

## Mortality Data Suggests that Men Are More Fragile but Women Age Faster

### Authors

Peter Lenart<sup>1,2</sup>, Daniela Kuruczova<sup>1,2</sup>, Julie Bienertová-Vašků<sup>1,2</sup>

<sup>1</sup>*Department of Pathological Physiology, Faculty of Medicine, Masaryk University, Kamenice 5, building A18, 625 00, Brno, Czech Republic*

<sup>2</sup>*Research Centre for Toxic Compounds in the Environment, Faculty of Science, Masaryk University, Kamenice 5, building A29, 625 00, Brno, Czech Republic*

### Abstract:

Although women on average live longer than men, differences in the pace of ageing are relatively unstudied and remain controversial. We thus employ mathematical methods previously established in model organisms to compare the pace of ageing between the sexes using freely available mortality data from 37 countries. Surprisingly, we found that the mortality rates of women almost universally increase faster than those of men, which is equivalent to faster ageing. This finding implies that the gap in life expectancy should continue to close with progress in healthcare since the longer lifespan of women is mainly due to the higher “starting” mortality of men. Our results may also help explain the mortality–morbidity paradox, i.e. why women live longer but are sicker than men.

### Main text:

The life expectancies of men and women are widely recognized as being different: women worldwide live longer than men. This logically leads to the question whether women also age slower than men. Both “yes” and “no” answers have found some support (1–3). The classical

argument against the notion that women age slower is the fact that men experience higher mortality rates at almost every age, i.e. that the reason for their shorter life span is that men are the less “robust” sex and as such exhibit higher background mortality (1,3). On the other hand, researchers suggesting that women indeed age slower than men note that this line of reasoning may not be altogether valid since men die from different causes at different ages (2). Interestingly both of these views fail to answer the existence of the mortality–morbidity paradox, in other words why women live longer but are sicker than men (3,4,5). Regardless of theoretical arguments, aging is defined as an age-dependent increase in mortality (2,6,7) and therefore, the pace of aging of men and women may be empirically calculated using available mortality data. In this article, we present the results of an analysis of mortality data from 37 countries which suggests that – contrary to all previous expectations – women in fact age faster than men.

One method of quantifying ageing relies on calculating the rate at which mortality increases with age<sup>8</sup>. The relationship between human age and mortality is usually modelled using a predefined distribution which explicitly defines the relationship between age and mortality rate. Distributions most commonly used for this purpose include Gompertz (or its extension Gompertz–Makeham), Weibull and logistic<sup>9</sup>. The choice of a specific distribution depends on the purpose of its use: the best fitting model is often desired when a prediction is sought while a different model may be more suitable for the interpretation of parameter values<sup>10,11</sup>. Since our objective was to demonstrate the difference between the pace of mortality rate increase in men and women, the Gompertz model<sup>12</sup> was selected as well-suited for this purpose. It is appropriate for accommodating human mortality data approximately between 30 and 80 years of age<sup>11,13</sup> and also offers a means for comparing mortality rate increase by means of mortality rate doubling time (MRDT), a parameter commonly used as an estimate of the rate of ageing<sup>14,15</sup>. Its

