LETTER

Evidence for a limit to human lifespan

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Driven by technological progress, human life expectancy has increased greatly since the nineteenth century. Demographic evidence has revealed an ongoing reduction in old-age mortality and a rise of the maximum age at death, which may gradually extend human longevity[1,2]. Together with observations that lifespan in various animal species is flexible and can be increased by genetic or pharmaceutical intervention, these results have led to suggestions that longevity may not be subject to strict, species-specific genetic constraints. Here, by analysing global demographic data, we show that improvements in survival with age tend to decline after age 100, and that the age at death of the world's oldest person has not increased since the 1990s. Our results strongly suggest that the maximum lifespan of humans is fixed and subject to natural constraints.

Maximum lifespan is, in contrast to average lifespan, generally assumed to be a stable characteristic of a species[3]. For humans, the maximum reported age at death is generally set at 122 years, the age at death of Jeanne Calment, still the oldest documented human individual who ever lived[4]. However, some evidence suggests that maximum lifespan is not fixed. Studies in model organisms have shown that maximum lifespan is flexible and can be affected by genetic and pharmacological interventions[5]. In Sweden, based on a long series of reliable information on the upper limits of human lifespan, the

maximum reported age at death was found to have risen from about 101 years during the 1860s to about 108 years during the 1990s[6]. According to the authors, this finding refutes the common assertion that human lifespan is fixed and unchanging over time[6]. Indeed, the most convincing argument that the maximum lifespan of humans is not fixed is the ongoing increase in life expectancy in most countries over the course of the last century[1,2]. Figure 1a shows this increase for France, a country with high-quality mortality data, but very similar patterns were found for most other developed nations (Extended Data Fig. 1). Hence, the possibility has been considered that mortality may decline further, breaking any pre-conceived boundaries of human lifespan[1,7].

As shown by data from the Human Mortality Database[8], many of the historical gains in life expectancy have been attributed to a reduction in early-life mortality. More recent data, however, show evidence for a decline in late-life mortality, with the fraction of each birth cohort reaching old age increasing with calendar year. In France, the number of individuals per 100,000 surviving to old age (70 and up) has increased since 1900 (Fig. 1b), which points towards a continuing increase in human life expectancy. This pattern is very similar across the other 40 countries and territories included in the database (Extended Data Figs 2, 3). However, the rate of improvement in survival peaks and then declines for very old age levels (Fig. 1c), which points
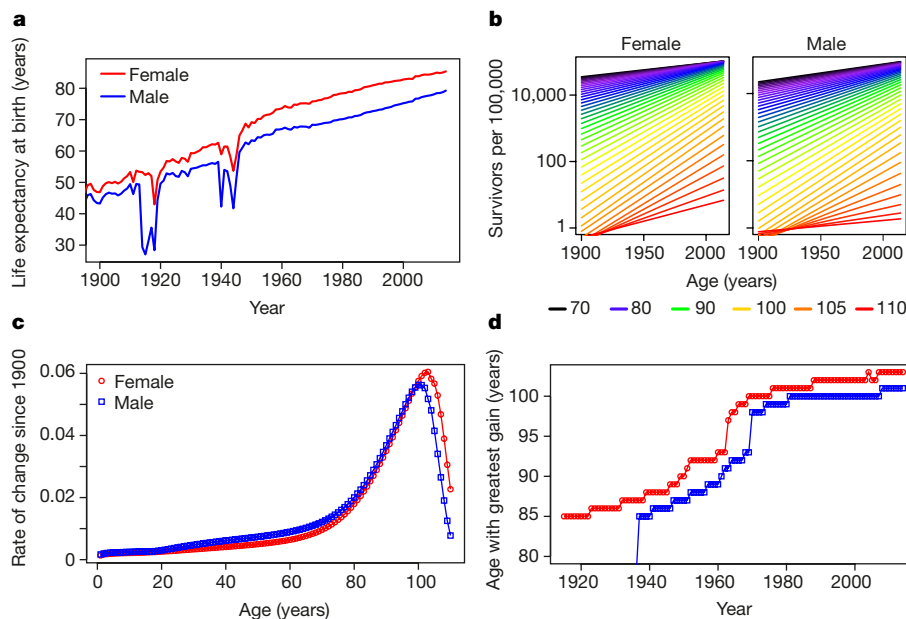

Figure 1 | Trends in life expectancy and late-life survival. a, Life expectancy at birth for the population in each given year. Life expectancy in France has increased over the course of the 20th and early 21st centuries. **b**, Regressions of the fraction of people surviving to old age demonstrate that survival has increased since 1900, but the rate of increase appears to be slower for ages over 100. **c**, Plotting the rate of

change (coefficients resulting from regression of log-transformed data) reveals that gains in survival peak around 100 years of age and then rapidly decline. **d**, Relationship between calendar year and the age that experiences the most rapid gains in survival over the past 100 years. The age with most rapid gains has increased over the century, but its rise has been slowing and it appears to have reached a plateau.

