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Supplementary appendix

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Trends in all-cause mortality among people with diagnosed diabetes in high-income settings: a multicountry analysis of aggregate data

Appendix

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1 Quality score algorithm

We used a modified Newcastle-Ottawa Quality Assessment Scale.

The scale includes items that assess representativeness of the data sources, sample size at each time point, the method of defining diabetes, whether people with gestational diabetes were excluded, completeness of the number of data points reported and the assesment of the outcome (death). The maximum score was 9.

Selection

1. Representativeness of the general population (sampling frame).
   (a) National scheme with $\geq$ 80% coverage of national population (2 points)
   (b) Random sample from national health insurance or national population-based survey with $\geq$ 80% response rate (1 point)
   (c) Regional representative or national scheme with $<$ 80% coverage of national population (0 points)
2. Sample size at each time point.
   (a) $> 10,000$ (1 point)
   (b) $\leq 10,000$ (0 points)
3. Assessment of diabetes status.
   (a) By blood glucose measurement (FPG, OGTT, HbA_{1c}) or by multiple approaches/ administrative algorithm where 2 or more criteria used (2 points)
   (b) Clinical diagnosis (e.g. ICD code or physician-diagnosed) (1 point)
   (c) Anti-diabetic medication or self-report of physician-diagnosed diabetes (0 points)
4. Exclusion of gestational diabetes
   (a) Yes (1 point)
   (b) No (0 points)

Completeness of trend data

1. How many time points are provided?
   (a) ≥ 10 (2 points)
   (b) 6 – 9 (1 point)
   (c) < 6 (0 points)

Outcome

1. By record linkage e.g. national death registry (1 point)
2. Other – regular follow-up (0 points)

Thus the total possible score is 9.

1.1 Quality score assessment

A study can be awarded a maximum of one or two points for each numbered item within each category. w Selection

The table A1, summarizes the data quality from the different sources used in the study.

Table A1: *Quality assessment of the included data sources.*

Country, Region	Origin of data	Representativeness of population	Sample size at time points	Assessment of diabetes	Exclusion of gestational diabetes	Completeness (no. of data points)	Assessment of death	Total Score
Range of allocated points:		0–2	0–1	0–2	0–1	0–2	0–1	0–9
Australia	National Diabetes Services Scheme	2	1	1	1	2	1	8
Canada	Canadian Chronic Disease Surveillance System	2	1	2	1	2	1	9
Denmark	National administrative databases	2	1	2	1	2	1	9
Hong Kong	Hong Kong Hospital Authority	2	1	2	1	2	1	9
Hungary	National Institute of Health Insurance Fund Management database	2	1	0	1	1	1	6
Israel(CHS)	Clalit Health Services (Insurance)	0	1	2	1	2	1	7
Israel(MHS)	Maccabi Health Care (Insurance)	0	1	2	1	2	1	7
Italy, Lombardy	Administrative health databases in Lombardy	0	1	2	0	2	1	6

Table continues next page

Table A1: *Quality assessment of the included data sources (cont'd).*

Country, Region	Origin of data	Representativeness of population	Sample size at time points	Assessment of diabetes	Exclusion of gestational diabetes	Completeness (no. of data points)	Assessment of death	Total Score
Range of allocated points:		0–2	0–1	0–2	0–1	0–2	0–1	0–9
Latvia	National diabetes registry	2	1	1	1	2	1	8
Lithuania	National Health Insurance information system "SVEIDRA"	2	1	1	1	1	1	7
Norway	Norwegian Patient Registry, Primary Care Database and Norwegian Prescription Data Base	2	1	1	0	1	1	6
Scotland	Scottish Care Information-Diabetes (SCI-Diabetes) database	2	1	1	0	2	1	7
Singapore	National administrative data hold by the Ministry of Health of Singapore	2	1	1	0	0	1	5
Spain	Information System for the Development of Research in Primary Care [SIDIAP]	0	1	1	1	2	1	6

