# Contesting the evidence for limited human lifespan

**ARISING FROM** X. Dong, B. Milholland & J. Vijg *Nature* **538,** 257–259 (2016); doi:10.1038/nature19793

In their Letter, Dong *et al.*[1] claimed that longitudinal mortality data indicate that human lifespan has a limit of around 115 years. We believe these authors' analyses, and, hence, their conclusions to be flawed. In this Comment, we outline four arguments to motivate our opinion. There is a Reply to this Comment by Dong, X. *et al. Nature* **546,** http://dx.doi.org/10.1038/nature22785 (2017).

First, the main result of Dong *et al.*[1] (shown in figure 2a of ref. 1) involved splitting the dataset at the year 1995, for which the only justification given was that a visual inspection of the data appeared to show the maximum age at death had reached a plateau around that time. It is well-known from statistical theory that the same dataset cannot be used for both hypothesis-generating and hypothesis-testing purposes, as this typically leads to severe overfitting and thus inaccurate results.

Second, whereas Dong *et al.*[1] reported a sample size of 534 in the text, they included only the oldest person who died in any given year in the linear regressions in their figure 2a, which therefore used sample sizes of just 21 (1968–1994) and 12 (1995–2006). It is not possible to draw any firm conclusions from such small samples; the uncertainty around the estimates is simply too large. Furthermore, these individuals are outliers among outliers; standard linear regression techniques are inappropriate under these circumstances. Instead, Dong *et al.*[1] should have used extreme value theory, a set of mathematical techniques specifically designed for analysing extreme events. This type of analysis involves the use of Poisson processes, and related stochastic processes, to model extreme value distributions[2], and dates back nearly a century[3].

Third, the conclusions of Dong *et al.*[1] are not supported even within the suboptimal regression framework. Dong *et al.*[1] did not compare the fit of their model to alternatives. Our re-analysis (full details and code for reproduction are available in the Supplementary Information) shows that there is no reason to favour the spline model the authors fit to the full ($n = 534$) dataset in their figure 2c. Depending on the relative fit index used, a basic linear model in which the maximal age at death increases monotonically each year fits just as well as (difference in the Akaike's information criterion = 1.1), or slightly better than (difference in the Bayesian information criterion = 7.5), a natural spline model that appears to plateau after the mid-1990s. (It should be noted that, in these models, the overall variance explained in age at death was very small; all adjusted $R^2$ values were approximately 0.03.)

Finally, and perhaps most importantly, the purported post-1995 decline in maximum longevity shown in figure 2a of ref. 1 seems to be entirely dependent on the exceptional case of Jeanne Calment. We created a dummy variable for the split used by Dong *et al.*[1] (pre- or post-1995), and tested for its interaction with year in predicting maximal age at death in the $n = 33$ dataset. This analysis showed that the slopes of the two split regression lines in figure 2a of ref. 1 are significantly different in a linear regression (year-by-split interaction $P = 0.02$). However, if Calment's age is reset to the modal age of 114 years, the lines are no longer significantly different (interaction $P = 0.09$). That is, without that single data point, there would be no statistical reason to consider 1995 as a change point in the series of life expectancies. In addition, had Calment died in 2004 instead of 1997 (at the same age of 122), for example, the apparent 'decline' in the data of Dong *et al.*[1] would be reversed (see Fig. 1, bottom; interaction $P = 0.94$). Even disregarding the serious problem of a wide-ranging claim hinging on just one observation, it is curious that the fact that this remarkable woman lived to the age of 122 should be such a crucial part of the argument that maximal human lifespan has plateaued at 115.

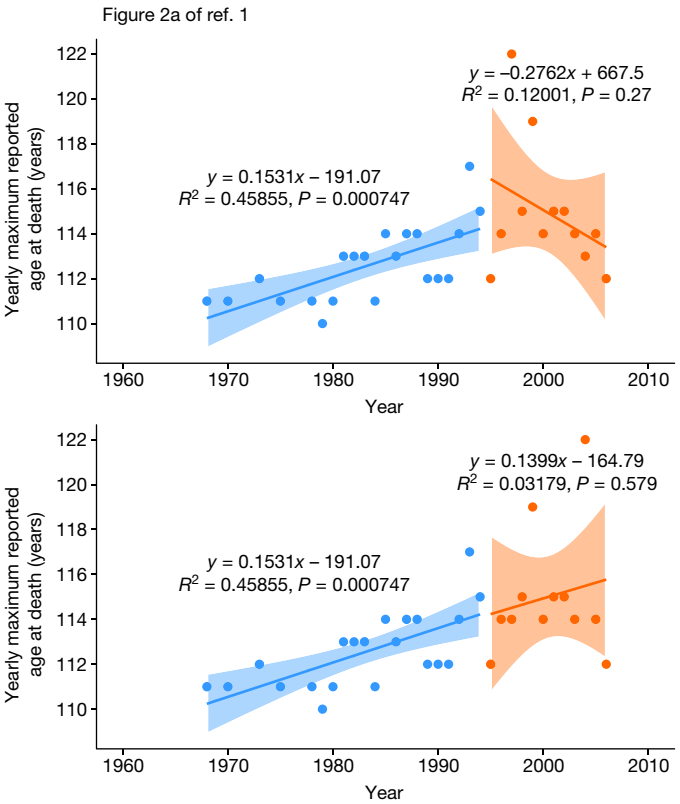


**Figure 1 | Regression lines predicting age at death from the oldest death in each given year, split between 1994 and 1995.** Top, the yearly maximum reported age at death (split pre-1995/1995 and after), as reported in figure 2a of ref. 1. Bottom, the yearly maximum reported age at death (split pre-1995/1995 and after), with Jeanne Calment's dates of birth–death changed from 1875–1997 to 1882–2004.