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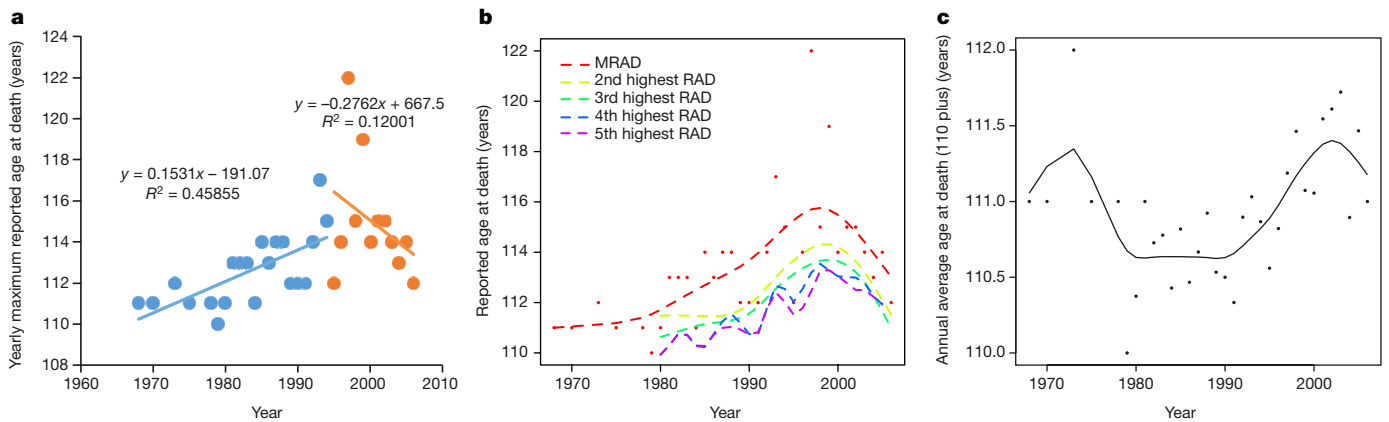
Figure 2 | Reported age at death of supercentenarians. All data were collected from the IDL database (France, Japan, UK and US, 1968–2006). **a**, The yearly maximum reported age at death (MRAD). The lines represent the functions of linear regressions. **b**, The annual 1st to 5th highest reported ages at death (RAD). The dashed lines are estimates of the RAD using cubic smoothing splines. The red dots represent the MRAD. **c**, Annual average age at death of supercentenarians (110 years plus, $n = 534$). The solid line is the estimate of the annual average age at death of supercentenarians, using a cubic smoothing spline.

towards diminishing gains in reduction of late-life mortality and a possible limit to human lifespan. The same pattern was found across other developed, low-mortality countries (Extended Data Fig. 4). However, we considered the possibility that the age experiencing the greatest increase in survivorship increases with calendar years; that is, the peak in the rate of increase in survivorship to old age will shift to the right over time. To test this, we plotted the age at which this peak occurred against calendar years (Fig. 1d). The results indicate that the age with greatest improvement in survival appeared to plateau around 1980. A similar pattern was seen in 88% of the 41 countries in the database (Extended Data Fig. 5). Together, these findings suggest, but do not prove, that human lifespan may have a natural limit. To further investigate this idea, we turned our attention from late-life mortality to maximum human lifespan itself and examined the ages at death of the world's oldest individuals.

We first plotted the yearly maximum reported age at death (MRAD) of France, Japan, UK and US, countries with the largest number of recorded supercentenarians (individuals aged 110 years old or more) in the International Database on Longevity[9] (IDL; $n = 534$, 1968–2006). As shown in Fig. 2a, although age at death increased rapidly between the 1970s and early 1990s, it reached a plateau around 1995, close to 1997, the year Jeanne Calment died. We partitioned the data into two groups (1968–1994 and 1995–2006) and modelled each group using linear regression. The results indicate a trend break between the two groups. Before 1995, the MRAD increased by 0.15 years per year ($r = 0.68$, $P = 0.0007$); however, after 1995 it no longer increased significantly and in fact decreased slightly by 0.28 years per year ($r = -0.35$, $P = 0.27$). When we considered MRAD records from another, independent resource, the Gerontological Research Group (GRG; http://www.grg.org/), we observed a similar trend—an increase by 0.12 years per year ($r = 0.71$, $P = 0.0002$) during the period 1972–1994, followed by a slight decrease by 0.14 years per year ($r = -0.36$, $P = 0.70$) during the period 1995–2015 (Extended Data Fig. 6). These results indicate that although the MRAD increased until the 1990s, no further increases were observed after that time; human yearly MRAD has plateaued at 114.9 (95% CI: 113.1–116.7) years. To approximate the absolute limit of human lifespan, we modelled the MRAD as a Poisson distribution; we found that the probability of an MRAD exceeding 125 in any given year is less than 1 in 10,000.