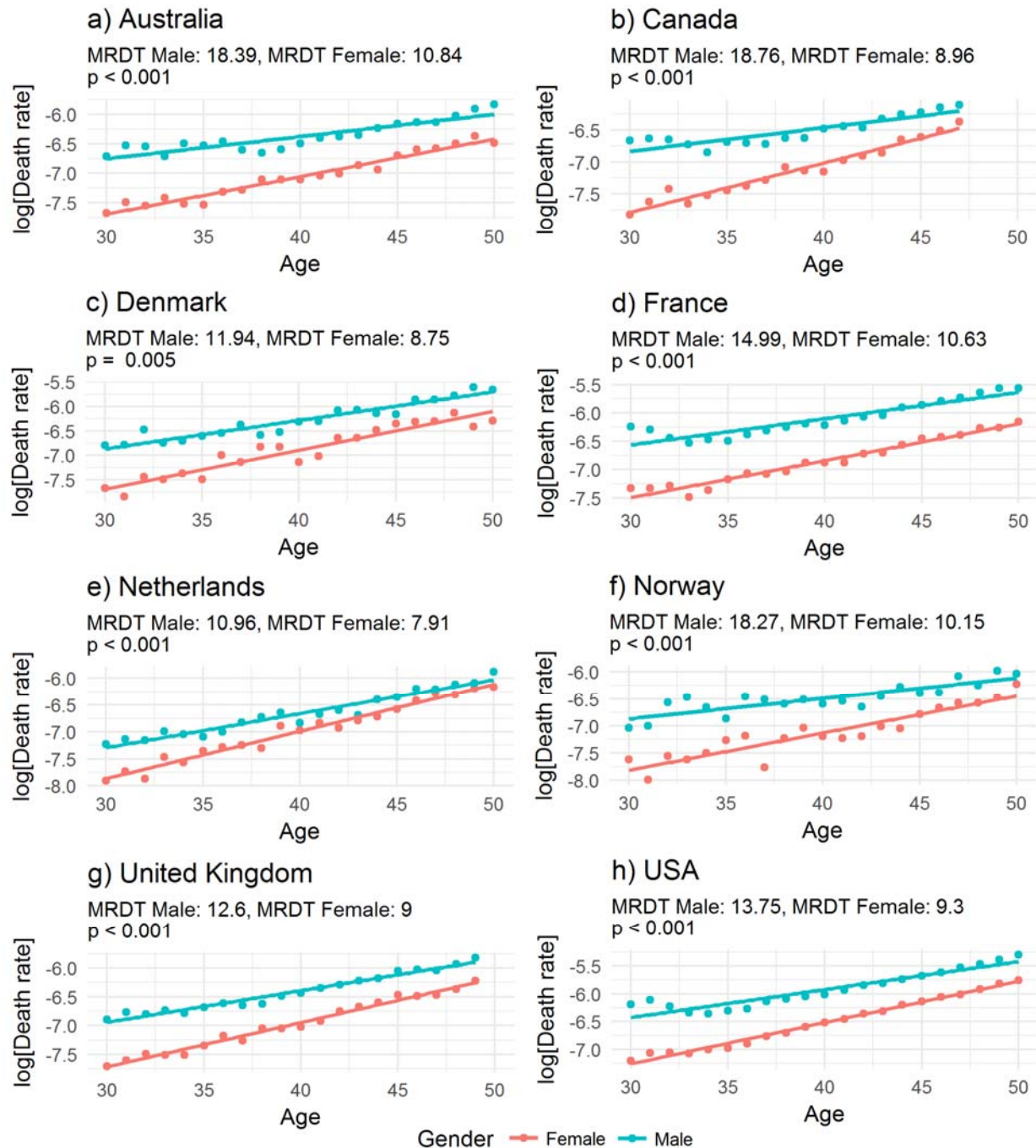
disadvantage, i.e. the inability to distinguish between intrinsic and extrinsic mortality rate, is not crucial, as the chosen interval of 30 to 60 years of age should be influenced mainly by intrinsic causes<sup>11</sup>. Furthermore, the Gompertz model may also be easily transformed and estimated as a linear model, which offers straightforward statistical tools for testing the difference between men and women.

In this study we used mortality data obtained from the Human Mortality Database<sup>16</sup> to calculate MRDTs for male and female populations in 37 countries. Furthermore, for each country, we also tested whether a statistically significant difference is to be found between the sexes in slopes of lines obtained by the log-linear Gompertz mortality rate model. Mortality rates may be affected by a great variety of external influences unrelated to ageing. One extreme example of such external influences was undoubtedly the Second World War (WWII) which dramatically altered mortality rates both directly by the deaths of millions of soldiers and civilians and indirectly by the late effects of injuries, starvation, psychological trauma, etc. Accordingly, mortality rates during the early life of a cohort are known to influence its mortality rates later in life<sup>17</sup>. Because most countries in the Human Mortality Database were more or less heavily involved in WWII, we thoroughly analysed mortality patterns only in people born at least 8 years after the end of this conflict. We calculated MRDTs for cohorts of people born in 1954 and 1964 using their mortality rates in periods starting in 1984 and 1994 respectively to the newest available data in the Human Mortality Database. In other words, investigated mortality rates for people born in 1954 and 1964 were from periods between their 30<sup>th</sup> and 60<sup>th</sup> or 30<sup>th</sup> and 50<sup>th</sup> birthdays. We also calculated MRDTs for people born in 1969 for a period starting with their 25<sup>th</sup> birthdays and ending with the most recent available records – generally 2014 or 2013 for most countries.

