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RESEARCH ARTICLE

REVISED The dynamic upper limit of human lifespan [version 2; peer review: 1 approved, 2 approved with reservations]

Saul Newman [ID] , Simon Easteal

John Curtin School of Medical Research, Australian National University, Acton, ACT, 2601, Australia

Abstract
We respond to claims by Dong *et al*. that human lifespan is limited below 125 years. Using the log-linear increase in mortality rates with age to predict the upper limits of human survival we find, in contrast to Dong *et al*., that the limit to human lifespan is historically flexible and increasing. This discrepancy can be explained by Dong *et al*.'s use of data with variable sample sizes, age-biased rounding errors, and log(0) instead of log(1) values in linear regressions. Addressing these issues eliminates the proposed 125-year upper limit to human lifespan.

Keywords
lifespan, human lifespan, contradictory findings, ageing, life history, refutation

This article is included in the Preclinical Reproducibility and Robustness gateway.

Open Peer Review

Reviewer Status ❓ ✔️ ❓

	Invited Reviewers		
	1	**2**	**3**
REVISED **version 2** published 09 Jun 2017			❓ report
version 1 published 26 Apr 2017	❓ report	✔️ report	

1 **Jean-Michel Gaillard**, University of Lyon, Villeurbanne, France

2 **Michael R. Rose**, University of California, Irvine, Irvine, USA

   Laurence D Mueller, University of California, Irvine, USA

3 **James Vaupel**, University of Southern Denmark, Odense, Denmark

   José Manuel Aburto [ID] , University of Southern Denmark, Odense, Denmark

Any reports and responses or comments on the article can be found at the end of the article.

Corresponding author: Simon Easteal (simon.easteal@anu.edu.au)

Recent findings by Dong et al.[1] suggested fixed upper limits to the human life span. Using the same data, we replicated their analysis to obtain an entirely different result: the upper limit of human life is rapidly increasing.

Dong et al. conclude that the maximum reported age at death (MRAD) is limited to 125 years in humans[1] and that lifespan

increases above age 110 are highly unlikely, due to the reduced rate of increase in life expectancy at advanced ages.

We repeated Dong et al.'s[1] analysis using identical data (SI). Replicating these findings requires the inclusion of rounding errors, treating zero-rounded values as log(1) and the incorrect pooling of populations.

The Human Mortality Database (HMD) data provide both the age-specific probability of survival (q_x) and the survival rates of a hypothetical cohort of 100,000 individuals (l_x). However, l_x survival rates are rounded off to the nearest integer value.

The magnitude and frequency of l_x rounding errors increases as the probability of survival approaches 1 in 100,000. These rounding errors mask variation in survival rates at advanced ages: over half of l_x survival data are rounded to zero above age 90 (Figure 1b).
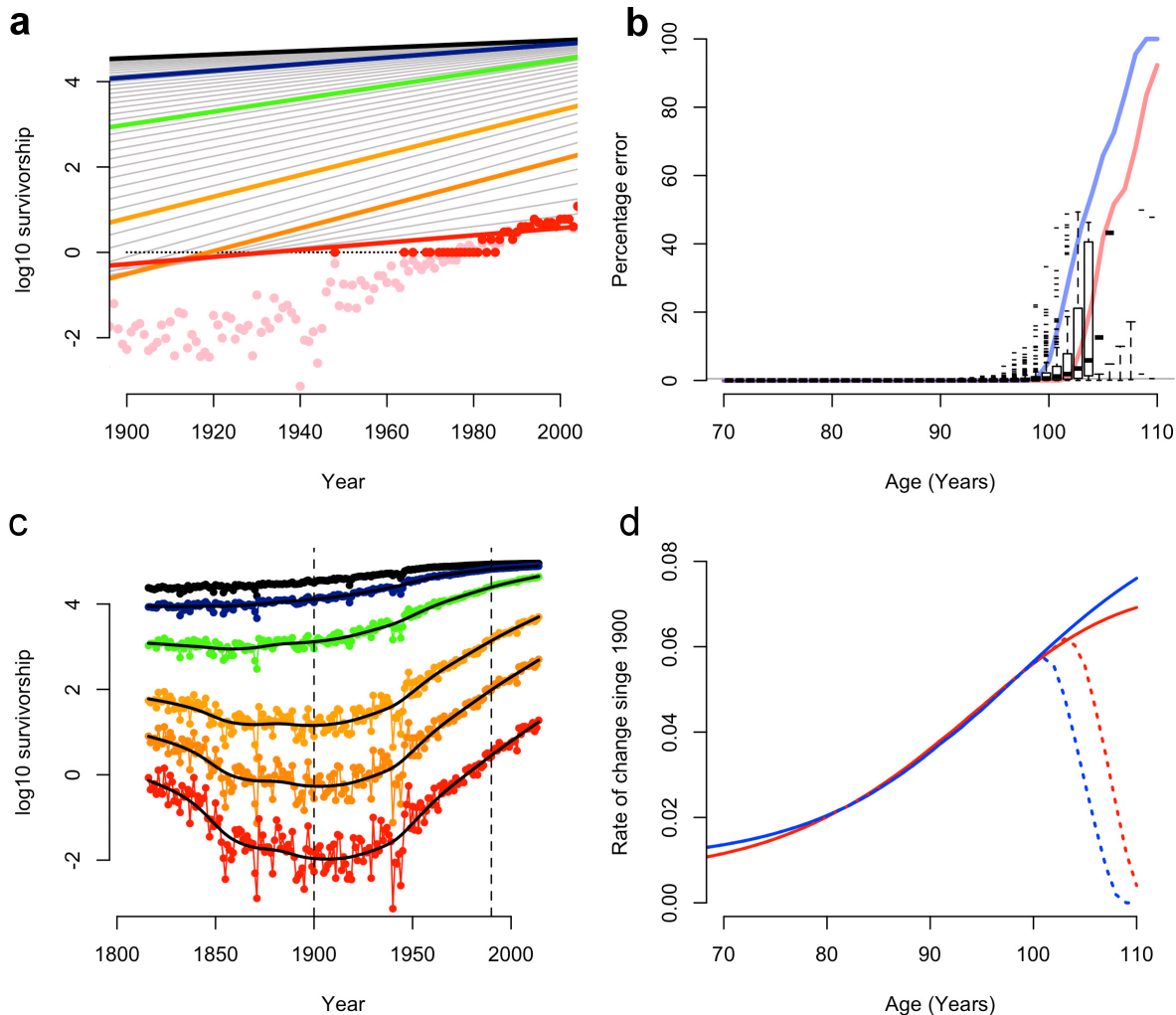
Figure 1. Rate of change in late-life survival for the French population 1816–2014. (a) Figure modified after Dong et al. Figure 1b, showing rounded survival data (red points), rounded survival data with log(0)=log(1) (black points), the resulting linear regression in Dong et al. (solid red line) and observed survival data (pink points). **(b)** Rounding errors in survival data (box-whisker plots; 95% CI) and the proportion of survival data rounded to zero in males (blue line) and females (red line). **(c)** Survival data from **(a)** with rounding errors removed, showing variation outside the 1900–1990 period (vertical dotted lines). **(d)** The rate of change in late-life mortality since 1900 with (dotted lines) and without (solid lines) rounding errors (after Dong et al. Figure 1c).