One potential confounder of our results is the fairly small number of reported MRAD cases, which could explain these results simply as fluctuations. To provide a robust statistical model that would strengthen the observed pattern, we considered several series of high reported age at death (HRAD), that is, the highest RAD (MRAD) and the second to the fifth highest RADs (Fig. 2b; data summarized from IDL).

All series showed the same pattern as the MRAD. Notably, even the annual average age at death for these supercentenarians has not increased since 1968 (Fig. 2c).

Hence, in contrast to previous suggestions that human longevity can be extended ever further[1], our data strongly suggest that the duration of life is limited. In the past, others have suggested that human lifespan is limited. For example, in 1980 Fries argued that increased prevention of premature deaths would lead to a compression of morbidity owing to a finite lifespan[10]. However, his arguments for such a limit to life, that is, the lack of a detectable increase in centenarians or in the maximum reported age at death, while correct at that time, have been refuted since[2,6]. Ten years later, Olshansky *et al.*[11] estimated the upper limits to human longevity based on hypothetical reductions in mortality rates, concluding that life expectancy at birth would not exceed 85 years. Like Fries, Olshansky *et al.* also suggested a biological limit to life based on the lack of an increase in the age of the verified longest-lived individual. However, as they mention, insufficient data prevented them from drawing definite conclusions. Now, more than two decades later, such data are becoming available. With the caveat that the ages at death of the supercentenarians in our present study are still noisy and made up of small samples, we feel that the observed trajectories in Fig. 2 are compelling and our results strongly suggest that human lifespan has a natural limit.

What could be the biological causes of this limit to human lifespan? The idea that ageing is a purposeful, programmed series of events that evolved under the direct force of natural selection to cause death has now been all but discredited[12]. Instead, what appears to be a 'natural limit' is an inadvertent byproduct of fixed genetic programs for early life events, such as development, growth and reproduction. Limits to the duration of life could well be determined by a set of species-specific, longevity-assurance systems encoded in the genome that counteract these inadvertent byproducts, which are likely to include inherent imperfections in transferring genetic information into cellular function[13,14]. To further extend human lifespan beyond the limits set by these longevity-assurance systems would require interventions beyond improving health span, some of which are currently under investigation[15]. Although there is no scientific reason why such efforts could not be successful, the possibility is essentially constrained by the myriad of genetic variants that collectively determine species-specific lifespan[16].

1. Oeppen, J. & Vaupel, J. W. Demography. Broken limits to life expectancy. *Science* **296,** 1029–1031 (2002).
2. Vaupel, J. W. Biodemography of human ageing. *Nature* **464,** 536–542 (2010).
3. Austad, S. N. in *Molecular and Cellular Biology of Aging* (eds Vijg, J., Campisi, J. & Lithgow, G.) Ch. 2 (The Gerontological Society of America, 2015).
4. Jeune, B. *et al.* in *Supercentenarians* (eds H. Maier *et al.*) (Springer, 2010).
5. Kenyon, C. The plasticity of aging: insights from long-lived mutants. *Cell* **120,** 449–460 (2005).
6. Wilmoth, J. R., Deegan, L. J., Lundström, H. & Horiuchi, S. Increase of maximum life-span in Sweden, 1861–1999. *Science* **289,** 2366–2368 (2000).
7. Blagosklonny, M. V. Why human lifespan is rapidly increasing: solving "longevity riddle" with "revealed-slow-aging" hypothesis. *Aging* **2,** 177–182 (2010).
8. *The Human Mortality Database* (http://www.mortality.org, 2016).
9. Maier, H. *et al. Supercentenarians* (Springer, 2010).
10. Fries, J. F. Aging, natural death, and the compression of morbidity. *N. Engl. J. Med.* **303,** 130–135 (1980).
11. Olshansky, S. J., Carnes, B. A. & Cassel, C. In search of Methuselah: estimating the upper limits to human longevity. *Science* **250,** 634–640 (1990).
12. Vijg, J. & Kennedy, B. K. The Essence of Aging. *Gerontology* **62,** 381–385 (2016).
13. Finch, C. E. *Longevity, Senescence, and the Genome* (Univ. Chicago Press, 1990).
14. Vijg, J. *Aging of the Genome* (Oxford, 2007).
15. Longo, V. D. *et al.* Interventions to slow aging in humans: are we ready? *Aging Cell* **14,** 497–510 (2015).
16. Vijg, J. & Campisi, J. Puzzles, promises and a cure for ageing. *Nature* **454,** 1065–1071 (2008).