Table continues next page

Table A1: *Quality assessment of the included data sources (cont'd).*

Country, Region	Origin of data	Representativeness of population	Sample size at time points	Assessment of diabetes	Exclusion of gestational diabetes	Completeness (no. of data points)	Assessment of death	Total Score
Range of allocated points:		0–2	0–1	0–2	0–1	0–2	0–1	0–9
South Korea	National Health Insurance Service – National Sample cohort	1	1	0	0	2	1	5
Taiwan	National Health Insurance Research database	1	1	2	1	2	1	8
USA(KPNW)	Kaiser Permanente Northwest health care delivery system	0	1	2	1	2	1	7
USA(Medicare)	Medicare claims data for beneficiaries	2	1	2	1	2	1	9
USA(NHIS)	National Health Interview Survey	1	0	0	1	2	1	5

2 Statistical methods

Data were provided from each data source separately for persons with diabetes[1] and persons without diabetes as number of deaths and person-years classified by sex, single calendar year and 5-year age classes, < 20, 20–24, ..., 75–79, 80–84 and 85+; some data sources used 70+ as the upper age-class.

In the analysis, age was used as a quantitative variable, `A` with values 12, 22.5, 27.5, ...82.5, and 78 and 88 for the 70+ and 80+ age-classes. Likewise, calendar time was scored as a quantitative variable, `P` (period), with value 2010.5 for the calendar year 2010 etc., so in quantitative terms we refer to 1 January 2010 as 2010.0, 3 July 2010 as 2010.5 and 31 December 2010 as 2010.997. For each observational unit in data we thus have the mean age and date of follow up, and from this we defined the mean date of birth, `C` (cohort), as `P-A`.

2.1 Age-period-cohort modeling of mortality rates

We fitted age-period-cohort models (APC models) for the log-mortality rates (a and p refer to the variables `A` and `P` defined above):

$$\log\big(\lambda(a,p)\big) = f(a) + g(p) + h(p-a)$$

where the three effects were modeled with natural splines with 6 knots for age, one knot per 4 years of period and 4 knots for cohort.

It is well-known that there is no way to identify the three separate effects, but we are only using the *predicted* rates from the model at pre-specified ages and dates. And these are well-defined, independent of the chosen parametrization [1].

For each data source, sex and ages 20, 21, ...90 we computed the predicted mortality rates at select dates (period), using dates 4 years apart across the range of data for the data source. These were plotted as functions of age, one for each chosen date. Confidence intervals were computed as Wald-confidence intervals (back transformed from log-rates ± 1.96 s.e.).

Also for each data source, sex and ages 40, 50, 60, 70 and 80 we computed the predicted mortality rates for a tightly spaced set of dates across the period of observation for the data source, that is 5 curves for each sex (with the exception of USA(Medicare), where we only used ages 70 and 80). These were plotted as functions of period, one for each of the 5 ages.

The curves were all plotted with shaded areas as confidence intervals; these are however so narrow for most data sources that they do not show up in the plots.

These plots shows how mortality rates in persons with diabetes depend on age and calendar time (period), and are shown in figures A9–A27 as reference.

2.1.1 Average mortality trends

For calculation of the time trends in mortality rates we fitted a model with a smooth age effect and a linear trend in calendar time:

$$\log\big(\lambda(a,p)\big) = f(a) + \beta p$$

[1] "Diabetes" covers either all diabetes or only type 2 diabetes, for details, see the main paper and table on page 6 below.

The trend in mortality rates is defined as $\exp(\beta)$ or in percentage terms, $(\exp(\beta) - 1) \times 100$. This was done separately for men and women, but also jointly for men and women with common trends for men and women and an interaction between sex and age, allowing for different age-specific mortality between men and women.

Time by age interaction We also investigated whether annual trends in mortality depended on age by amending the model with the product `age` × `per` in the model and graphing the estimated annual trend as function of age. Formal test of the model with the interaction term versus the model without (the average trend model) was done too.

2.1.2 Direct standardization

We computed the age-distribution of person-years among persons with diabetes (except for USA(Medicare) and USA(NHIS)) and used these as weights in direct standardization on the log mortality scale.

