile of adult lifespan, Q_{90}, and the average of the top 10th percentile of adult lifespan, e_{90}, appear to be the best alternatives to using MRLS as a comparative metric for extreme lifespan. Both correlate well with MRLS when sample size is corrected for, correlate weakly with population size, and demonstrate relatively little sampling variance. Furthermore, both can accommodate right-censored data. Neither measure seems to have a clear advantage over the other based upon the sampling characteristics analyzed here. However, one may prefer Q_{90} over e_{90} if extreme lifespan exaggeration was considered to be a problem, because Q_{90} is expected to be more robust to this effect than e_{90}. We recommend that future aging studies consider using the 90th quantile lifespan as a comparative metric.

The metrics that took the average of a set number of elite individuals (MxLS) performed poorly as candidate metrics for extreme lifespan. Not surprisingly, MxLS measures correlated extremely well with MRLS when population size was held constant. However, the positive correlation between the measure and population size *increased* for this family of measures. Our rank persistence analysis illustrated problems inherent in the use of MxLS as a comparative metric. When population sizes were not randomized, MRLS and the closely related M4LS performed well, as indicated by high rank persistence to resampling. Similar methods that correlate well to MRLS (M16LS and M32LS) also performed well under these conditions. However, when population sizes were randomized to decouple the effects of biology and animal collection size, these performed very poorly compared to other measures. The reason for this is evident if we recognize that MxLS is the mean of the top $1 - (n\text{-}x)/n$ percentile of the population. Because the threshold for inclusion is sensitive to population size, variation in population size varies the lifespans of the individuals included in the measure.

Judged as univariate descriptors of longevity, measures based upon parameterized demographic models performed poorly as a group, with the exception of the Weibull intercepts, W_A. Estimates of these metrics seemed to be more sensitive to our choice of method for delineating the aging and non-aging segments of each species life history. These metrics correlated poorly with MRLS, holding population size constant. With respect to the Weibull-based omega values, our results (using T_1 as our definition of adulthood, the partial correlation was -0.238 and the total correlation was -0.464) contrast sharply with a full correlation between and MRLS of -.83 across 150 captive vertebrate species recently reported by Ricklefs (2010b). At least two reasons may account for this discrepancy. First, our analytical methods differ: Ricklefs uses least-squares regression to fit a three-parameter Weibull model to death records at all ages (we use maximum likelihood to fit a two parameter model to adult events) and he does not consider right-censored observations (we do). Second, the numbers of animal records per species tend to be far greater in our study. If small sample sizes upwardly bias estimates of omega (this is speculation on our part), then the variance in sample size across species (such as both studies find) will generate excess negative correlations between omega and MRLS. The results from the rank persistence analyses suggested that the demographic parameters, especially those that describe the slopes of mortality functions, are subject to high sampling variance. The Weibull intercept, however, demonstrated high partial correlations with MRLS and low sampling variances. Our only reason for not recommending this measure is that it correlated more strongly with population size, which suggests that it is a more biased measure than some of the nonparameteric alternatives.

While much attention in comparative biogerontology focuses on measures of extreme lifespan, investigators might consider using measures of central tendencies instead. There are at several reasons for doing so. First, as we show here, mean adult lifespan exhibits the least amount of sampling variance. It is the most repeatable measure that we investigated. Second, compared to MRLS, there is far less association between population size and metric estimates. As we have argued, there is reason to believe that mean lifespan should be the measure that is *least* biased by small sample size. Third, mean lifespan is highly correlated with MRLS (correcting for population size), with a partial correlation coefficient of between 0.91 and 0.93. Other measures, such as Q_{90}, may perform better in this respect, but it appears that a great deal of the biological information that is parameterized by maximum lifespan is also expressed by the mean lifespan of those animals that live at least as long as the ages measured by T_1 and T_2. Last, the most familiar definitions and predictions of the evolutionary change of phenotypes from one generation to the next are expressed as changes in the means (Robertson 1966; Price 1970; Price 1972; Lande & Arnold 1983). In evolutionary biology, it is changes in the means, and occasionally the variances, of phenotypes that are nearly always the subject of study. We note, though, that the means and medians used for our calculations are for samples that exclude perinatal and a high proportion of juvenile mortality, and cannot be used to evaluate issues related to life expectancy at birth or proportions of offspring surviving to reproductive age.