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Author Information Reprints and permissions information is available at www.nature.com/reprints. The authors declare no competing financial interests. Readers are welcome to comment on the online version of the paper. Correspondence and requests for materials should be addressed to J.V. (jan.vijg@einstein.yu.edu).
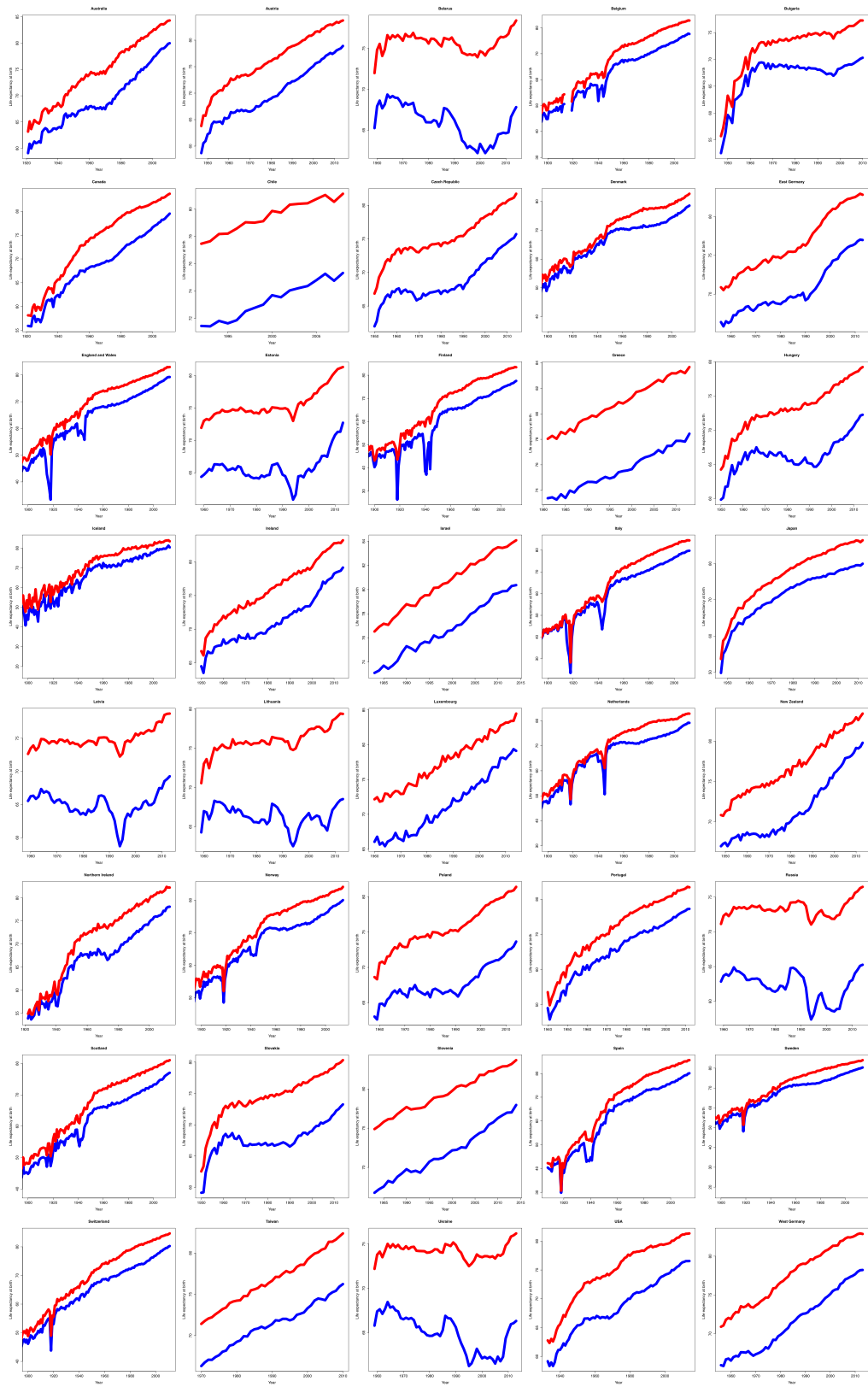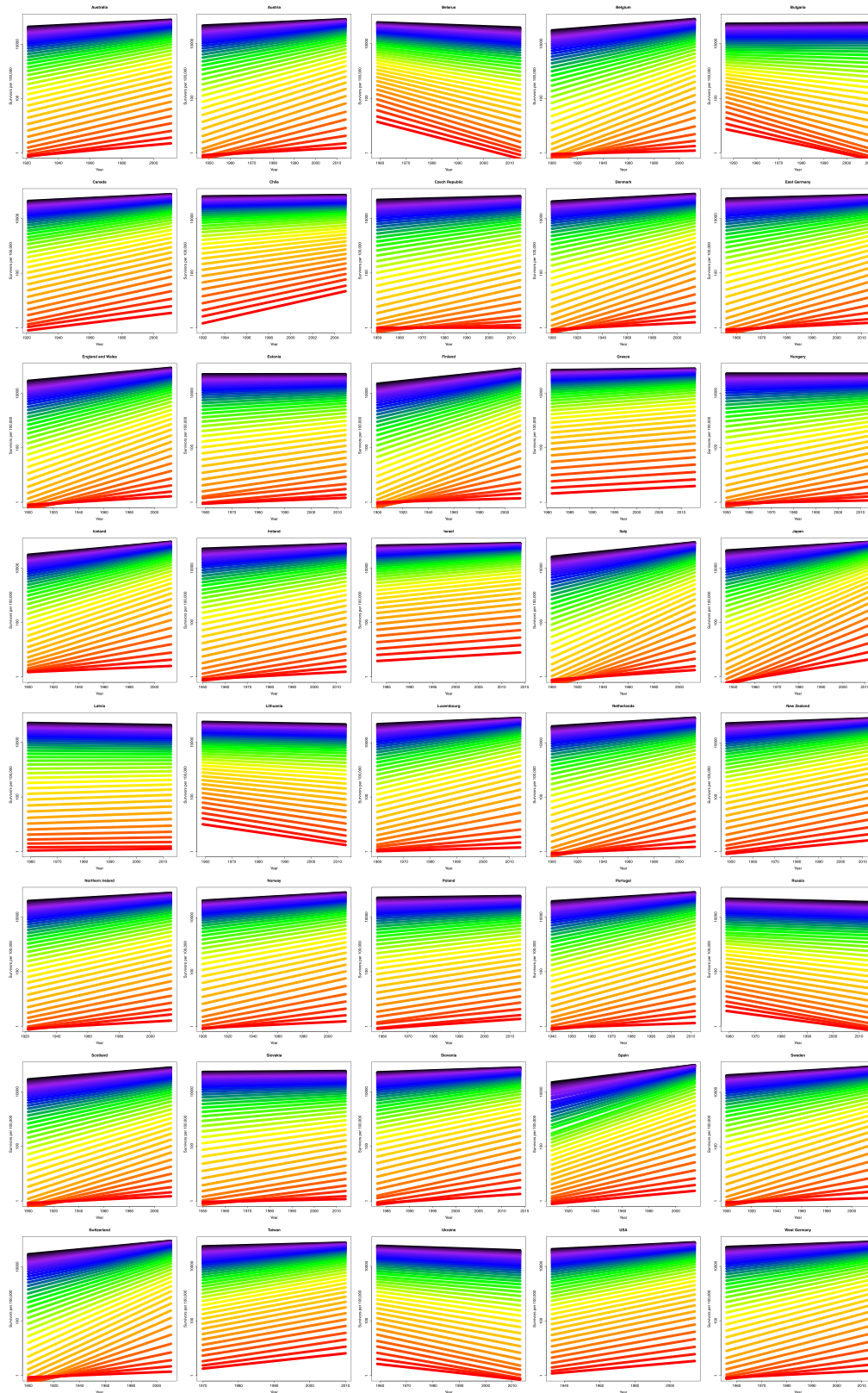
