Maximum human lifespan may increase to 125 years

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

In their Letter, Dong *et al.*[1] argue that there is a limit to human lifespan of around 115 years, with their main rationale being that the maximum reported age at death (MRAD) in Japan, France, the United Kingdom and the United States has not increased since 1995. However, this does not necessarily indicate that no one will survive beyond age 115 in the future. Here we show that even if the death probabilities do not change in the future, Japanese women will reach an age of 118 before 2070, simply because of the rise in the number of supercentenarians. If we take into account the evidence that mortality has been delayed to older ages in the past, we can even project that an age of 125 years will be reached by 2070, and this projected increase in the MRAD suggests that a limit to human lifespan is not yet in sight. There is a Reply to this Comment by Dong, X. *et al. Nature* **546,** http://dx.doi.org/10.1038/nature22793 (2017).

The MRAD value can be considered the limit to human lifespan only if the probability of death equals one at that age. Since Jeanne Calment survived to age 122 in 1997[2], we know that the death probabilities below age 122 are smaller than one, and that the limit to human lifespan is at least 122. The finding that in recent years no person has survived to such a high age does not indicate that a natural limit to human lifespan has been reached, but rather that the probability of reaching that age is small. Given the recent and expected strong increase in the number of centenarians[3], the probability that in the future one person will survive to such an old age will, however, increase substantially. The highest age that can be reached in the foreseeable future depends on the death probabilities at older ages and on the size of the older population rather than on past trends in the MRAD (see Extended Data Fig. 1 and Supplementary Information).

Given the scarcity of data on the death probabilities in very old age, we estimate the death probabilities for ages 110 and above by applying a logistic-type model to mortality data of Japanese women up to age 109 (Human Mortality Database (HMD); http://www.mortality.org). We study Japanese women because a large number of very old women live in Japan. The logistic model is considered superior to the widely known Gompertz model[4–9]. Whereas the Gompertz model overestimates the acceleration of the increase in the death probabilities at the oldest ages, our logistic-type model describes this increase very accurately: $R^2 = 99.97\%$ (see Fig. 1). Using our logistic-type model, we estimate that the maximum death probability equals 0.6. Our estimate is slightly more conservative than that of Gampe in *Supercenterians*[10], who concluded, based on the analysis of 637 supercentenarians, that death probabilities after age 110 are flat at a constant level of around 0.5.

We define the MRAD value by the highest age at which at least one woman is alive and at which the probability that at least one woman will survive to the next age is smaller than 50%. If the death probabilities estimated by our logistic-type model do not change in the future, the probability that a Japanese woman aged 85 on 1 January 2015 will reach age 118 is 1 in 450,000. The number of Japanese women who were aged 85 on 1 January 2015 was 482,000 (HMD; http://www.mortality.org). Thus, we expect that one of these Japanese women will reach age 118 by 1 January 2048 (see Fig. 2).

Given the declines in the death probabilities and the delay of mortality to older ages that occurred in the past[9], it is, however, unlikely that the death probabilities will remain constant in the future. If we assume that survival to age 100 continues to improve at the same pace over the next 55 years as it did over the past 55 years, the number of centenarians will increase from 56,000 in 2015 to 750,000 in 2050. This increases the likelihood that some of these women will survive to 120, even if we assume that the survival rate among centenarians does not improve (see Fig. 2). Assuming a continuation of the observed decline in the death probabilities at ages 100 or over (see Extended Data Fig. 2), we anticipate that 1 in 840,000 women who were aged 70 on 1 January 2015 will survive to age 125 in the year 2070 (see Fig. 2).

According to all three projections, no Japanese woman is expected to survive to an age beyond 116 before 2025. This stagnation in the MRAD over the next 10 years, however, does not indicate that the limit to human lifespan is reached, as was suggested by Dong *et al.*[1] By contrast, the projected increase in the MRAD in the long run suggests that a limit to human lifespan is not yet in sight.