Dong *et al*. appear to have used these rounded-off survival data in their models[1] and incorrectly treated log(0) values as log(1) in log-linear regressions (Figure 1a–d; SI).

These errors have considerable impact. Re-calculating cohort survival from raw data or excluding zero-rounded figures eliminates the proposed decline in old-age survival gains (Figure 1d; SI).

Likewise, recalculating these data removed their proposed limits to the age of greatest survival gain (SI), which in 15% of cases were the result of the artificial 110-year age limit placed on HMD data[2].

We also found that variation in the probability of death was masked by date censoring[1]. Major non-linear shifts in old-age survival occur outside the 1900–1990 period used by Dong *et al*. (Figure 1c). Why these data were excluded from this regression, but included elsewhere, is unclear.

Evidence based on observed survival above age 110 appears to support a late-life deceleration in survival gains[1]. For the period 1960–2005 Dong *et al*. present data[1] from 4 of the 15 countries in the International Database on Longevity[3] (IDL). In their pooled sample of these countries, there is a non-significant (p=0.3) reduction in MRAD between 1995 and 2006 (Figure 2a).

The declining MRAD reported by Dong *et al*.[1] arises from the use of falling sample sizes. According to the Gerontology Research Group (GRG), 62% of validated supercentenarians alive in 2007 resided in France and the USA. However, these countries are not surveyed[3] by the IDL after 2003 (Figure 2a). The proposed post-1995 decline in MRAD results from this dramatic fall in sample size.

Viewed individually, all four countries have an upward trend in the mean reported age at death (RAD; Figure 2b) of supercentenarians (SI) and the top 5 ranked RADs (Figure 2c). All four countries achieved record lifespans since 1995, as did 80% of the countries in the IDL. Without the pooling of IDL data used by Dong *et al*. there is no evidence for a plateau in late-life survival gains.

We attempted to reproduce Dong *et al*.'s supporting analysis of GRG records. The text and Extended Data Figure 6 of Dong *et al*. do not match annual MRAD records from 1972 as stated[1]. However, they do match deaths of the world's oldest person titleholders from 1955 (GRG Table C, Revision 9) with all deaths in May and June removed (SI).

Actual MRAD data from the GRG support a significant decline in the top-ranked age at death since 1995 (r = -0.47; p = 0.03, MSE = 3.2). However, this trend is not significant if only Jeanne Calment is removed (p = 0.9). Linear models fit to lower-ranked RADs have an order of magnitude better fit, and all indicate an increase in maximum lifespan since 1995 (Supplementary Figure S1; N= 64; SI).

Collectively, these data indicate an ongoing rebound of upper lifespan limits since 1950, with a progressive increase in observed upper limit of human life. To estimate theoretical limits, we developed a simple approximation of the upper limit of human life.