Extended Data Figure 1 | Life expectancy over time since 1900 (or the earliest year for which data was available) in 40 countries and territories. There is a generally positive trend over time; life expectancy in Japan appears to be reaching a plateau, but the increase looks unabated in many of the other countries. The data represent the entire population for each region, except Scotland, where it represents only the civilian population. The colour scheme is as in Fig. 1a.
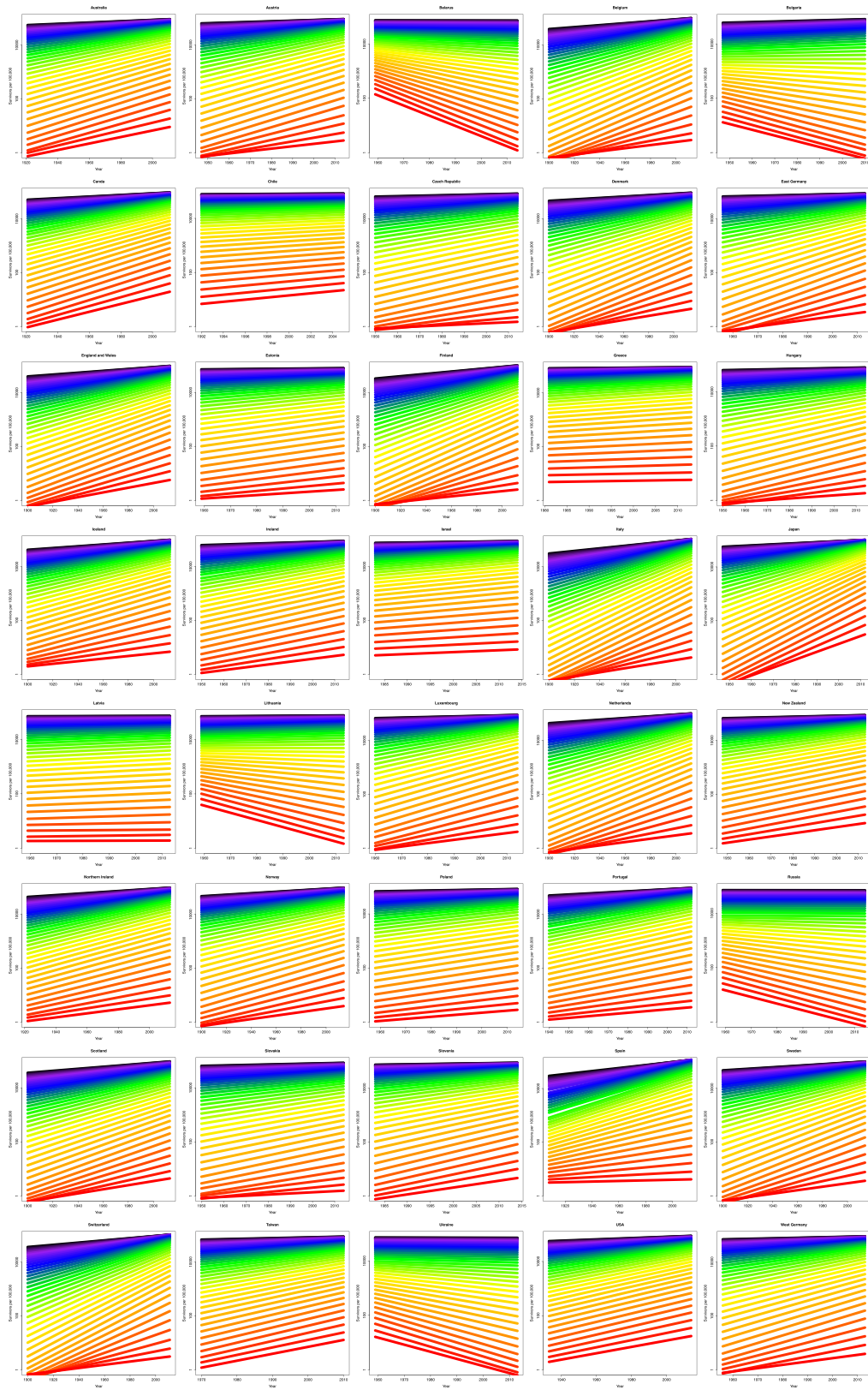
Extended Data Figure 2 | Proportion of the population surviving to old age among females in 40 countries and territories. The data represent the entire population for each region, except Scotland, where it represents only the civilian population. The colour scheme is as in Fig. 1b.