There are three reasons why we expect that the MRAD will increase in the long term. First, the increase in the number of centenarians makes it likely that some of these women will survive beyond age 116, even if death probabilities would not decline. Second, the projected improvement in survival up to age 100, which is in line with past trends, will lead to a further increase in the number of female Japanese centenarians, which in turn increases the likelihood that some of these women will survive to very old ages. Third, continued improvements in survival among centenarians may be expected to result in a further increase in the age at death beyond the 122 years reached by Jeanne Calment.

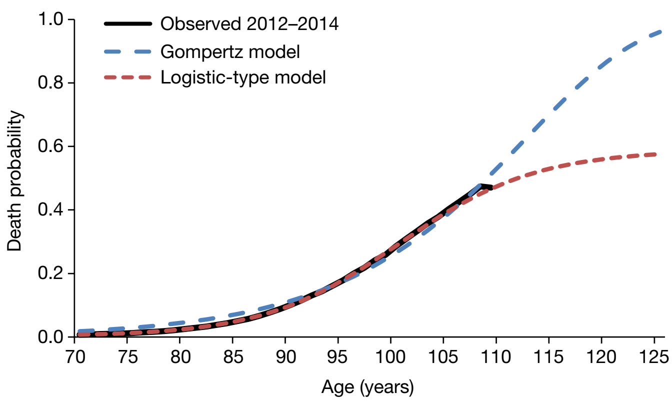

Figure 1 | Death probabilities in Japanese women. The death probability is the probability that an individual will die within one year. The solid black line shows the average observed values for the years 2012–2014 for ages 70–109. The dashed blue line shows the fit of the Gompertz model for ages 70–109 and the projection for ages 110 and over. The Gompertz model overestimates the acceleration of the increase in death probabilities in old age: the Gompertz model underestimates the death probabilities around age 100, and overestimates the death probabilities around age 110. Note that the oldest recorded age at death is 122 years[2]. This indicates that the death probabilities up to age 122 are smaller than 1.0. The dashed red line shows the fit of our logistic-type model, which is more accurate than that of the Gompertz model (see Extended Data Fig. 1 and Supplementary Information for further evidence). The logistic-type model projects that the death probability increases from 0.5 at age 110 to 0.6 at age 125.

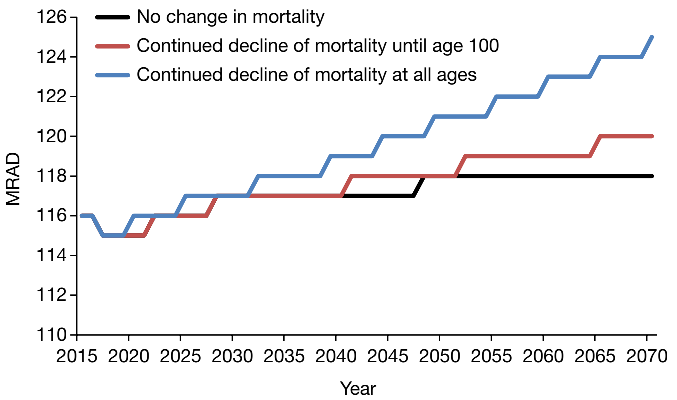

Figure 2 | MRAD of Japanese women, on 1 January 2015–2070. On 1 January 2015, the oldest living Japanese woman was aged 116. She died in 2015 after her 117th birthday (Gerontology Research Group (GRG); http://www.grg.org/). On 1 January 2016, the oldest Japanese woman was aged 115. She celebrated her 116th birthday in August 2016. Note that no Japanese woman is expected to survive beyond age 116 before 2025. This does not, however, suggest that the limit to lifespan is reached, as the MRAD is expected to rise in the long term. The black line shows the development of the MRAD based on the assumption that the death probabilities do not change between 2015 and 2070. The increase in the maximum age is due to the increase in the number of centenarians to 150,000 in 2050. This substantial increase makes it likely that some of these women will survive to age 118. The red line is based on the assumption that the decline in the death probabilities up to age 100 observed in the 1960–2014 period will continue in the years 2015–2070. The projected delay of mortality will lead to a further increase in the number of female Japanese centenarians to 750,000 in 2050. This in turn increases the likelihood that some of these women will survive to 120 and beyond. The blue line is based on the assumption that the death probabilities at the oldest ages will also decline (see Extended Data Fig. 2). The resulting improved survival of centenarians is expected to result in an increase in the maximum age to 125 years in 2070.