Ultimately, the choice of whether to compare means or extremes may depend upon the nature of the comparative question that is under study. We recommend, however, that this decision is made explicit and justified by each study. Comparative biogerontologists have prepared extensive compilations of MRLS data, and for many meta-analyses MRLS may, unfortunately, be the only available measure currently available. Compilation of similar lists of Q_{90} values and mean lifespans of animals surviving at least to T_1 or T_2, would be a worthwhile project for field biologists and zoo consortia to tackle as a service to aging research, and we recommend that such statistics be routinely included in reports about lifespan and aging in wild, captive, and experimental populations. In this respect, our study

makes an important contribution by providing these estimates for nearly 200 bird and mammal species.

Experimental procedures

Obtaining animal records

We obtained records for 200 species of captive-born birds and mammals from the International Species Information System (ISIS), an international non-profit membership organization of zoos and aquariums. ISIS maintains an extensive database derived from over 800 zoological institutions in 77 countries, including life history information on over 2.4 million individual animals, of which over 1.5 million have exactly recorded birthdates. ISIS data has contributed to previous studies of demographic parameters related to lifespan evolution (Ricklefs 2000; Ricklefs 2010a; Ricklefs 2010b), in which the absence of predation in zoological settings was believed to be an advantage in determining intrinsic mortality rates. Because information in the ISIS database differs greatly among species in the number of individuals, the degree of right censoring, the extent of missing data, and the pooling of information from zoos of varying size and environmental characteristics, these data provide an excellent opportunity to compare statistical estimates of extreme longevity in a realistic context.

Animal records included sex, birth dates and death dates (or last recorded observations). Animals with unknown or estimated birth dates were removed from the analysis. We also removed all animals with life-spans that exceeded 120% of the maximum recorded lifespan as reported by AnAge (de Magalhaes & Costa 2009). We chose this value to allow for the possibility that the ISIS records included valid ages of animals that exceeded the AnAge values (many record-breaking individuals were identified), but we did not want to include records of animals that were suspiciously old. We used two methods (explained below) to determine the initial age of our analysis of aging (T) for each species. Most (181 species) had 50 or more individuals (n 50) with ages at death that exceeded T–values determined by one or both methods. These species (Supplemental Table 1) were chosen for further analysis.

Determining T

Populations from the ISIS datasets exhibited U-shaped mortality functions of age. The close monitoring of individual animals in the zoological setting, especially starting with birth or hatch, generates data on early mortality. As we were only interested in the distribution of lifespans that are associated with senescence, we discarded deaths that occurred before the onset of aging (T). This age was determined in two different ways: First, we ignored all deaths that occurred before the age of first reproduction as determined by the literature (see Table S1 in the Supplemental Information). When sex-specific ages of first reproduction were available and different, we took the greater of the two ages to be the truncation age (T_1) for both sexes.

The second method found the age at which mortality was minimized (T_2). For each reduced population, we used a simple iterative routine to find T_2:

1. We calculated L_X values using the 'Survival' package in R 2.11.0 (R Development Core Team 2011; Therneau & Lumley 2011). Individuals with known death dates (complete) and dates of last observation (right-censored) were used. We binned the population into groups of similar lifespans, defined by regular age intervals. The bin number is defined by the "Sturges" algorithm (Sturges 1926), where the number of classes is a function of sample size, $N = 1+\log_2(n)$. This function is commonly used to construct histograms.

2. The age mid-point of the class with the lowest mortality value was the provisional T_2 value.

3. A new population was defined by individuals from this class and those from either of the flanking classes.

4. We repeated steps 1-3 using the new population until age bins appeared with no deaths or until the Sturges function no longer returned more than two classes.