Mortality rates double with age in human populations (Figure 3a and b). Log-linear models fit to this rate-increase closely approximate the observed age-specific probability of death[4]. These models also provide a simple method of predicting upper limits to human life span that is independent of population size.
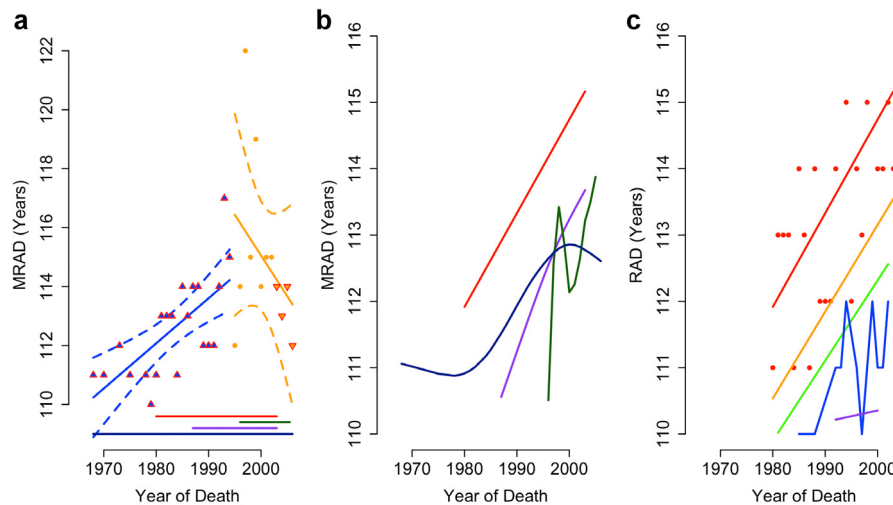
Figure 2. Maximum reported age at death of supercentenarians. (**a**) Reproduction of Dong *et al*. Figure 2a, including 95% CI for increasing (p<0.0001) and falling (p=0.3) maximum recorded age at death (MRAD), showing data biased by the addition and removal (up and down arrows) of populations. (**b**) Locally weighted smoothed splines of MRAD in Japan (green), the USA (red), the UK (dark blue) and France (purple). (**c**) Locally weighted trends of MRAD in the USA across the oldest 5 reported ages at death (red, orange, green, blue and purple lines show rank 1–5 respectively).
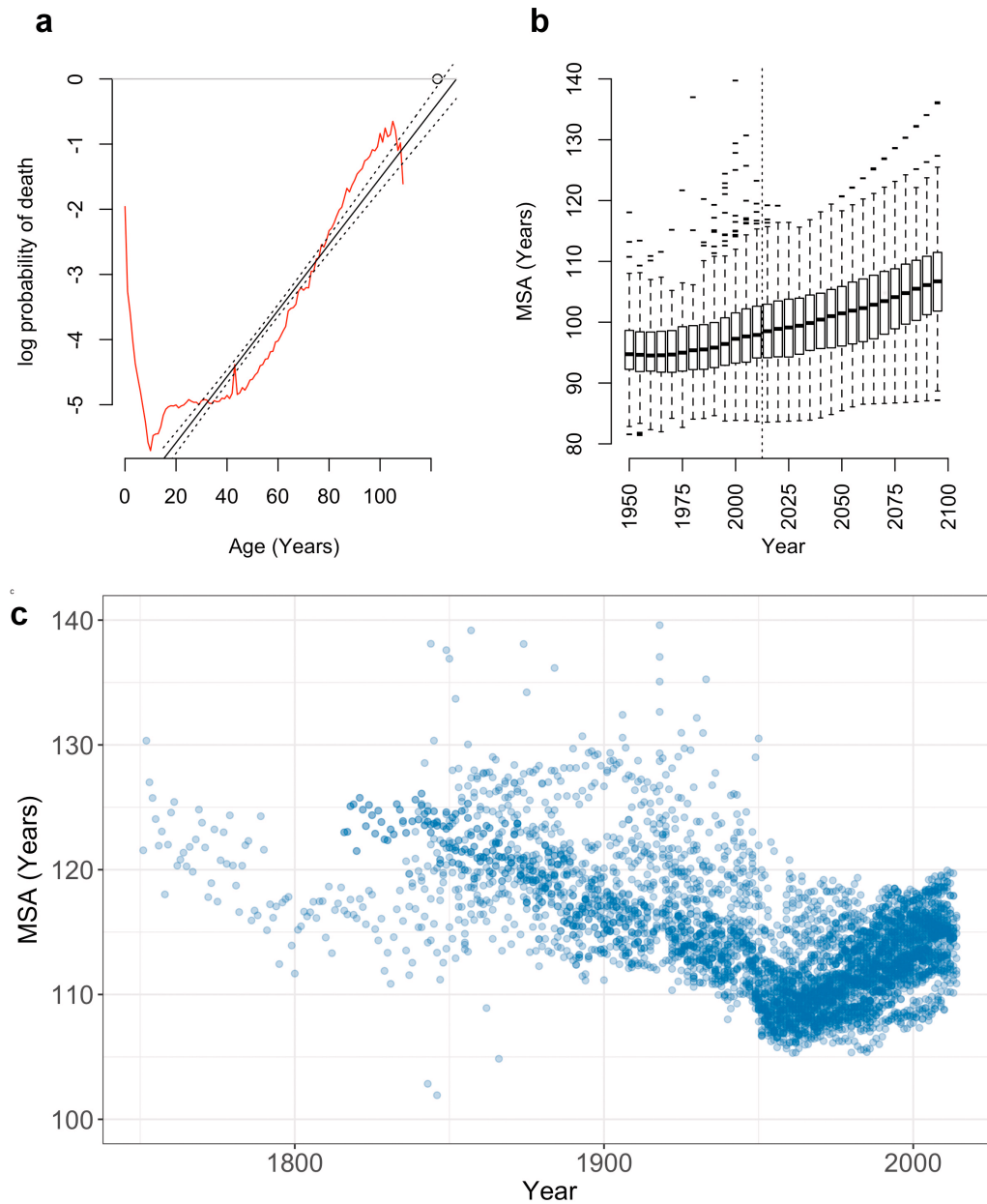
Figure 3. Observed and projected variation in the maximum survivable age (MSA). (**a**) In humans, the probability of death q at age x (q_x; red line) increases at an approximately log-linear rate with age (black lines; 95% CI), shown here for the birth cohort of Jeanne Calment (d.122.5 years; circle). Projection of this log-linear increase to $\log(q) = 0$ provides the MSA, the upper limit of human survival, shown here for (**b**) observed and projected global populations[5] and (**c**) 40 historic HMD populations 1751–2014.

We fit log-linear models to age-specific mortality rates from the HMD data used by Dong *et al.*[1], and used these models to predict the age at which the probability of death intercepts one. This maximum survivable age (MSA) provides a simple, conservative estimate of the upper limit of human life (Figure 3c).

Log-linear models closely approximate the observed probability of death in HMD populations for both period and cohort life tables (median $R^2 = 0.99$; 4501 population-years). The MSA limit is compatible with observed ages at death in the GRG database with 330 out of 331 supercentenarians approaching, but not exceeding, their predicted lifespan limit (Supplementary Figure S2; SI). These models predict an MSA exceeding 125 years within observed historic periods (Figure 3b and c; SI).

Furthermore, period HMD data indicate that MSA is steadily increasing from a historic low c.1956 (Figure 3b and c), tracking the increasing MRAD during the same period. The United Nations[5]

global mortality data from 194 nations support this trend, with projected population data from the UN predicting a gradual rise in MRAD and MSA through the year 2100 (Figure 3b).