Methods

We used population data and unsmoothed mortality data from the HMD (http://www.mortality.org), obtained on 11 October 2016. To estimate death probabilities for ages beyond 109 and for projecting future age-specific death probabilities, we used the CoDe 2.0 model. The CoDe 2.0 model is a continuous version of the recently published and validated CoDe model[9], which describes the full age pattern of mortality (see Extended Data Fig. 2) and assesses mortality delay and compression. The model includes a logistic-type term that describes the age pattern of the death probabilities at older ages (see Extended Data Fig. 1). To project the values of the parameters of the CoDe 2.0 model, we used a multivariate stochastic time-series model (see Extended Data Fig. 3). For more information about the model and the projections, see the Supplementary Information.

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

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1. Dong, X., Milholland, B. & Vijg, J. Evidence for a limit to human lifespan. *Nature* **538,** 257–259 (2016).
2. Robine, J. & Allard, M. in *Validation of Exceptional Longevity* (eds Jeune, B. & Vaupel, J. W.) (Odense Univ. Press, 1999).
3. Robine, J. M. & Caselli, G. An unprecedented increase in the number of centenarians. *Genus* **61,** 57–82 (2005).
4. Gompertz, B. On the nature of the function expressive of the law of human mortality, and on a new mode of determining the value of life contingencies. *Philos. Trans. R. Soc. Lond*. **115,** 513–583 (1825).
5. Kannisto, V. *Development of Oldest-Old Mortality, 1950–1990: Evidence From 28 Developed Countries* (Odense Univ. Press, 1994).
6. Wilmoth, J. R. & Robine, J. The world trend in maximum life span. *Popul. Dev. Rev.* **29,** 239–257 (2003).
7. Thatcher, A. R., Kannisto, V. & Vaupel, J. W. *The Force of Mortality at Ages 80 to 120* (Odense Univ. Press, 1998).
8. Bebbington, M., Green, R., Lai, C. & Zitikis, R. Beyond the Gompertz law: exploring the late-life mortality deceleration phenomenon. *Scand. Actuar. J.* **2014,** 189–207 (2014).
9. De Beer, J. & Janssen, F. A new parametric model to assess delay and compression of mortality. *Popul. Health Metr.* **14,** 1–21 (2016).
10. Gampe, J. in *Supercentenarians* (eds Maier, H. *et al.*) (Springer Verlag, 2010).

Supplementary Information accompanies this Comment.

Author Contributions J.d.B. developed the model and calculated the population projections, A.B. estimated the time series model and projected the parameters, J.d.B. and A.B. drafted the Supplementary Information, F.J. aided in interpreting the results, J.d.B. and F.J. wrote the manuscript.

Competing Financial Interests Declared none.