MRDTs calculated for people born in 1954 were longer for males in 32 of 37 investigated countries (Table S1) with a mean MRDT difference in these 32 countries of 0.902 years (average of 1.187 years). While MRDTs were found to be longer for women in Greece, Japan, Portugal, Slovakia and Taiwan, in three of these five countries the differences between MRDTs of men and women were not statistically significant (Greece: 0.498, Portugal: 0.253, Slovakia: 0.055 years). The two countries with a significantly slower increase in mortality in women in comparison with men were Japan with a 1.240 years longer female MRDT ( $p < 0.001$ ) and Taiwan with an 0.768 years longer female MRDT ( $p = 0.037$ ). Furthermore, it is interesting to note that most of these countries experienced various destabilizing post-WWII events which may have affected the analysed mortality rates: Greece underwent civil war<sup>18</sup>, as did Taiwan, which in its current form is a direct result of the Chinese Civil War<sup>19</sup>, while Slovakia (Czechoslovakia at the time) forcibly expelled over two million ethnic Germans<sup>20</sup> and experienced a communist coup<sup>21</sup>. Finally, mortality rates in Portugal may have been influenced by the Portuguese Colonial War and the subsequent influx of refugees from former colonies<sup>22</sup>. While it seems likely that mortality rates in these countries may have been influenced by the above mentioned events, universally higher MRDTs in males are found in the case of prosperous western countries which had enjoyed significantly more stable conditions (Figure S1).

MRDTs calculated for people born in 1964 are even more suggestive. Out of 37 analysed countries, males had longer MRDTs in 36 of them (table 1). The only country with longer MRDT in females was Taiwan. However, while differences in MRDTs in Taiwan were not statistically significant ( $p = 0.055$ ), male MRDTs were found to be significantly longer in a total of 27 analyzed countries. The median difference between male and female MRDTs for these cohorts in all analysed countries is 3.2 years (average 5.3 years). Furthermore, in most first world

countries the differences between the MRDTs of men and women were found to be robust and highly significant ( $p < 0.001$ ) (figure 1).



**Figure 1:** Lines resulting from the logarithmic transformation of the Gompertz curve which represents the rate of mortality increase over time. The significant difference between the slopes of these lines is equivalent to the significant difference between MRDTs.

MRDTs calculated for people born in 1969 show the same trend: MRDTs of men are longer in all analysed countries with the exception of Taiwan. Since only limited data is available for this cohort, MRDTs were calculated from a different age interval starting at a lower age and are thus more susceptible to outlier influence. Nevertheless, the aim of comparing MRDTs in this “young” cohort is only to show that trend of higher male MRDT is consistently apparent even at different intervals. Furthermore, it is important to note that while the absolute differences between MRDTs in men and women depend on a great variety of external conditions and differ from cohort to cohort and from country to country, the longer MRDTs of men seem to be almost universal. Therefore, the main result of this study is not the precise estimate of differences in ageing between sexes but the simple statement that – against all previous expectations – women seem to age faster.

Our results strongly suggest that the longer MRDTs of men are a world-wide phenomenon and as such must be based on an underlying cause. We believe that the most coherent explanation is the faster rate of ageing in women. Other possible explanations such as the world-wide systematic negligence of women’s healthcare or the lower tendency of women to consult their health issues with medical doctors seem to be directly contradicted by existing data<sup>7</sup>. The faster rate of female ageing is not only the most coherent explanation but it is also the most powerful one. It predicts that the life expectancy gap between men and women should slowly close or even disappear as medicine progresses and further reduces average mortality rates. This scenario already seems to be taking place in developed western countries<sup>23</sup>.

Furthermore, the age at which female mortality rates should catch up with male mortality rates may be easily calculated for each cohort and country. For example, for a cohort born in the USA in 1954 the predicted age of mortality rate equality for both sexes is 86.7. However, a cohort born in the USA in 1964 should reach equal mortality rates at age 64.7. We speculate that the lower predicted age of equal mortality rates in the younger cohort, which is also evident in other countries, is caused by the decrease of background mortality rates due to improvements in health care.