5. The estimate of the mortality minimum was the last meaningful T_2 value (Table S1).

Estimating metrics

We estimated longevity using the post-T (aging) populations. Longevity metrics were of two types. Non-parametric estimates were functions of longevity quantiles, based upon survival curves generated from the survival analysis described above. Parametric estimates derived from functions of Gompertz or Weibull parameters fit to each aging population. Model fitting was accomplished using the 'Survomatic' package in R 2.11.0 (Bokov & Gelfond 2010; R Development Core Team 2011). Metrics are described in detail in Table 1, and estimates are presented in Supplemental Table S2.

Rank persistence

We were interested in discriminating between populations represented by their longest-lived individuals. One way to evaluate the merits of candidate metrics is to perform rank persistence analyses of re-sampled species-specific populations. We began with a collection of P species, each of size N_p. We re-sampled each species twice with replacement, taking N_p draws from each population p. For each metric m, there was a ranking sequence specific to each sample set. For example, the MRLS rankings for five sample species ($p = 1$ to 5) may have been

$$R1\,(m{=}MRLS) = \{1, 2, 3, 4, 5\}$$
$$R2\,(m{=}MRLS) = \{1, 3, 4, 2, 5\}$$

In this case, species 1 always has the longest-lived individual and species 5 always has the lowest maximum aged individual. Species 2, 3, and 4 exchange rank. Using the same re-sampled data, a metric other than MRLS might return rankings that are more persistent:

$$R1\,(m{=}X) = \{1, 3, 2, 4, 5\}$$
$$R2\,(m{=}X) = \{1, 2, 3, 4, 5\}$$

We can quantify rank persistence using two slightly different measures. The first measure is Spearman's Footrule Distance: $D_{ij} = \sum_{k=1}^{n} \left| x_{ik} - x_{jk} \right|$, where i and j are R1 and R2, x is the rank and k is the population. For the examples above, $D_{R1R2}\,(MRLS) = 4$ and $D_{R1R2}\,(X) = 2$. Persistence increases with decreased D (low values are superior to high values). The second measure is r_{ij}, the rank correlation across the samples, which increases with rank persistence (high values are superior to low values). In our example, $r_{R1R2}\,(MRLS) = +0.7$ and $r_{R1R2}\,(X) = +0.9$. Note that the measures are very similar; the only fundamental difference between the two measures is that r weights changes in rank by the square of the change and D scales the changes linearly. By both measures, the rankings derived using metric X would seem to more robust to changes in the populations resulting from re-