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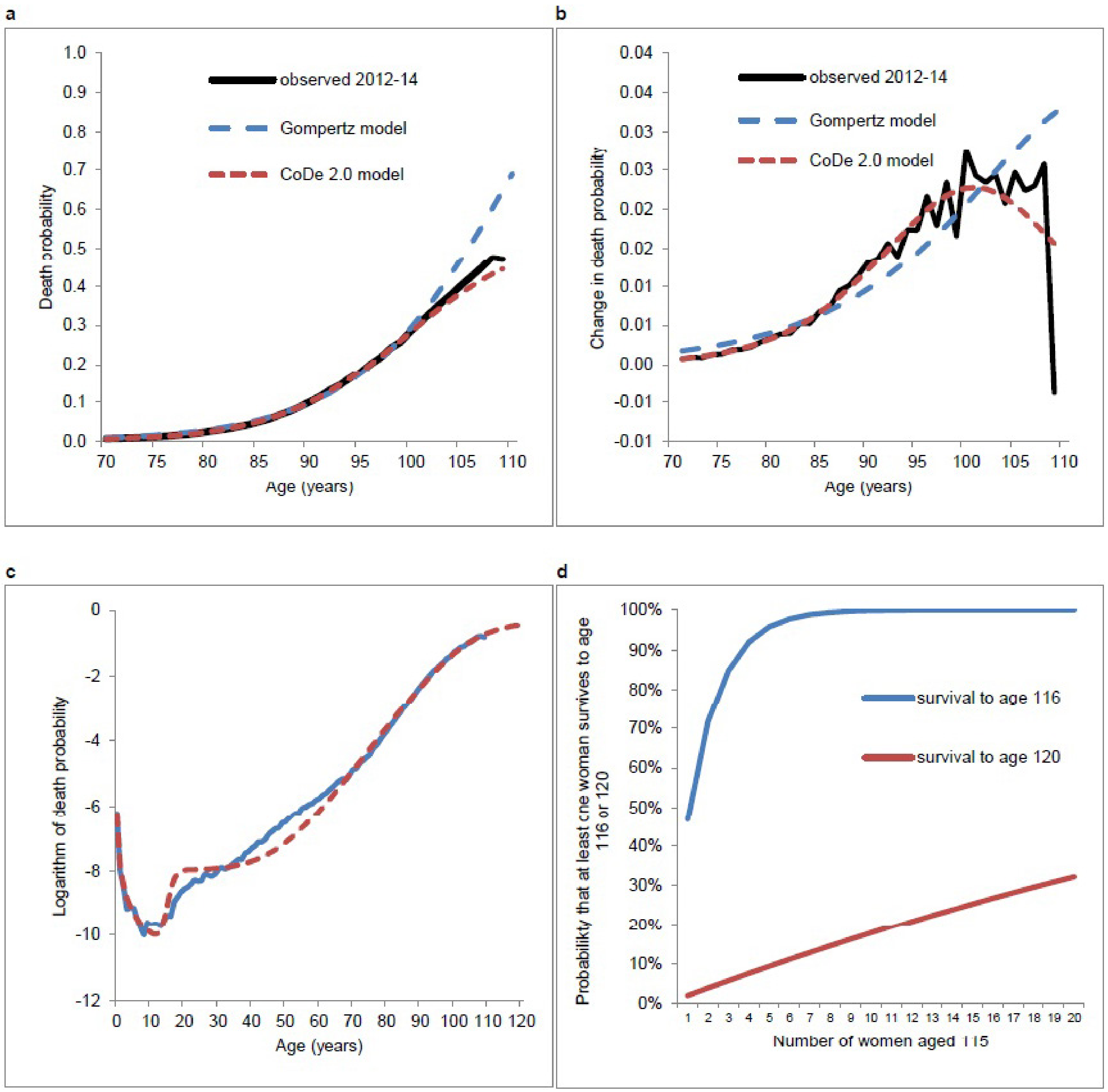