It is also worth noting that common opinion among laymen is that women age faster. While it may be argued that the subjective perception of youthfulness in women is highly influenced by sexual attractiveness related to fertility<sup>2</sup>, our data indicate that this faster subjective deterioration of women is at least partially related to the ageing process itself. Furthermore, the faster ageing of women makes perfect sense in evolutionary terms. Due to the inherently lower mortality of women and relatively short lifespan of humans throughout most of our species' history, it seems very likely that the evolutionary pressure to reduce the speed of ageing has historically been lower in females than in males.

## **Methods**

Mortality rate data were acquired from [www.mortality.org](http://www.mortality.org) on 12 July 2017. The Human Mortality Database (HMD) contained data about mortality rates for 39 sovereign countries and several others smaller areas and populations. Iceland and Luxembourg were excluded from our analysis due to population size criteria (under 1 million). Croatia was excluded due to a very

limited range of available data (2001–2015). Chile and Bulgaria were excluded due to missing mortality rate data for 17 and 4 years respectively.

## Statistics

The Gompertz model<sup>12,14</sup> of exponential hazard growth was used to model the relationship between age and mortality rate. The basic form of the Gompertz model is

$$h(t) = ae^{bt}$$

where  $a$  and  $b$  are constants,  $t$  is time (in our case age) and  $h(t)$  is the hazard (mortality) rate.

Using the logarithmic transformation, a simple linear model is obtained

$$\log h(t) = b_0 + b_1 t.$$

where  $b_0$  signifies the intercept (overall shift of the line in the direction of the y-axis) and  $b_1$  expresses the slope of the line. MRDT is subsequently calculated from the slope as

$$MRDT = \log(2) / b_1$$

and expresses the time it takes for the mortality rate to double.

To determine the difference in the rate of ageing between sexes, we modified the linear model by adding a dummy variable indicating the male sex

$$\log h(t) = b_{01} + b_{02} Male + (b_{11} + b_{12} Male)t.$$

Coefficients  $b_{02}$  and  $b_{12}$  express the difference in the intercept and the slope for males. Statistical testing may be employed to determine whether these coefficients are significantly different from zero, i.e. whether there is a difference between sexes. Testing the difference of the slope between the sexes is equivalent to testing the difference of the MRDT.



The above described model was fitted on data for each individual country using an age interval beginning at 30 years of age. The Gompertz model accurately fits human mortality dynamics roughly between 30 and 80<sup>11,13</sup>, which was subsequently confirmed during exploratory analysis of the data from HMD. The model proved to be a good fit for HMD data with a median  $R^2$  of 0.98 for the 1954 cohort and 0.96 for the 1964 cohort (see table TBD). MRDTs for all selected countries were subsequently calculated using the slope coefficients from the fitted model. The fitted models for several selected countries were further used to determine the age, at which male and female mortality rates will become equal.

Differences between slopes were tested across multiple countries which led to multiple hypothesis testing situations. As our main goal was to provide a descriptive analysis in order to show the effect on multiple datasets, no correction was used. Naturally, one should be more cautious when relying on p-values in this case, but they still serve as reliable measure of the effect and the comparison between MRDTs provides a suitable means of expressing the magnitude of the effect.

## **Code availability**

Code is available at [http://www.math.muni.cz/~xkuruczovad/Gompertz\\_calc.R](http://www.math.muni.cz/~xkuruczovad/Gompertz_calc.R) or upon request.

## **References:**

1. Austad, S. N. Why women live longer than men: Sex differences in longevity. *Gend. Med.* 3, 79–92 (2006).

2. Blagosklonny, M. V. Why men age faster but reproduce longer than women: mTOR and evolutionary perspectives. *Aging* 2, 265–273 (2010).
3. Austad, S. N. & Fischer, K. E. Sex Differences in Lifespan. *Cell Metab.* 23, 1022–1033 (2016).
4. Vaupel, J. W. Biodemography of human ageing. *Nature* 464, 536–542 (2010)
5. Oksuzyan, A., Juel, K., Vaupel, J. W. & Christensen, K. Men: good health and high mortality. Sex differences in health and aging. *Aging Clin. Exp. Res.* 20, 91–102 (2008).
6. Kirkwood, T. B. L. & Austad, S. N. Why do we age? *Nature* 408, 233–238 (2000).
7. Lenart, P. & Bienertová-Vašků, J. Keeping up with the Red Queen: the pace of aging as an adaptation. *Biogerontology* 18, 693–709 (2017).
8. Pletcher, S. D., Khazaeli, A. A. & Curtsinger, J. W. Why do life spans differ? Partitioning mean longevity differences in terms of age-specific mortality parameters. *J. Gerontol. A. Biol. Sci. Med. Sci.* 55, B381-389 (2000).
9. Pham, H. Mortality Modeling Perspectives. in *Recent Advances in Reliability and Quality in Design* 509–516 (Springer, London, 2008). doi:10.1007/978-1-84800-113-8\_25
10. Ricklefs, R. E. & Scheuerlein, A. Biological Implications of the Weibull and Gompertz Models of Aging. *J. Gerontol. Ser. A* 57, B69–B76 (2002).
11. Nash, F. R. *Reliability Assessments: Concepts, Models, and Case Studies.* (CRC Press, 2016).