This analysis provides an estimate of human lifespan limits that is conservatively low. Log-linear mortality models assume no late-life deceleration in mortality rates[6], which, if present, would increase the upper limits of human lifespan[7]. In addition, these models are fit to population rates and cannot provide an estimate of individual variation in the rate of mortality acceleration.

Given historical flexibility in lifespan limits and the possibility of late-life mortality deceleration in humans[8], these models should, however, be treated with caution.

A claim might be made for a general, higher 130-year bound to the human lifespan. However, an even higher limit is possible and should not be ruled out simply because it exceeds observed historical limits.

Methods

Life table data were downloaded from the United Nations[5] (UN) and the Human Mortality Database (HMD) and lifespan records from the International Database on Longevity (IDL) and the Gerontology Research Group (GRG).

Least squared linear models were fit to life table data on the log-transformed age-specific probability of death (q_x), and projected

to q_x=1 to predict the maximum survivable age in each population (Figure 1b and c; SI). Maximum lifespan within GRG and IDL data was annually aggregated and fit by locally weighted smoothed splines[9] (Figure 3b and c).

We reproduced the analysis of Dong *et al.* in R version[10] 3.2.1 (SI), using the code in Supplementary File 1.

An earlier version of this article can be found on bioRxiv (doi: 10.1101/124800).

Data availability

The authors declare that all data are available within the paper and its supplementary material.

Author contributions

S.J.N. wrote the analysis and code, and reproduced Dong *et al.'s* analysis. S.J.N. and S.E. developed the analysis, methods and statistical design, and co-wrote the manuscript.

Competing interests

No competing interests were disclosed.

Grant information

The author(s) declared that no grants were involved in supporting this work.

Supplementary material

Supplementary File 1: Supplementary information guide. The supplementary information supplied here constitutes two sections of integrated code in the R statistical language:

1. R code required to calculate the maximum survivable age or MSA from both public data and the human mortality data used by Dong *et al.*, and required to reproduce our findings in full.

2. R code required to reproduce Dong *et al.*[1] with original errors, often including several error-corrected or partially corrected versions.

Both sections are wrapped in the same script, and require several package dependencies and datasets outlined in the annotated code.
Click here to access the data.

Supplementary Figure S1. Trends across ranked supercentenarian recorded ages at death from the GRG.
Click here to access the data.

Supplementary Figure S2. Relationship between the maximum reported age at death and the theoretical maximum survivable age. Of 331 GRG supercentenarians born into populations with a known lifespan limit, only Jeanne Calment exceeded the theoretical gender-pooled lifespan limit (diagonal line). However, Jeanne Calment did not exceed the theoretical limit of her female cohort (see Figure 3a).
Click here to access the data.

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Open Peer Review

Current Peer Review Status: ? ✔ ?

Version 2

Reviewer Report 10 July 2018

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James Vaupel
Max Planck Institute for Demographic Research, Rostock, Germany
José Manuel Aburto (iD)
University of Southern Denmark, Odense, Denmark

Newman and Easteal[1] challenge the findings of Dong et al[2] on the evidence of a limit for human lifespan. They highlight rounding errors and inappropriate selection of data. These errors have been documented in a series of communications to Nature[3-6] and in a recent article[7] questioning Dong et al's results. Newman and Easteal provide code to reproduce their results, which is highly valuable.

Newman and Easteal state that "we fit log-linear models to age-specific mortality rates", which, called the Gompertz model, is common practice in demography for some ages (usually between 30 and 90). However, the authors do not fit a Gompertz model to the age-specific mortality rates (denoted m_x by demographers). Instead they fit log-linear models to the age-specific probabilities of death (which demographers denote by q_x). They do so to estimate the Maximum Survivable Age (MSA), as can be seen from lines 950-989 of the provided code.

There is a fundamental problem with this approach. A linear model fit to the log probabilities predicts probabilities exceeding one at high ages. To avoid this fallacy, Newman and Easteal postulate that the MSA is the age when their model predicts a probability of death of one. This is arbitrary and unconvincing, especially in light of evidence suggesting that age-specific probabilities of death reach a plateau at advanced ages at a value of about 0.5[8-9]. Although the authors acknowledge this evidence, they disregard it.

Moreover, they fit their model using the Ordinary Least Squares approach, which assumes normally distributed errors that are identical over age. This is an assumption that does not hold, implying that their estimated coefficients and standard errors are not correctly calculated.

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Is the work clearly and accurately presented and does it cite the current literature?
Yes

Is the study design appropriate and is the work technically sound?
Partly

Are sufficient details of methods and analysis provided to allow replication by others?
Yes

If applicable, is the statistical analysis and its interpretation appropriate?
Partly

Are all the source data underlying the results available to ensure full reproducibility?
Yes

Are the conclusions drawn adequately supported by the results?
Partly

Competing Interests: No competing interests were disclosed.

We have read this submission. We believe that we have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however we have significant reservations, as outlined above.

Version 1

Reviewer Report 30 May 2017

https://doi.org/10.5256/f1000research.12350.r22232

Michael R. Rose
Department of Ecology and Evolutionary Biology, University of California, Irvine, Irvine, CA, USA
Laurence D Mueller
Department of Ecology and Evolutionary Biology, University of California, Irvine, CA, USA

Evidently the Dong et al. *Nature* article[1] made some major, though elementary, mistakes: (a) an incorrect rounding procedure; and (b) choosing data from an historical period (1900-1990) that generally fit a limited lifespan expectation, while neglecting to consider other data. Newman and Easteal[2] correct the rounding error and look at human cohort data from a broader range of historical dates. However, they fit log-linear Gompertz models to the data, though doing so is questionable as they themselves admit, if in fact human mortality rates plateau[3]. It is often the case that extrapolating regression models beyond the range used to fit them is fraught with danger.