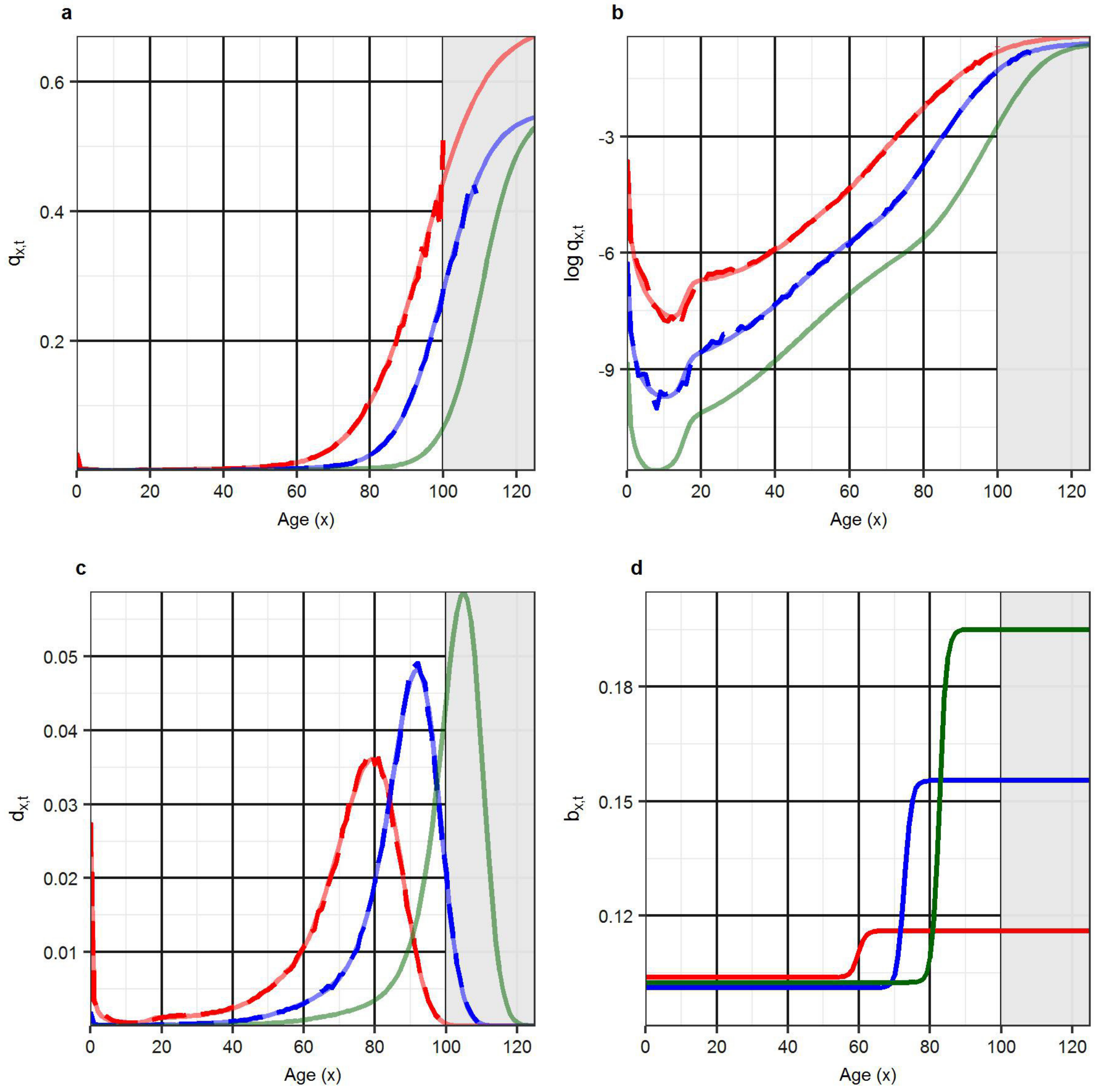
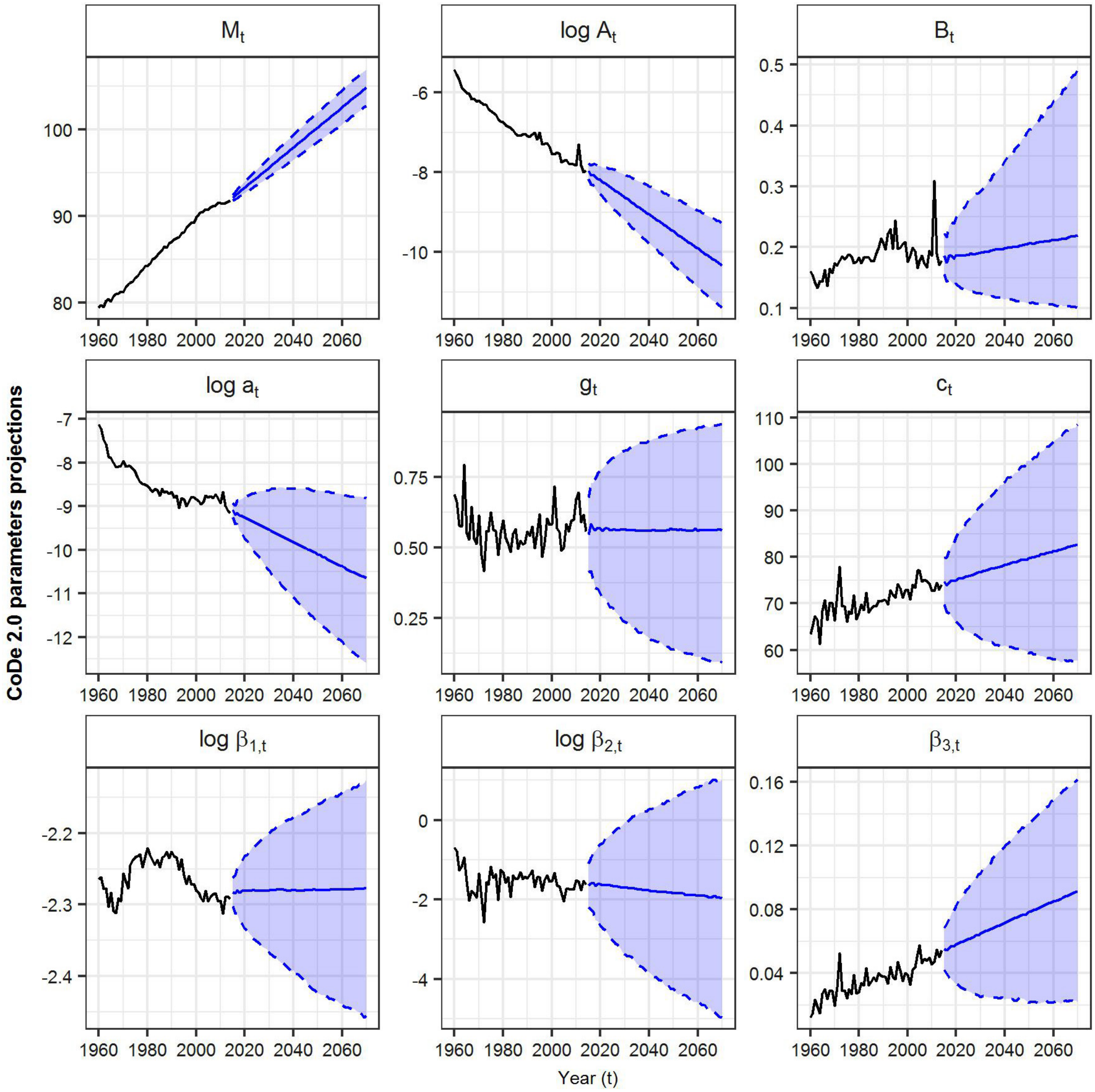