sampling. In terms of rank persistence alone, we would conclude that X is a superior longevity metric to $MRLS$.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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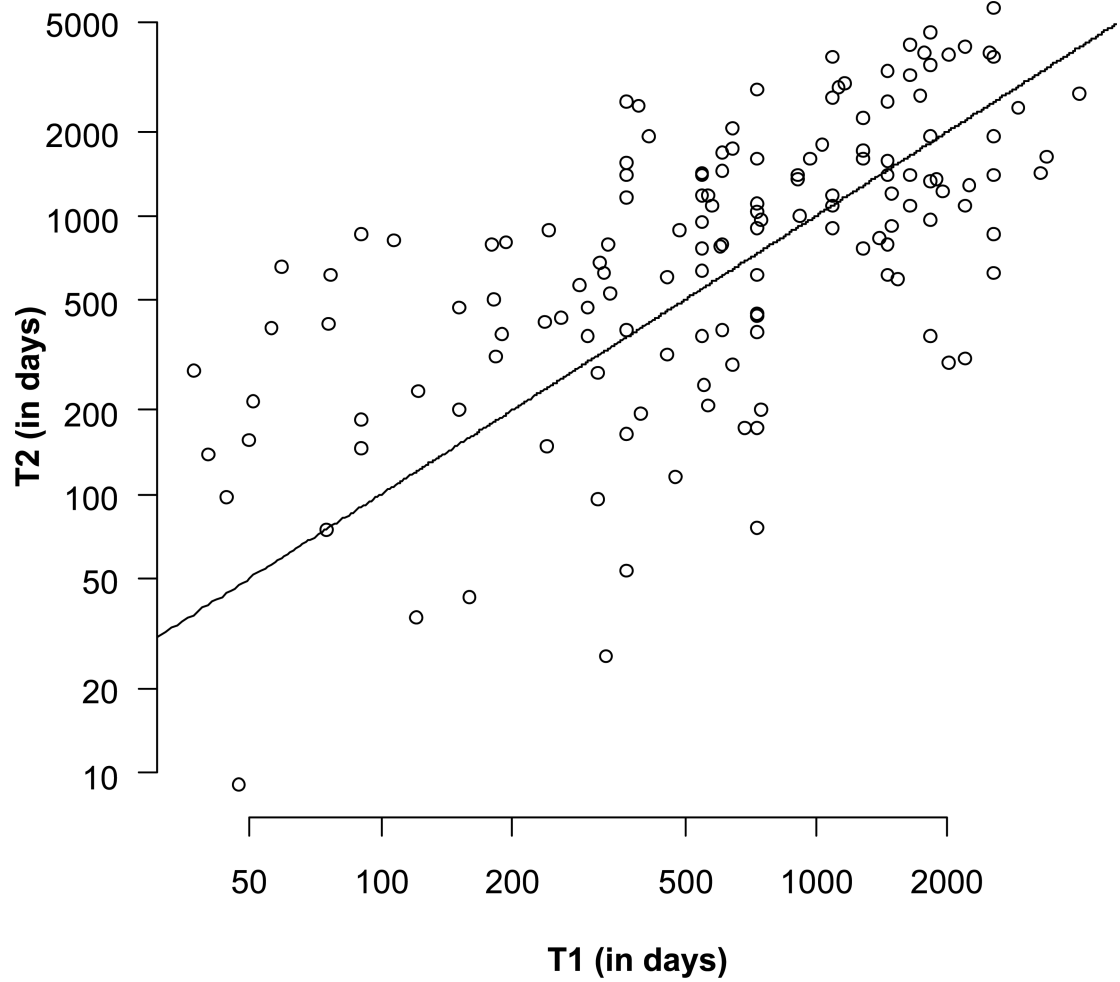
Figure 1. Two methods of determining age of onset
shows the joint distribution between 1) the oldest of the two sex-specific values for the first age of reproduction and 2) age at minimal mortality for 163 species with 50 or more adults (as defined by both definitions). The line defines the $T_2 = T_1$ relationship.
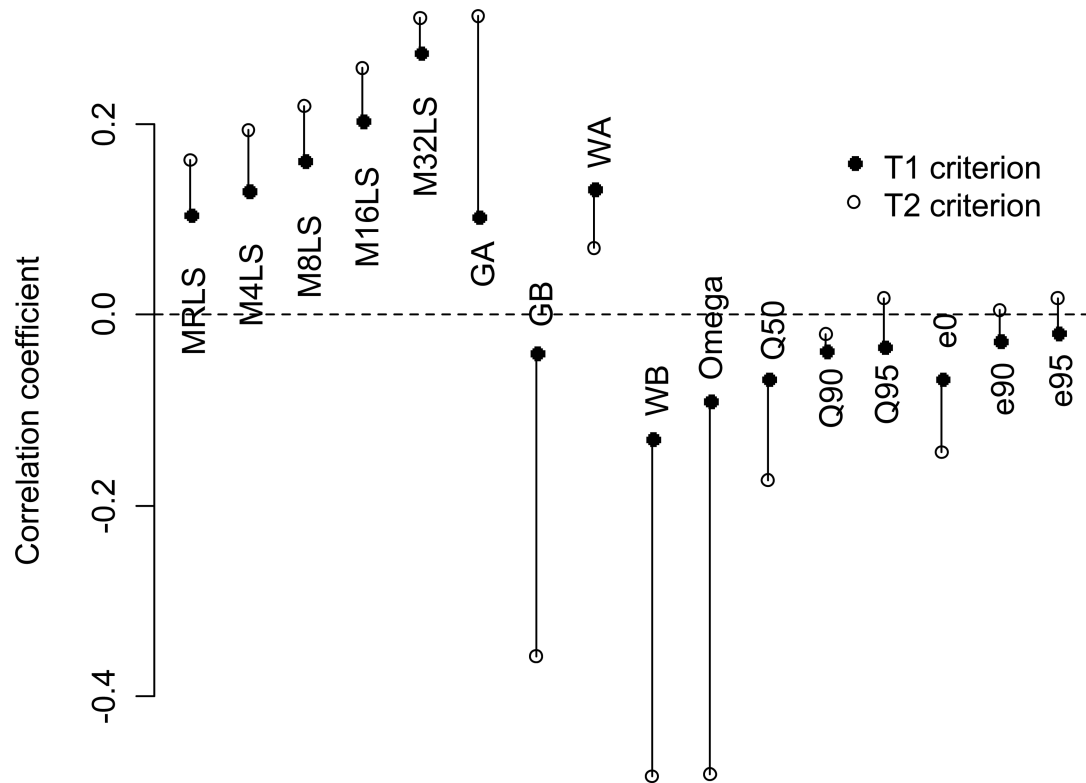
Figure 2. Correlations between longevity metrics and population size
illustrates the correlations between candidate metrics and population size. Correlations are sensitive to the definition of adult (T) used to estimate the measures. For each measure, bars connect the T_1 and T_2-derived estimates. Long bars indicate high sensitivity of the correlation to the choice of T.