Specifically, we used the age-period-cohort model to provide estimates (and the corresponding variance-covariance matrix) of the log-mortality rates for ages in 1-year classes at the midpoint of each year. We then computed directly standardized rates as the weighted average of these age-specific log-mortality rates using the standard population distribution as weights. The calculation was done as a matrix multiplication of the log-rates, which allows a parallel calculation of the variance of the weighted average. These were then exponentiated to the standardized rates with confidence intervals.

These calculations were done separately for men and women, as well as across men and women using equal weights for men and women.

Thus, the standardized rates are based on estimates from age-period-cohort models, a smoothed version of the observed rates, as can be seen from comparing figures A1 and A2. The data source-specific standardized rates as functions of time are in figure A5.

2.2 Standardized Mortality Ratio (SMR)

We computed the SMR as the mortality rate-ratio between persons with diabetes and persons without diabetes, specifically:

Mortality in non-diabetes represent the death in people without diabetes (type 1, type 2 and other kinds of diabetes)	Australia, Canada, Hong Kong, Israel(CHS), Italy, Lithuania, Singapore, South Korea, USA(Medicare), USA(NHIS)
Mortality in non-diabetes represent the death in people without type 2 or type 1 diabetes	Denmark, Israel(MHS), Latvia, Scotland, Spain, USA(KPNW)
Mortality in non-diabetes represent the death in people without type 2 diabetes	Hungary, Norway, Taiwan

The dataset used for mortality calculations among persons with diabetes (deaths, person-years, sex, age, date) was combined (head-to-foot) with the corresponding dataset for persons without diabetes, defining a diabetes status variable indicating if a record was diabetes or non-diabetes. For the combined dataset we used a model with age, period and cohort effects, each with an interaction with the diabetes / non-diabetes variable. This corresponds to an age-period-cohort model for the SMR.

If we by $d = (\text{diabetes}, \text{no diabetes})$ denote the diabetes status variable the model is:

$$\log\big(\lambda(a,p,d)\big) = f_d(a) + g_d(p) + h_d(p-a)$$

and the SMR is defined as the ratio of estimated rates between diabetes and no diabetes. These were computed for select values of age and period as outlined for the mortality rates above.

For calculation of the time trends in SMR we fitted a model with different age effects between persons with and without diabetes, but with common period and cohort effects, and a linear trend interaction with diabetes status:

$$\log\big(\lambda(a,p,d)\big) = f_d(a) + g(p) + h(p-a) + \beta_d p$$

The trend in SMR is defined as $\exp(\beta_{\text{diabetes}} - \beta_{\text{no diabetes}})$. This was done separately for men and women, and also jointly for men and women with common trends for men and women and an interaction between sex and diabetes status.

2.3 Documentation of analyses

All analysis code underlying the results in the paper and the Appendix are available in the document http://bendixcarstensen.com/IDI/global/globDM-m.pdf.

References

[1] B Carstensen. Age-Period-Cohort models for the Lexis diagram. *Statistics in Medicine*, 26(15):3018–3045, July 2007.

3 Statistical tables

Table A2: *Deaths person-years and crude rates (per 1000 PY) by source and diabetes status.*

	Diabetes			No diabetes		
Country	Deaths	PY(1000)	Rate	Deaths	PY(1000)	Rate
Australia	292,628	10,222	28.6	1,680,285	291,239	5.8
Canada	789,710	27,111	29.1	1,894,650	376,288	5.0
Denmark	158,749	3,517	45.1	983,071	111,005	8.9
Hong Kong	171,749	5,375	32.0	410,828	92,973	4.4
Hungary	246,429	5,906	41.7	784,416	73,425	10.7
Israel(CHS)	172,182	4,252	40.5	194,246	51,296	3.8
Israel(MHS)	26,033	1,160	22.4	56,510	25,801	2.2
Italy	182,439	3,962	46.0	732,107	97,952	7.5
Latvia	47,446	986	48.1	474,715	35,624	13.3
Lithuania	58,625	1,274	46.0	532,538	42,484	12.5
Norway	39,452	1,116	35.4	211,902	29,971	7.1
Scotland	95,285	2,393	39.8	556,932	60,120	9.3
Singapore	37,959	1,436	26.4	52,856	18,007	2.9
South Korea	10,431	414	25.2	31,864	7,290	4.4
Spain	114,294	3,265	35.0	315,788	53,326	5.9
Taiwan	17,630	656	26.9	31,163	8,845	3.5
USA(KPNW)	18,011	589	30.6	49,977	9,480	5.3
USA(Medicare)	6,979,017	83,231	83.9	13,131,982	229,648	57.2
USA(NHIS)	11,463,555	325,319	35.2	38,728,508	4,021,753	9.6