Of most interest for us was whether the fundamental concept of inferring a species-wide maximum lifespan from one or even many cohorts of demographic data is cogent at all. With that in mind, we used mortality data from a twenty-cohort study of *Drosophila melanogaster* that we and our colleagues recently published[4]. Specifically, we used "A-type" populations to predict sex-specific "maximum lifespans" for populations of "C-type" populations. Each of the ten pairs of A and C type populations share a common ancestral population in our laboratory, though they have since evolutionarily diverged.

We took the initial sample size of, say, cohort CO-i, sex-j (N_{ij}), and then computed the age at which the probability of survival in the matching ACO-i, sex-j cohort is $<= 1/(10*N_{ij})$. We plotted the maximum lifespans predicted from the 20 "A" sex-specific cohorts versus the observed maximum lifespan in the 20 corresponding "C" cohorts (see Figure 1) using a double plateau Gompertz model[4]. If the concept of species-wide maximum longevity were cogent, we would expect all the observed maximum lifespans to be near or well below the y=x line. In fact, most are well above that line, and show no correlation with the predicted values. Effectively, the maximum lifespan estimation procedure is not generally reliable. In the case of the example that we give here, the maximum lifespan was altered by substantial genetic changes caused by natural selection.

We have long used experimental evolution to reconfigure the onset and end of periods of aging in carefully handled cohorts, as illustrated in publications 3 and 4. We do not regard maximum lifespans as characteristic of entire species, however they might be defined demographically. Rather, we view them as phenotypes that depend on both genotype and environment even in so-called "wild-type" populations, like most components of life history, as the extensive evolutionary literature on life history and aging has long suggested. More importantly, in cohorts that show a cessation of aging[3] we doubt that the concept of maximum lifespan has any biological cogency.

Figure 1. The predicted maximum lifespan based on 10 A-type populations[4] and the observed maximum lifespan in 10 C-type populations:

https://f1000researchdata.s3.amazonaws.com/supplementary/11438/8c2e3298-9ed0-4ac5-8b85-ce6233

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Is the work clearly and accurately presented and does it cite the current literature?
Yes

Is the study design appropriate and is the work technically sound?
Yes

Are sufficient details of methods and analysis provided to allow replication by others?
Yes

If applicable, is the statistical analysis and its interpretation appropriate?
Yes

Are all the source data underlying the results available to ensure full reproducibility?
Yes

Are the conclusions drawn adequately supported by the results?
Yes

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Aging; Evolution of demography

We have read this submission. We believe that we have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.

Author Response 08 Jun 2017
Saul Newman, Australian National University, Acton, Australia

We wish to thank MRR and LDM for their review. We agree with the ideas expressed, particularly with the risk of extrapolating log-linear models and the potential for improving estimates of lifespan limits using alternate models of old age survival.

There is little about maximum human lifespan or lifespan limits can be concluded with certainty. Therefore, our focus was on implementing the simplest available methods. The appended figure S2 supported the rationale for our use of log-linear models for projecting lifespan limits.

This figure reproduces the plot presented by MRR and LDM for *Drosophila* using human data. It

plots the upper observed lifespan (MRAD) of individuals in the GRG against their calculated lifespan limit.

We could match 331 validated maximum lifespan observations to a historical gender-pooled MSA estimate. Of these, 330 approached but do not exceed their predicted limit. The only exception was Jeanne Calment, who outlived the gender-pooled MSA limit by 3 years but fell short of the female-cohort limit shown in Figure 3a. Unlike *Drosophila*, these calculated limits seem to fit reasonably well with MRAD.

However, there are many problems involved in human data that do not affect *Drosophila*. Human populations are not directly observable past their maximum age, individual variation in mortality acceleration is unknown, and ascertainment and validation problems abound.

Therefore, we still consider these projection methods, the GRG and IDL data, and much of the discussion of MRAD, problematic.

Finally, we agree that in species with a cessation of ageing or negative senescence there will be an unbounded, finite maximum lifespan with intrinsic limit. By extension, if there were a complete cessation of ageing in humans at extreme old ages there would be no intrinsic limit, but many probabilistic constraints, to human lifespan.

Competing Interests: The authors disclose no competing interests

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Reader Comment 28 Jun 2017

Xiao Dong, Brandon Milholland and Jan Vijg, Albert Einstein College of Medicine, USA

In their review, Rose and Mueller briefly express their approval of Newman and Easteal's paper before moving on to a lengthier discussion of their own experiments with *Drosophila*. As to the first point, we believe that even a cursory examination of our work and the material produced by Newman and Easteal will show that the accusations of errors are themselves erroneous; see our comment for an in-depth critique. As for the results in fruitflies, Rose and Mueller's findings are potentially very interesting, but their immediate relevance to humans is unclear. If as Rose and Mueller say "extrapolating regression models…is fraught with danger" extrapolating from flies to humans must be similarly fraught.

Xiao Dong, Brandon Milholland and Jan Vijg

Competing Interests: No competing interests were disclosed.

Reviewer Report 18 May 2017

? **Jean-Michel Gaillard**

Laboratory of Biometrics and Evolutionary Biology(LBBE), CNRS (French National Center for Scientific Research), UMR5558, University of Lyon, Villeurbanne, France

This manuscript challenges the recent findings by Dong *et al*. that human lifespan has an upper limit and proposes that human lifespan is rapidly increasing. While I am quite convinced by all the problems the authors identified in the analysis performed by Dong *et al*. and by the maximum survivable age of about 125 years the authors estimated for humans, I am not convinced at all by the claim that maximum reported age at death is expected to rise over the next century.
In particular, I do not understand the rationale of removing Jeanne Calment from the analysis. This data point has been validated. Contrary to the authors' interpretation, the mere existence of a lifespan of 122 observed 20 years ago without being even approached since then seems to indicate that some saturation in the maximal age at death is occurring. It is required to estimate the probability of not observing older ages at death for 20 years under different scenarios of increasing trends in maximal age at death.

Detailed comments:
p. 3 second column 3rd paragraph l. 1: Remove "significant"
p. 3 second column 3rd paragraph l. 1: Should be "Calment", not "Clament"!