Extended Data Figure 3 | Proportion of the population surviving to old age among males in 40 countries and territories. The data represent the entire population for each region, except Scotland, where it represents only the civilian population. The colour scheme is as in Fig. 1b.
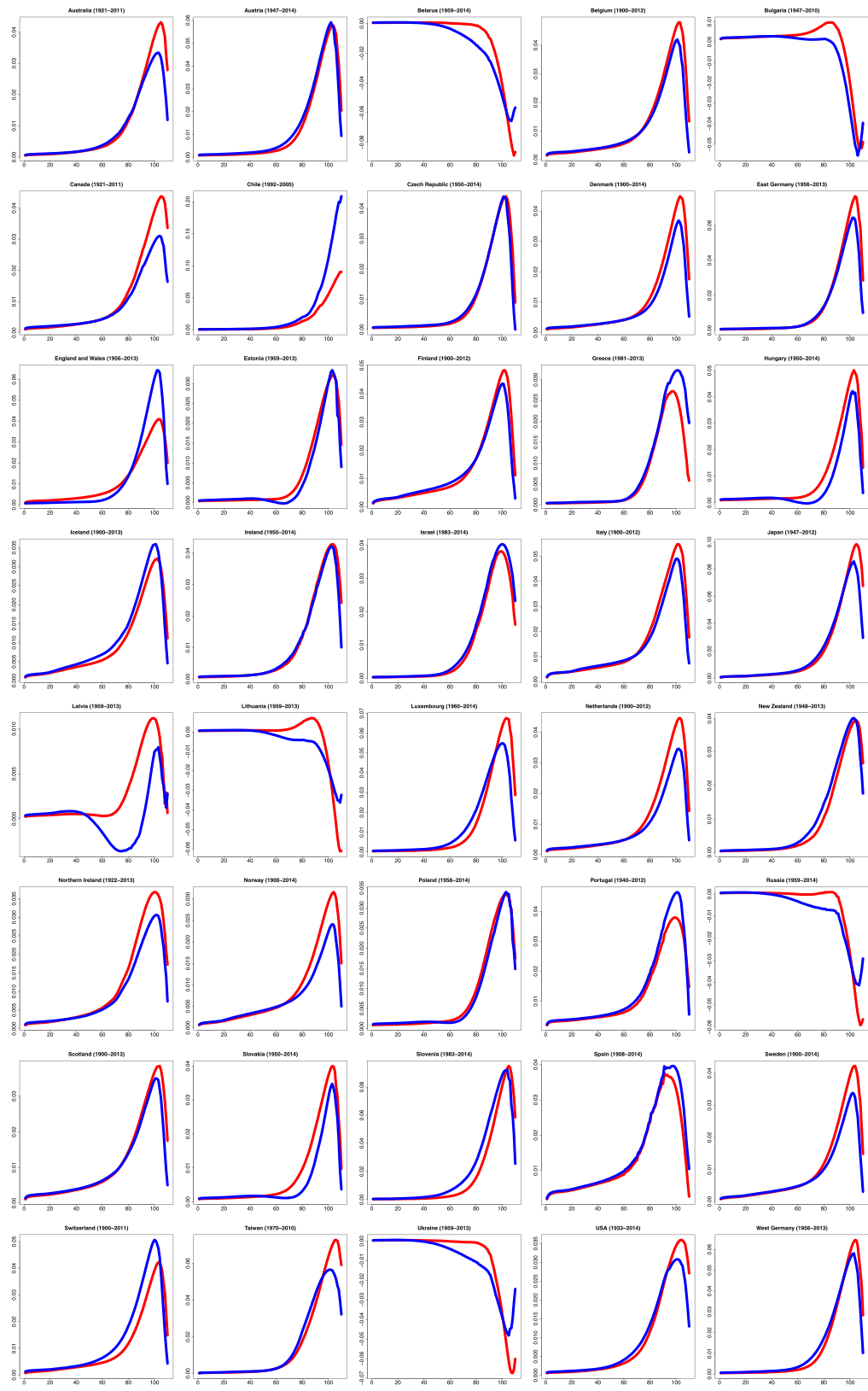
Extended Data Figure 4 | Rate of change in survival since 1900 (or the earliest year for which data was available) to a given age as a function of that age in 40 countries and territories. The rate of change is the slope of the line calculated by an exponential regression, that is, b in the equation $y = a + bx$, where x is age and y is the logarithm of the number of survivors to that age per 100,000. Including France, 90% (37/41) of the regions examined exhibited the pattern depicted in Fig. 1c.
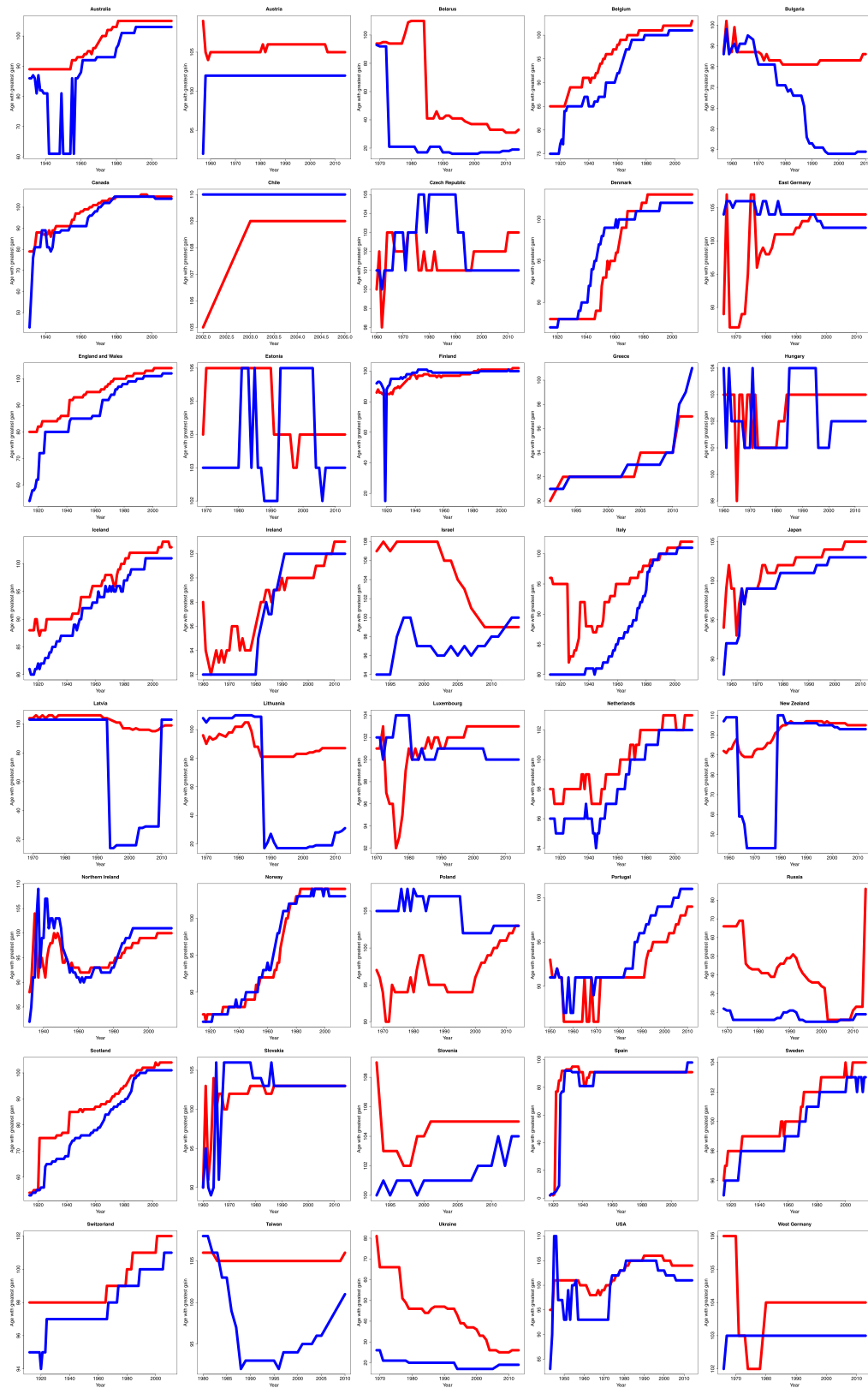
Extended Data Figure 5 | Age with the greatest increase in survival as a function of calendar year in 40 countries and territories. For each year, the age with the greatest increase in survival over the past 100 