12. 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).
13. Easton, D. M. & Hirsch, H. R. For prediction of elder survival by a Gompertz model, number dead is preferable to number alive. *Age 30*, 311–317 (2008).
14. de Magalhães, J. P., Cabral, J. A. S. & Magalhães, D. The Influence of Genes on the Aging Process of Mice. *Genetics* 169, 265–274 (2005).
15. de Magalhães, J. P., Costa, J. & Church, G. M. An Analysis of the Relationship Between Metabolism, Developmental Schedules, and Longevity Using Phylogenetic Independent Contrasts. *J. Gerontol. A. Biol. Sci. Med. Sci.* 62, 149–160 (2007).
16. Human Mortality Database. Available at: <http://www.mortality.org/>. (Accessed: 30th June 2017)
17. Beltrán-Sánchez, H., Crimmins, E. M. & Finch, C. E. Early Cohort Mortality Predicts the Cohort Rate of Aging: an Historical Analysis. *J. Dev. Orig. Health Dis.* 3, 380–386 (2012).
18. Marantzidis, N. & Antoniou, G. The Axis Occupation and Civil War: Changing Trends in Greek Historiography, 1941-2002. *J. Peace Res.* 41, 223–231 (2004).
19. Dunbabin, J. P. D. *The Cold War: The Great Powers and Their Allies*. (Pearson Education, 2008).
20. Glassheim, E. National Mythologies and Ethnic Cleansing: The Expulsion of Czechoslovak Germans in 1945. *Cent. Eur. Hist.* 33, 463–486 (2000).

21. Taborsky, E. Communism in Czechoslovakia, 1948-1960. (Princeton University Press, 2015).
22. Carrington, W. J. & De Lima, P. J. F. The Impact of 1970s Repatriates from Africa on the Portuguese Labor Market. *ILR Rev.* 49, 330–347 (1996).
23. Regan, J. C. & Partridge, L. Gender and longevity: why do men die earlier than women? Comparative and experimental evidence. *Best Pract. Res. Clin. Endocrinol. Metab.* 27, 467–479 (2013).

## Acknowledgements

We would like to thank the CETOCOEN PLUS project CZ.02.1.01/0.0/0.0/15\_003/0000469.

## Authors' contributions

P. L. formulated the research problem, chose data sources and interpreted the results. D. K. analysed the data and J. B. V supervised the project. All authors co-wrote the manuscript.

Country	MRDT male (years)	MRDT female (years)	p	R <sup>2</sup>
Australia	12.9	10.4	< 0.001	0.977
Belarus	8.4	8.0	= 0.342	0.976
Belgium	10.3	9.4	= 0.017	0.982
Canada <sup>(2011)</sup>	11.5	9.0	< 0.001	0.990
Czechia	8.9	8.6	= 0.265	0.980
Denmark	10.1	9.2	= 0.068	0.972
East Germany	10.8	10.6	= 0.761	0.982
West Germany	9.4	9.2	= 0.291	0.997
Estonia <sup>(2013)</sup>	11.0	9.2	= 0.143	0.908
Finland	12.0	8.9	< 0.001	0.980
France	10.9	10.4	= 0.016	0.995
Greece <sup>(2013)</sup>	8.9	9.4	= 0.210	0.982
Hungary	9.5	9.4	= 0.860	0.980
Ireland	10.2	8.6	= 0.029	0.934