Is the work clearly and accurately presented and does it cite the current literature?
Yes

Is the study design appropriate and is the work technically sound?
Partly

Are sufficient details of methods and analysis provided to allow replication by others?
Yes

If applicable, is the statistical analysis and its interpretation appropriate?
Partly

Are all the source data underlying the results available to ensure full reproducibility?
Yes

Are the conclusions drawn adequately supported by the results?
Partly

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Biodemography

I have read this submission. I believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however I have significant reservations, as outlined above.

Author Response 06 Jun 2017

Saul Newman, Australian National University, Acton, Australia

We thank J-MG for these comments, and welcome the opportunity to clarify our analysis and expand our rationale for this study.

We wish to clarify that our projected increase in MRAD over the coming century is not based on IDL or GRG lifespan data, and these projections do not require either removal or inclusion of Jeanne Calment. Rather, these projections are based on theoretical lifespan limits calculated using HMD and WHO life table data, including the WHO population projections through 2100.

Our statement that "period data indicate that MSA is steadily increasing from a historic low c.1956 (Figure 3b and c) and that the MRAD is expected to rise over the next century" is based on observed HMD and WHO data for the "historic low" in 1956 and on WHO population projections over 2015-2100 for the 'steady rise'. We can see that we did not make this distinction sufficiently clear and we have amended the text to make it clearer.

The rationale for removing Jeanne Calment from the regression of observed trends was to demonstrate her singular effect on recent MRAD trends. Jeanne Calment is a remarkable statistical outlier from historic trends in both Dong *et al*. and our linear models, with a Cook's distance of 1.97 (Cook, 1982).

A large Cook's distance is not necessarily grounds for ignoring a well-validated data point. Our finding that the inferred decline in MRAD is eliminated by removal of one outlier demonstrates that the inference is tenuous rather than invalid.

We find it notable that such broad conclusions on lifespan limits depend on the status of a single data point. We agree that the 20-year streak set by Jeanne Calment is remarkable, and we consider it valid. However, we disagree that this indicates a saturation of old-age survival.

Jeanne Calment's record-holding streak is not unprecedented in length. Mary Kelly held the overall lifespan record for 17 years from 1964 to 1981. Gert Adrians-Boomgaard held the male lifespan record for 68 years. Mathew Beard broke this record, and held it for another 21.9 years (1985-2007). Like Jeanne Calment, Mathew Beard exceeded the next-lowest record by three years for this period.

We consider that these record-holding streaks do not reflect saturation of the MRAD, but the uncertain ascertainment and stochastic nature of lifespan records. Therefore, we suggest Jeanne Calment's survival reflects a rare statistical event where survival has approached the calculated upper limit of lifespan in her cohort. We think this event is a result of stochastic variation, and is biasing the projection of short-term trends. The simulated removal of Jeanne Calment was intended to indicate this.

More broadly, we feel that too much emphasis is placed on this single data point. Jeanne Calment's predecessor Carrie White held a well-verified claim to the world's oldest and then

second-oldest woman for 24 years, before the claim was recognised as a clerical error in 2012 and retracted.

In the unlikely event that Jeanne Calment's lifespan claim is also false, demographers would be depending on conclusions about lifespan limits from a single, false data point that is an outlier from the aggregate trend across 1626 other supercentenarians in the GRG (see figure S1).

Furthermore, a declining or flat trend in lifespan limits is inconsistent with our analysis of 3.3 billion lifespan records in 194 nations. We maintain that statistical trends in data for billions of deaths should not be ignored in favour of a single data point in 1997.

Finally, we accept our spelling error for Jeanne Calment's name. Yet we do not understand the request to remove the word 'significantly' from the text: the negative trend was significant (p=0.03).

Competing Interests: The authors have no competing interests.

Reader Comment 28 Jun 2017
Xiao Dong, Brandon Milholland and Jan Vijg, Albert Einstein College of Medicine, USA

Gaillard is correct to express reservations about this paper: the "problems" that Newman and Easteal claim to have identified do not actually reflect the contents of our paper; see our comment for more detail. Gaillard is "not convinced at all by the claim that maximum reported age at death is expected to rise over the next century" and neither are we. As our correctly conducted analysis shows, the MRAD is likely to remain stagnant in the future.

Xiao Dong, Brandon Milholland and Jan Vijg

Competing Interests: No competing interests were disclosed.

Comments on this article

Version 2

Author Response 30 Jun 2017
Saul Newman, Australian National University, Acton, Australia

Dear Sirs,

Your assertion that our use of the 1900-1990 census period for figure 1c invalidates our findings is false. We have already calculated your regressions using data from 1900-present. We have posted the near-identical and highly error prone figure that results from using these dates as a supplementary figure.

The statement that your errors are "*greatly overstated by the omission of all data since 1990*" is demonstrably false. The error rate of zero-rounded data from 1900-1990 is *lower* than the error rate of the

1900-2014 data. The magnitude of your errors are not "*greatly overstated*" in our analysis, they are understated by 16%.

The statement that your data were truncated at 1990 was based on our attempts to reproduce your figures in the absence of any code. This was only possible for figure 1c if we performed a 1900-1990 censoring. Other analysis did not use this census period, and we did not use this census period throughout our paper.

Furthermore, we have previously used data from 1900-present, without the 1990 censoring, for all analyses. We found no difference in the outcome or the scope of your errors when using this data, except that use of 1900-1990 data reduces the error rate and better reproduces fig. 1c.

Therefore, the 1900-1990 truncation had no material effect on our analysis. All of our data was also calculated from 1900-present, 1925-present, from 1850-present, from 1800-present, from 1950-present, and across many other time periods, in the hope that we may arrive at a trend that supported your original findings.

Not one of these periods illustrated any plateau in MRAD.