years (or since the earliest year for which data was available), that is, the peak of a graph like that from Extended Data Fig. 4, was determined. Including France (Fig. 1d), a total of 82 data sets were considered (males and females in each region); we used linear regressions of segments of the data to look for evidence of plateaus. A data set was considered to be plateauing if one

of the following criteria applied: the second half of the data had a negative slope; the first half of the data had a negative slope (as an increase in the second half would likely reflect a return to some equilibrium after being negatively perturbed); the first half of the data had a slope greater than that of the second half of the data; or the final 10% of the data had a slope less than that of the preceding 40%. In 88% (72/82) of the data sets, there was evidence of a plateau.
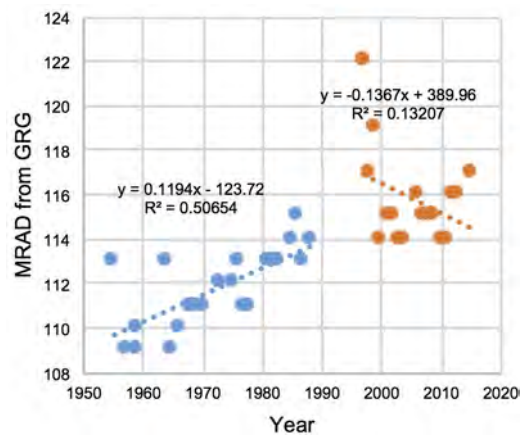
Extended Data Figure 6 | The yearly maximum reported age at death from the GRG database (worldwide, 1972–2015). The lines represent the functions of linear regressions.