**Data Availability** All data are available from the corresponding author upon reasonable request.

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# Dong *et al.* reply

**REPLYING TO** N. J. L. Brown, C. J. Albers & S. J. Ritchie *Nature* **546,** http://dx.doi.org/10.1038/nature22784 (2017)

In the accompanying Comment[1], Brown *et al.* question our analyses and hence the evidence for a limit to human lifespan[2]. However, we do not believe that their arguments undermine our results.

First, there is value to data-driven (as opposed to hypothesis-driven) research[3]. We are surprised by the opposition towards the visual inspection of data. We thought that the field of statistics had decades ago dispensed with the notion that 'actually looking at the data is cheating' and acknowledged that graphs are not only useful but also essential for choosing one's model[4]. Cubic smoothing splines of data from the International Database on Longevity (figure 2b of ref. 2) suggested a trend break around the mid-1990s, which could be parsimoniously modelled with a segmented regression. But even within the framework of hypothesis proposal and testing, our work is valid because it relies on multiple datasets. Data from the Human Mortality Database (HMD; http://www.mortality.org/) indicate that there have been limited gains in survival to very old age (see figure 1 and extended data figures 1–5 of ref. 2), suggesting that there might be a limit to human lifespan. This limit was confirmed by a segmented regression, using the breakpoint suggested by smoothing splines, on the maximum reported age at death (MRAD; figure 2 of ref. 2); the stagnation in MRAD since the 1990s found by this model is corroborated with data from the Gerontology Research Group (GRG; extended data figure 6 of ref. 2).

Regarding sample size, in the figure 2 legend of our paper[2], we wrote 534 as the number of supercentenarians for figure 2c. Brown *et al.*[1] misinterpret the 534 as applying to figure 2a. We apologize if the legend was ambiguous. Next, Brown *et al.*[1] claim that it is not possible to draw any firm conclusions from the 33 observations over 40 years (1968–2006) because of this limited sample size, but no statistical justification was provided to support this claim; although more data would increase the strength of our conclusions, we were still able to arrive at a fairly narrow 95% confidence interval for the level at which the MRAD has plateaued. In addition, they suggest using extreme value theory (EVT)[1]. Additional investigation of the data using EVT may indeed prove insightful, but this does not undermine the value of the analyses presented in our Letter. Brown *et al.*[1] do not seem to provide any statistical justification to demonstrate why EVT is suitable and our analyses are not, and they do not apply EVT in their subsequent analyses. Recently, another group applied EVT to mortality at old ages and found evidence for a finite 'ultimate age', arriving at results that they say are 'very close' to ours[5].

To demonstrate that a single linear model is a better fit for the data, Brown *et al.*[1] first examine the average age at death of supercentenarians, performing a comparison of alternatives to our spline model from figure 2c of ref. 2. However, their analyses are undermined by several issues. First, the spline model to which they compare their models is not the one from our figure 2c. We modelled the yearly average age at death of supercentenarians, but they did not perform the averaging when constructing their model. Also, their linear model has $R^2 = 0.03$. This suggests that there is no linear correlation between calendar year and age at death of supercentenarians, a result that supports our claim.

Finally, Brown *et al.*[1] claim that our results are due to the outlier data point of Jeanne Calment, and claim to show this by finding a steady increase in lifespan after they relocate Jeanne Calment's data point. We agree that Jeanne Calment's death is an influential point, but our findings, far from being "entirely dependent" on this data point, as they assert, do not require its presence at all: a regression split at 1995 would still find a plateau if Jeanne Calment were omitted entirely. The alternative models suggested by Brown *et al.*[1] consist of changing Jeanne Calment's age and dates of birth and death without any biological or statistical justification. With this data manipulation, Brown *et al.*[1] seem to have altered the data to fit their model, rather than vice versa. Even after these changes, the alternative model still supports our claim that there is no significant increase in the maximum age at death after 1995 (figure 1 of ref. 1, bottom panel, $R^2 = 0.032$, $P = 0.579$), indicating the robustness of our result. Brown *et al.*[1] note that it is "curious" that Jeanne Calment is a critical part of our argument for a limit to human lifespan; however, our evidence for a limit to lifespan is not dependent on Jeanne Calment. Our findings are unchanged by the omission of this one data point, which is completely inessential to our conclusions. By contrast, their results seem to require not only its presence but also its relocation.

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