There are several other points that you have misconstrued. The first is that the reasoned criticisms of JMG support your findings, despite his statement that "*I am quite convinced by all the problems the authors identified in the analysis performed by Dong et al*.". JMG has provided an insightful comment on our methodology, which we believe results from a simple misunderstanding and has no bearing on the errors in your paper.

 The "improperly formed" boxplots of error rates reflect the calculated maximum, median, 95th percentile and 75th percentile of error rates all reaching 100%. That is, the frequency of your zero-rounding errors becomes so high, and error rates below 100% are so rare, there is no longer a 'box' forming in these boxplots.

This was the rationale for including the red and blue lines, showing the overall fraction of data rounded to zero.

As for your comments on the IDL and GRG data, we would highlight several problems. First, you cannot ignore your incorrect pooling of the IDL data because of trends in another database.

There is no evidence that the proposed plateau in MRAD occurs in any single one of these populations. The 'plateau' trend that appears when you pool these data is, as we have shown in our code, a result of poor assumptions. You cannot pool four populations in this way, when two of them are only present to 2003 and one to 2006. You have done nothing to address these problems, other than repeating your initial mistake.

Your 'obvious' plateau in the GRG is, as we have stated before, based on a single data point. Removal of that data point removes your proposed plateau in these data. It also makes a simple increasing linear model, with no post-1995 plateau in MRAD, the best fit for observed data under the R squared metric, the Bayesian information criteria and the Akaike information criteria.

We find it remarkable that a selected-by-eye regression, with a worse fit than a linear model when Jeanne Calment is removed, is a core supporting argument for your paper.

As we highlighted for JMG, before Jeanne Calment the record-holder for lifespan, Mary Beard held this record. Mary Beard's record was retracted after being considered valid for 24 years, when it was recognized her extreme age was a straightforward clerical error. As you admit, a similar clerical error for Jeanne Calment would undo your proposal for a significant fall in MRAD.

The GRG acknowledge this inherent unreliability, stating quite clearly that their data are not complete surveys of the oldest old. They also state that many supercentenarian records are subsequently found to be false positives, or are impossible to verify. Therefore, the analysis presented in Nature depends on a single data point, drawn from unreliable data, gathered from incomplete surveys with a high false positive rate, conducted in a small number of countries.

I suggest you ask a statistician whether they consider it good practice to extract species-wide trends from such data.

In contrast, we have based our analysis on surveys of global populations, conducted by national statistical bodies. None of our calculated limits depend on GRG or IDL data.

Your comment that the median MSA we observed, of around 100 years, supports your results is unfounded. That MSA reflects diversity across all countries in the UN database. It better reflects the limit of lifespan in Namibia than in France, or in any of the developed countries you measured. Furthermore, this median is increasing linearly. Like almost all global populations, the MSA is increasing, with no sign of a plateau.

We have provided data on the correspondence between our MSA estimates and observed data: of 311 observations, 310 were consistent with limits calculated under MSA (our figure S2).

Your suggestion that these data are implausible is not based on any apparent analysis. You have not provided any indication why these estimates are incorrect, beyond your own opinion. Where is your code?

We would also highlight that there is nothing historically remarkable about the current length of the Jeanne Calment's lifespan record. We have heard the argument that holding an unbroken lifespan record for two decades somehow suggests an MRAD plateau, an argument you repeated in response to Rozing, Kirkwood and Westendorp (Nature 546, E12 (29 June 2017) doi:10.1038/nature22789).

However, the overall lifespan record was previously held for 17 consecutive years (Mary Kelly, 1964-1981). The male lifespan record was held for 68 consecutive years (Gert Adrians-Boomgaard) and then 21.9 years (Mathew Beard 1985-2007) by a margin of 3 years. None of these broken records indicated a plateau in MRAD.

Neither does the lifespan record of Jeanne Calment. We suggest the Jeanne Calment record simply reflects the uncertain ascertainment, and rarity of adequate documentation, required to validate the oldest-old.

Finally, I consider the findings of Dong *et al*. are invalid as a result of methodological errors, errors you have not corrected or addressed. Pointing to data you feel supports your view, in this paper or others, does not answer any of the problems raised by ourselves or other authors.

Were our results to entirely support your proposed MRAD plateau this would do nothing to excuse or explain your errors in analysis.

I cannot speak for my (currently traveling) co-author, but I find it disturbing that you have failed to acknowledge or correct even the most basic errors in typesetting and analysis, even those that have little material effect on the result (your Extended Data figure 6 still has incorrect axes, is not the data you said it was in the text, and is still missing all the people who died in May and June).

It seems to many observers that you have committed basic errors that you refuse to acknowledge or repair.

Despite our reproduction of your analysis, you have not provided a single piece of code. We have repeatedly requested this code. Should you ever provide it, in accordance with the editorial guidelines of Nature, I will gladly highlight these errors for you.

In the mean time, I suggest that you reflect on the possibility of honest errors driving your results.

Regards,
Saul Newman

https://f1000researchdata.s3.amazonaws.com/linked/166727.Fig_1_HiRes_2014.tiff

Competing Interests: I disclose no competing interests.

Reader Comment 29 Jun 2017

F1000 Research, UK

Thank you for bringing the errors when downloading the supplementary data to our attention – this was caused by an issue with how the files were uploaded, and has now been rectified.

Competing Interests: No competing interests were disclosed.

Reader Comment 28 Jun 2017

Xiao Dong, Brandon Milholland and Jan Vijg, Albert Einstein College of Medicine, USA

In their paper, Newman and Easteal dispute our findings of evidence for a limit to human lifespan[1]. However, their work is based on several incorrect assertions about our original paper, and the evidence they provide for an increasing human lifespan is entirely unconvincing.