Table 1

Univariate longevity metrics

	Parametric?	**Details**
MxLS	no	Mean lifespan of the x longest-lived individuals x=1,4,8,16, 32 (where M1LS represents MRLS)
G_A	yes	intercept of the maximum likelihood Gompertz model ($\mu = Ae^{Bx}$)
G_B	yes	slope of the maximum likelihood Gompertz model
W_A	yes	intercept of the maximum likelihood Weibull model ($\mu = Ax^B$)
W_B	yes	slope of the maximum likelihood Weibull model
Ω	yes	Omega index based upon a Weibull model $\Omega = A^{1/(B+1)}$
Q_X	no	The xth lifespan quantile $x = .5, .9, .95$
e_x	no	The mean lifespan above the xth lifespan quantile $x = 0, .9, .95$

Table 2

Partial correlations using ISIS species data, holding sample size constant

MRLS	.992	.986	.977	.964	-.789	-.570	-.928	.280	-.238	.883	.950	.950	.927	.973	.980
.991	M4LS	.997	.991	.980	-.802	-.563	-.937	.297	-.223	.890	.961	.974	.936	.984	.990
.983	.997	M8LS	.997	.989	-.808	-.550	-.936	.314	-.204	.896	.967	.977	.941	.986	.990
.970	.989	.996	M16LS	.996	-.817	-.534	-.938	.331	-.186	.905	.973	.980	.950	.986	.988
.958	.980	.989	.997	M32LS	-.825	-.511	-.934	.348	-.168	.913	.975	.977	.955	.981	.979
-.698	-.719	-.727	-.739	-.755	G_A	.148	.880	-.641	-.143	-.912	-.856	-.842	-.902	-.837	-.824
-.733	-.718	-.704	-.681	-.652	.186	G_B	.627	.390	.779	-.270	-.485	-.522	-.373	-.533	-.550
-.938	-.948	-.947	-.946	-.942	.828	.628	W_A	-.300	.243	-.912	-.951	-.959	-.940	-.957	-.953
.120	.148	.162	.185	.217	-.635	.452	-.206	W_B	.811	.522	.378	.345	.462	.336	.314
-.297	-.273	-.258	-.234	-.201	-.252	.770	.230	.877	Ω	.028	-.141	-.176	-.045	-.187	-.209
.869	.883	.889	.901	.913	-.858	-.442	-.914	.421	.027	Q50	.947	.919	.986	.921	.907
.941	.956	.964	.972	.975	-.793	-.604	-.956	.244	-.170	.947	Q90	.991	.978	.990	.979
.957	.973	.979	.983	.983	-.773	-.643	-.959	.214	-.204	.930	.994	Q95	.965	.997	.993
.907	.922	.928	.937	.945	-.844	-.511	-.941	.362	-.044	.991	.974	.963	e_0	.966	.954
.971	.982	.985	.985	.981	-.766	-.633	-.963	.195	-.224	.924	.990	.997	.958	e_{90}	.997
.981	.990	.989	.984	.977	-.748	-.690	-.961	.170	-.251	.907	.976	.989	.944	.996	e_{95}