Israel	9.4	8.6	= 0.172	0.955
Italy <sup>(2012)</sup>	10.7	9.5	< 0.001	0.994
Japan	8.8	10.1	< 0.001	0.995
Latvia <sup>(2013)</sup>	9.9	9.1	= 0.413	0.932
Lithuania <sup>(2013)</sup>	9.3	8.9	= 0.556	0.959
Netherlands	9.0	8.5	= 0.063	0.986
New Zealand <sup>(2013)</sup>	13.1	10.7	= 0.018	0.925
Norway	10.8	8.7	< 0.001	0.961
Poland	9.7	8.8	< 0.001	0.995
Portugal	12.0	12.3	= 0.630	0.985
Russia	9.3	8.4	= 0.204	0.944
Slovakia	8.9	9.0	= 0.875	0.985
Slovenia	11.5	9.3	= 0.002	0.964
Spain	10.5	10.4	= 0.512	0.995
Sweden	11.8	9.6	= 0.001	0.956
Switzerland	12.2	10.4	= 0.009	0.965
Taiwan	11.2	11.9	= 0.037	0.992
Ukraine <sup>(2013)</sup>	8.3	7.9	= 0.506	0.967
United Kingdom <sup>(2013)</sup>	9.2	8.6	< 0.001	0.996
England and Wales <sup>(2013)</sup>	9.2	8.7	= 0.003	0.995
Northern Ireland <sup>(2013)</sup>	9.2	8.1	= 0.140	0.913
Scotland <sup>(2013)</sup>	9.5	8.1	= 0.002	0.971
USA	11.7	9.1	< 0.001	0.996

**Table S1.** Summary of MRDTs for men and women in 37 analyzed countries. Years listed in brackets (upper indices in the Country column) indicate the last year with mortality rates