Extended Data Figure 1 | Death probabilities of Japanese women. **a**, The solid black line shows the average observed death probabilities for the years 2012–2014 for ages 70–109. The dashed blue line shows the fit of the Gompertz model for ages 70–100. Using the estimated parameters of the Gompertz model, the death probabilities are projected for ages 101–109. The dashed red line shows the fit and projection of the logistic-type function used in the CoDe 2.0 model. **b**, The solid black line shows the changes in the average observed values of the death probabilities between successive ages. The dashed blue line shows that the Gompertz model projects an acceleration of the increase in the death probabilities. The dashed red line shows that the logistic-type model used in the CoDe 2.0 model describes the levelling off of the increase in the death probabilities at ages 90 and over. **c**, The solid line shows the logarithm of the observed death probabilities in 2014. The dashed line shows the fit of the CoDe 2.0 model if the slope parameter of the logistic model *b* would not change with age. **d**, The blue line shows the probability that at least one woman aged 115 will reach age 116, and the red line shows the probability that at least one woman will reach age 120. These probabilities depend on both the size of the population at risk and the level of death probabilities.



Extended Data Figure 2 | Death probabilities and age-at-death distribution of Japanese women. The red lines show the values for 1960, the blue lines those for 2014, and the green lines the projection for 2070. The dashed lines show the observed values, the solid lines show the fit of the CoDe 2.0 model. The grey area represents the ages for which we extrapolate our estimations. The projections for 2070 are calculated using the CoDe 2.0 model in which the parameter values are assumed to equal the median values of the projections of the parameters for 2070. **a**, The increase in the death probabilities *q* levels off at older ages. **b**, The decrease in the logarithm of the death probabilities between 1960 and 2014 is smaller at older ages than at young and adult ages. **c**, The age-at-death distribution in 2014 is more compressed around the modal at death than in 1960. **d**, The slope parameter *b* of the logistic term increases more strongly at older ages in 2014 than in 1960. This results in compression of mortality in old age. This development is projected to continue up to 2070.