Each cell gives the partial correlation between two measures of longevity taken over ISIS species, holding sample sizes constant. The diagonal cells define the measures. Elements above the diagonal report the corresponding partial correlation using the T_1 truncation method and those below use the T_2 method. For example, the cell at row 1, column 2 is the partial correlation between MRLS and M4LS, which is .992 using T_1. Using T_2, the cell at row 2 and column 1 indicates that correlation between these measures is .991. Shaded cells indicate metric pairs where the absolute value of the partial correlation coefficient is at least 0.95.

Table 3

Rank persistence analysis (fixed population size)

Metric	$n \geq 50$				$n \geq 150$				$n \geq 500$				$n \geq 1500$			
	T_1		T_2		T_1		T_2		T_1		T_2		T_1		T_2	
	D	ρ	D	ρ	D	ρ	D	ρ	D	ρ	D	ρ	D	ρ	D	ρ
MRLS	913	.980	804	.980	588	.983	440	.982	139	.982	104	.983	5.4	.986	4.9	.981
M4LS	997	.983	872	.983	631	.987	464	.986	146	.985	106	.985	7.7	.980	5.5	.980
M8LS	918	.987	794	.987	571	.990	417	.989	124	.989	91	.989	7.8	.981	4.8	.984
M16LS	827	.989	704	.990	514	.992	375	.992	106	.992	79	.991	6.4	.985	3.7	**.989**
M32LS	**725**	**.992**	**602**	**.993**	**457**	**.994**	332	.994	99	.992	70	.993	5.8	.987	**3.2**	**.990**
G_A	1162	.982	1121	.974	692	.988	509	.987	109	.992	81	.991	5.5	.986	**2.6**	**.993**
G_B	2026	.929	1656	.944	1197	.955	881	.953	190	.975	181	.952	10.4	.970	9.1	.953
W_A	**629**	**.990**	**595**	**.993**	**368**	**.994**	**282**	**.996**	**62**	**.997**	**58**	**.995**	**3.0**	**.991**	3.4	.986
W_B	1831	.924	1603	.951	1062	.951	834	.964	174	.970	129	.980	7.5	.976	6.5	.974
Ω	1939	.912	1689	.945	1150	.941	867	.960	191	.964	159	.967	9.3	.968	5.9	.979
Q_{50}	**757**	**.991**	**627**	**.992**	501	.993	**314**	**.995**	**86**	**.994**	**58**	**.995**	**2.3**	**.995**	**1.3**	**.997**
Q_{90}	802	.990	679	**.990**	**467**	**.994**	324	.994	94	.993	**64**	.994	**5.0**	.986	**3.1**	.989
Q_{95}	897	.986	772	.986	514	.992	340	.993	109	.991	69	.993	6.5	.982	5.6	.974
e_0	**547**	**.996**	**463**	**.996**	**347**	**.997**	**222**	**.997**	**55**	**.998**	**50**	**.996**	**1.3**	**.997**	**1.3**	**.996**
e_{90}	**772**	**.990**	**667**	**.990**	**450**	**.994**	**310**	**.994**	**91**	**.994**	**59**	**.995**	**5.1**	**.989**	4.3	.982
e_{95}	830	.989	740	.987	483	.993	347	.993	**91**	**.994**	65	**.994**	5.2	**.990**	4.2	.983

Graphs in Tables 3 and 4 correspond to the *D*-values for each metric specific to each treatment (lowest values are best). Within each graph, the values correspond in order, from left-to-right, with the metrics defined in the first column on the table (e.g., starting with MRLS and ending with e_{95}). Values are standardized in terms of the largest *D* for the treatment. Open circles are values for M*x*LS metrics, open triangles are values for parametric longevity measures, and sold circles are quantile-based measures. Bold-faced values are top-five performers, and the shaded boxes indicate bottom-five performers.