### Supplementary Materials:

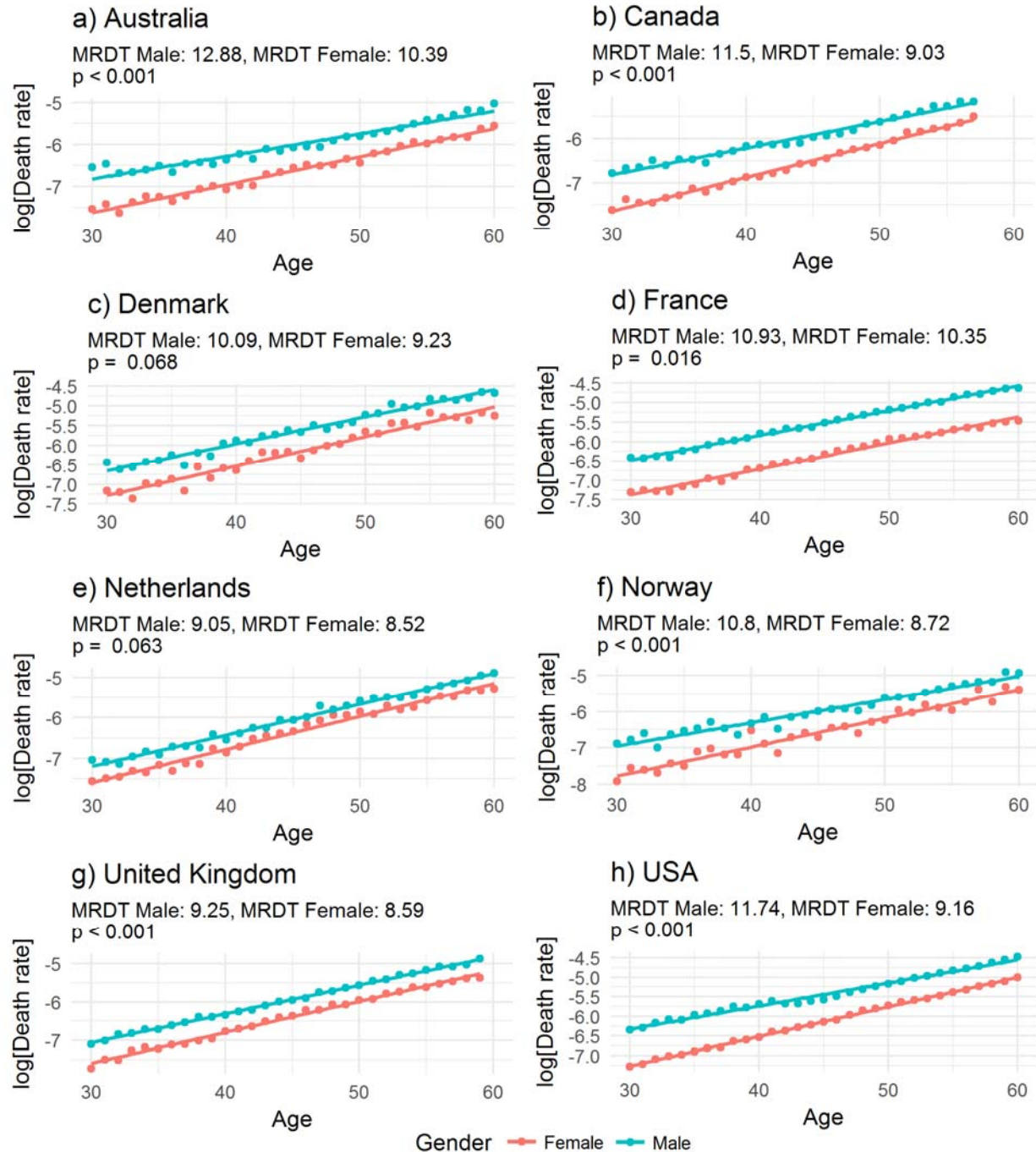
Table S1

Figure S1

<b>Table S1 Summary of MRDTs for cohort born in 1954 (30–60)</b>				
Country	MRDT male (years)	MRDT female (years)	p	R <sup>2</sup>
Australia	12.9	10.4	< 0.001	0.977
Belarus	8.4	8.0	= 0.342	0.976
Belgium	10.3	9.4	= 0.017	0.982
Canada <sup>(2011)</sup>	11.5	9.0	< 0.001	0.990
Czechia	8.9	8.6	= 0.265	0.980
Denmark	10.1	9.2	= 0.068	0.972
East Germany	10.8	10.6	= 0.761	0.982
West Germany	9.4	9.2	= 0.291	0.997
Estonia <sup>(2013)</sup>	11.0	9.2	= 0.143	0.908
Finland	12.0	8.9	< 0.001	0.980
France	10.9	10.4	= 0.016	0.995
Greece <sup>(2013)</sup>	8.9	9.4	= 0.210	0.982

Hungary	9.5	9.4	= 0.860	0.980
Ireland	10.2	8.6	= 0.029	0.934
Israel	9.4	8.6	= 0.172	0.955
Italy <sup>(2012)</sup>	10.7	9.5	< 0.001	0.994
Japan	8.8	10.1	< 0.001	0.995
Latvia <sup>(2013)</sup>	9.9	9.1	= 0.413	0.932
Lithuania <sup>(2013)</sup>	9.3	8.9	= 0.556	0.959
Netherlands	9.0	8.5	= 0.063	0.986
New Zealand <sup>(2013)</sup>	13.1	10.7	= 0.018	0.925
Norway	10.8	8.7	< 0.001	0.961
Poland	9.7	8.8	< 0.001	0.995
Portugal	12.0	12.3	= 0.630	0.985
Russia	9.3	8.4	= 0.204	0.944
Slovakia	8.9	9.0	= 0.875	0.985
Slovenia	11.5	9.3	= 0.002	0.964
Spain	10.5	10.4	= 0.512	0.995
Sweden	11.8	9.6	= 0.001	0.956
Switzerland	12.2	10.4	= 0.009	0.965
Taiwan	11.2	11.9	= 0.037	0.992
Ukraine <sup>(2013)</sup>	8.3	7.9	= 0.506	0.967
United Kingdom <sup>(2013)</sup>	9.2	8.6	< 0.001	0.996
England and Wales <sup>(2013)</sup>	9.2	8.7	= 0.003	0.995
Northern Ireland <sup>(2013)</sup>	9.2	8.1	= 0.140	0.913
Scotland <sup>(2013)</sup>	9.5	8.1	= 0.002	0.971
USA	11.7	9.1	< 0.001	0.996

**Table S1.** Summary of MRDTs for men and women in 37 analyzed countries. Years listed in brackets (upper indices in the Country column) indicate the last year with mortality rates recorded in the Human Mortality Database. In case no number is included, mortality rates were last recorded in 2014.



**Figure S1.** Curves resulting from the logarithmic transformation of the Gompertz curve which represents the rate of mortality increase over time. The significant difference between the slopes of these lines is equivalent to the significant difference between MRDTs.