Extended Data Figure 3 | Estimates and projections of the parameter values of the CoDe 2.0 model. The solid lines show the estimates for the period 1960–2014 and the median values of the projections for the period 2015–2070. The dashed lines show the 95% projections intervals. The increase in the modal age at death, M_t, indicates that the CoDe 2.0 model projects a continuation of the delay of mortality. Note that the projection interval is relatively narrow. Thus, based on the observed increase in the modal age at death in the 1960–2014 period, our time-series model projects that it is highly likely that the delay of mortality to older ages will continue. The projected decrease in the values of A representing infant mortality and a representing the increase in mortality in adolescence indicate further reduction in mortality in young age contributing to compression of mortality. The increase in the value of β_3, representing the increase in the slope of the logistic term with age, indicates that a continuation of the compression of mortality at older ages is projected. The projected constant level of the asymptotic value g indicates that the death probabilities in very old age will be constant.

Dong *et al.* reply

REPLYING TO J. de Beer, A. Bardoutsos & F. Janssen & *Nature* **546,** http://dx.doi.org/10.1038/nature22792 (2017)

In the accompanying Comment[1], de Beer *et al.* question our finding of a limit to human lifespan[2]. However, we feel that their criticisms are based on misinterpretation of our results, unsubstantiated assumptions and extrapolation without support from real data. The authors claim out that our findings do not necessarily suggest that no one will survive beyond age 115 in the future. We agree, and that is why we made the distinction between the level at which yearly maximum reported age at death (MRAD) has plateaued (115 years) and the absolute maximum age beyond which it is unlikely anyone will live, which we estimated to be 125 years[2]. de Beer *et al.*[1] calculated that by 2070, at least one person in Japan will live to age 118 when assuming no change in mortality, which does not contradict our model. They also present models in which ages 120 and 125 are reached owing to a decrease in mortality before age 100 and a decrease in mortality at all ages, respectively. However, we do not think that these latter two scenarios are plausible in light of the evidence.

The results of the authors are substantially based on an extrapolation of death probabilities from data up to age 109 to beyond age 110 using the CoDe 2.0 model (figure 1 in ref. 1). de Beer *et al.*[1] argue that a logistic-type model (such as CoDe 2.0), which suggests little further increase in death probability with age beyond age 110 (red line), is more appropriate for this purpose than a Gompertz model, which suggests a substantial increase in death probability with ages beyond age 110 (blue line). However, the only actual data available do not reach further than age 109, during which time the predictions from the two models are practically on top of each other. It is only after age 109 that the models diverge. Since death probabilities display an accelerating increase before this point, it seems biologically implausible to conclude, in the absence of compelling evidence, that they would then asymptotically approach a value much less than 1. Extended data figure 1 of ref. 1 is a zoomed-in view of figure 1 (ref. 1), in which the two models begin to visibly diverge around age 105. Here, the actual data appear to lie somewhere in between the two models. Looking at the changes in death probabilities (extended data figure 2 of ref. 1), the actual data is still in between the two models, especially towards older ages. In addition, the data show several fluctuations not accounted for, including a sharp drop at the end, which could be construed as support for the CoDe 2.0 model, but which is more likely to be an artefact. Therefore, there is little reason to choose the CoDe 2.0 model over the Gompertz model when modelling mortality beyond age 110. In light of this, the evidence does not support the proposition of ref. 1 that maximum human lifespan will increase to 125 years.

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1. de Beer, J., Bardoutsos, A. & Janssen, F. Maximum human lifespan may increase to 125 years. *Nature* **546,** http://dx.doi.org/10.1038/nature22792 (2017).
2. Dong, X., Milholland, B. & Vijg, J. Evidence for a limit to human lifespan. *Nature* **538,** 257–259 (2016).

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