Table 4

Rank persistence analysis (randomized population size)

Metric	$n \geq 50$				$n \geq 150$				$n \geq 500$				$n \geq 1500$			
	T_1		T_2		T_1		T_2		T_1		T_2		T_1		T_2	
	D	ρ	D	ρ	D	ρ	D	ρ	D	ρ	D	ρ	D	ρ	D	ρ
MRLS	1787	.949	1511	.952	1258	.951	926	.951	335	.924	255	.919	24.4	.866	19.0	.859
M4LS	1855	.952	1561	.955	1289	.954	938	.954	347	.922	263	.915	27.5	.837	21.0	.834
M8LS	1980	.946	1642	.951	1392	.948	1012	.948	384	.906	292	.896	31.4	.793	23.5	.799
M16LS	2270	.931	1848	.938	1616	.931	1174	.931	449	.873	344	.858	37.1	.719	26.9	.740
M32LS	2789	.899	2244	.909	2027	.896	1461	.895	551	.815	426	.788	44.7	.600	31.8	.643
G_A	1860	.957	1733	.948	1224	.963	929	.959	244	.961	187	.956	16.7	.931	**10.9**	**.945**
G_B	3187	.846	2631	.873	2122	.865	1585	.865	413	.876	383	.804	27.4	.822	26.4	.712
W_A	**1028**	.974	**968**	**.978**	**646**	**.982**	**504**	**.987**	**126**	**.984**	**126**	**.979**	**11.8**	**.956**	**10.3**	**.942**
W_B	2859	.841	2559	.879	1803	.878	1452	.900	358	.874	290	.898	25.3	.800	17.4	.881
Ω	3070	.814	2692	.867	2005	.844	1537	.885	408	.837	340	.853	25.6	.820	19.1	.847
Q_{50}	**1196**	**.981**	972	**.984**	**840**	**.981**	**551**	**.985**	**173**	**.979**	**131**	**.978**	**9.3**	**.968**	**6.0**	**.978**
Q_{90}	**1257**	**.978**	1039	**.98**	822	**.981**	570	**.983**	197	**.972**	138	**.974**	15.8	.928	**9.0**	**.956**
Q_{95}	1366	.973	1146	.975	880	.978	604	.980	217	.966	151	.969	16.7	.928	12.3	.926
e_0	**872**	**.99**	714	**.991**	**600**	**.991**	395	**.992**	**125**	**.989**	**102**	**.987**	**7.0**	**.983**	**4.2**	**.986**
e_{90}	**1211**	**.979**	1016	**.981**	**788**	**.983**	**548**	**.984**	**192**	**.974**	**134**	**.976**	**14.2**	**.944**	11.2	.933
e_{95}	1321	**.975**	1120	.976	862	.979	605	.980	206	.971	145	.972	**14.3**	**.946**	12.0	.927
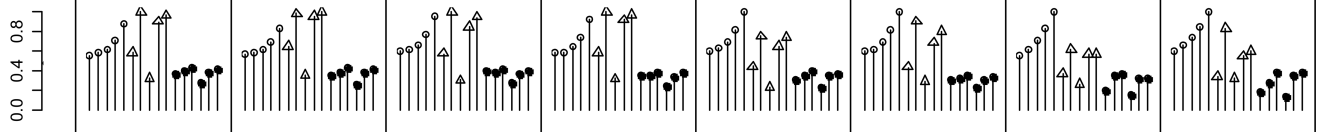
Table 5

Sensitivity of metric performance to treatment and assessment changes

population size	fixed				random			
	D and ρ		T_1 and T_2		D and ρ		T_1 and T_2	
	T_1	T_2	D	ρ	T_1	T_2	D	ρ
n 50	.950	.979	.994	.965	.950	.979	.994	.976
n 150	.968	.985	.974	.950	.976	.988	.988	.982
n 500	.982	.988	.976	.950	.979	.997	.997	.976
n 1500	.941	.974	.812	.721	.965	.994	.956	.891