In the first part of their paper, Newman and Easteal criticize our analysis of data from the Human Mortality Database, but their statements reflect a fundamental misunderstanding of the work that we did. Newman and Easteal's entire premise is based on their incorrect statement that, in our paper, data outside the range 1900-1990 were excluded from some plots but included in others; to them, the "major non-linear shifts in old-age survival" that occur outside of this range invalidate our results. With regards to data prior to 1900, it is true that some major non-linear shifts did occur: these likely represent the major changes caused by the Industrial Revolution, which it would be sensible to leave out since these changes are neither novel nor relevant to the maximum human lifespan. However, we did not exclude any data from after 1990. In our paper, the axes from Fig. 1a, both charts in Fig. 1b and Fig. 1d all clearly extend past

1990 and even past 2000; Fig. 1c is based on Fig. 1b and so obviously reflects post-1990 data as well. All told, our paper contains over 200 graphs, and in every single one of them it is clear from the axes, the legend, or the graph titles that our analysis extends well into the 2000s and even 2010s, stopping only with the limit of available data. We are simply baffled as to how Newman and Easteal could have gotten the impression we had done otherwise.

The fact that we did not truncate the data at 1990 severely undermines the findings of Newman and Easteal's Fig. 1. In this figure, they claim to show that "rounding errors", caused by our use of survival probabilities effectively rounded to 0.0001, explain our results, but the proportion and effect of any such errors are greatly overstated by the omission of all data since 1990. The x-axis of their Fig. 1a, inexplicably, terminates at the year 2000, exaggerating the proportion of years with alleged rounding errors. Truncating the analysis at 1990, as Newman and Easteal did, also exaggerates the proportion of years with rounding errors as shown in their Fig. 1b. Of note, these errors seem to be mainly very minor. Interpretation of the Newman and Easteal data is somewhat hampered by the fact that many box plots are not properly formed, but it appears that for only one age (106) does the median magnitude exceed 20%, and there does not appear to be any pattern in their magnitude after that. A proper analysis, making use of the additional data from 1990 and later, would display an even smaller proportion and magnitude of rounding errors. Their Fig. 1c contains, as far as we can tell, no major errors; but observe that, contrary to Newman and Easteal's assertion, there does not seem to be any "non-linear shifts" in the post-1990 range.

Of note, their Fig. 1d is completely invalidated. It is clear from the contents of the figure and their R code that they have limited their analysis to data from prior to 1990, but this is not accurately reflected in their y-axis label "rate of change singe [since] 1900". By contrast, we made use of all data available after 1900 in our paper; the discrepancy between what we did and what Newman and Easteal claim we did could explain the difference in results depicted in their Fig. 1d. In addition, Newman and Easteal's conclusion that survival increases ever more rapidly until age 110 would be difficult to reconcile with our finding, from an independent data source, that life expectancy for 110 year olds has not increased in several decades (Fig. 2c of our paper). Indeed, our findings were recently confirmed by the observation that there has not been any improvement in mortality among centenarians in the past 30 years[2]. As we have shown in our original paper, the period since 1990 is critical for evidence of a limit to human lifespan, so it is not surprising that when Newman and Easteal remove it, they come to a different conclusion. What is surprising is that they thought it should be removed at all.

Next, Newman and Easteal criticize our findings of a plateau of the human MRAD based on data from the IDL and GRG. They argue that in the IDL database MRAD correlates with the number of countries, i.e., with cohort size. When they split up the IDL among the different countries (US, UK, Japan, France) they no longer see the MRAD plateauing, at least not consistently. However, first, apart from the fact that we pooled MRAD data among countries to increase the sample size and reliability of the analysis, we also see the same plateau using the independent GRG database, which runs to 2015 (the IDL only to 2007). We have conducted our own analysis of cohort size and MRAD and found that after a certain point the MRAD plateaus, even as the cohort size continues to increase (unpublished). The literature also abounds with information that makes it clear that increases in cohort size are insufficient to drive an increased human lifespan. For example, in spite of the dramatic (exponential) increase in the number of centenarians over the last decades[3], the MRAD in the GRG database has not significantly increased since the 1990s.

When analyzing the data from the GRG, Newman and Easteal come to the same conclusion that we do: MRAD has not increased and has even decreased since the 1990s. Upon removing Jeanne Calment from the data, however, they find that the decline is no longer statistically significant. But this does not undermine our results: the apparent decline is likely just due to regression to the mean after the high point

of Jeanne Calment, and at no point in our paper do we attribute any practical significance or importance to it. After removing Jeanne Calment, there is no significant decrease, but neither is there a significant increase. Therefore, the evidence for a stagnation in MRAD, reflecting a limit to human lifespan, is both strong and robust.

We were unable to evaluate the supplementary results. The supplementary figures were apparently corrupted, as they could not be read by any of the programs we tried.

Finally, Newman and Easteal propose an alternative metric, the maximum survivable age (MSA). Although potentially interesting, the MSA does not appear to provide a parsimonious reflection of human lifespan, nor does it provide convincing evidence for a continued increase in human lifespan. In Fig. 3a, the probability of death reaches 1 shortly after age 122, a finding consistent with our results. In Fig. 3b, the median MSA remains below 100 for the real data and below 110 for the projected data—an even lower limit to lifespan than the one we found in our paper. Looking at Fig. 3c, the MSA seems to be subject to massive fluctuations. It does not seem plausible that, shortly after 1750, the MSA was over 130, nor do any of the various peaks near 140 seem realistic. Of note, the last of these occurred some time in the first quarter of the 20th century. Over the entire time period, there is no clear upward trend, and the MSA has not returned to the highs it reached in previous centuries. Since 1950, the MSA has rarely exceeded 120, and over the past 20 years, the MSA seems firmly rooted between 110 and 120—exactly the range one would expect based on our findings. Although we have taken exception to many of the choices Newman and Easteal have made in their paper, we do appreciate this final piece of inadvertent support for our results.

Xiao Dong, Brandon Milholland and Jan Vijg

1. Dong X, Milholland B, Vijg J: Evidence for a limit to human lifespan. *Nature*. 2016; **538** (7624): 257-259 PubMed Abstract | Publisher Full Text
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Competing Interests: No competing interests were disclosed.

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