Table A3: *Deaths, person-years and crude rates (per 1000 PY) by source and diabetes status, men only*

	Diabetes			No diabetes		
Country	Deaths	PY(1000)	Rate	Deaths	PY(1000)	Rate
Australia	165,251	5,376	30.7	845,643	144,998	5.8
Canada	425,480	14,249	29.9	933,100	185,503	5.0
Denmark	85,673	1,879	45.6	477,110	54,843	8.7
Hong Kong	89,973	2,613	34.4	235,002	43,672	5.4
Hungary	117,273	2,677	43.8	391,575	35,075	11.2
Israel(CHS)	83,540	2,087	40.0	94,832	25,015	3.8
Israel(MHS)	13,724	623	22.0	29,125	12,494	2.3
Italy	94,880	2,094	45.3	343,160	47,369	7.2
Latvia	16,778	322	52.1	238,975	16,468	14.5
Lithuania	24,402	488	50.0	280,868	19,755	14.2
Norway	21,211	612	34.7	100,786	15,027	6.7
Scotland	49,893	1,314	38.0	261,742	28,910	9.1
Singapore	19,664	723	27.2	29,399	8,829	3.3
South Korea	5,764	220	26.2	17,331	3,621	4.8
Spain	60,314	1,744	34.6	159,001	26,235	6.1
Taiwan	9,913	326	30.4	20,098	4,510	4.5
USA(KPNW)	9,662	301	32.1	24,203	4,592	5.3
USA(Medicare)	3,140,100	36,763	85.4	5,497,535	92,005	59.8
USA(NHIS)	6,014,992	159,606	37.7	20,103,968	1,925,084	10.4

Table A4: *Deaths, person-years and crude rates (per 1000 PY) by source and diabetes status, women only*

	Diabetes			No diabetes		
Country	Deaths	PY(1000)	Rate	Deaths	PY(1000)	Rate
Australia	127,377	4,846	26.3	834,642	146,241	5.7
Canada	364,230	12,861	28.3	961,550	190,785	5.0
Denmark	73,076	1,638	44.6	505,961	56,162	9.0
Hong Kong	81,776	2,762	29.6	175,826	49,301	3.6
Hungary	129,156	3,230	40.0	392,841	38,350	10.2
Israel(CHS)	88,642	2,165	40.9	99,414	26,281	3.8
Israel(MHS)	12,309	537	22.9	27,385	13,307	2.1
Italy	87,559	1,868	46.9	388,947	50,582	7.7
Latvia	30,668	664	46.2	235,740	19,157	12.3
Lithuania	34,223	786	43.5	251,670	22,729	11.1
Norway	18,241	504	36.2	111,116	14,944	7.4
Scotland	45,392	1,079	42.1	295,190	31,210	9.5
Singapore	18,295	714	25.6	23,457	9,178	2.6
South Korea	4,667	194	24.0	14,533	3,668	4.0
Spain	53,980	1,521	35.5	156,787	27,091	5.8
Taiwan	7,717	330	23.4	11,065	4,335	2.6
USA(KPNW)	8,349	288	29.0	25,774	4,887	5.3
USA(Medicare)	3,838,917	46,468	82.6	7,634,447	137,643	55.5
USA(NHIS)	5,448,563	165,713	32.9	18,624,540	2,096,669	8.9

Table A5: *Standardized rates (per 1000 PY) of mortality among persons with diabetes by data source 1995–2002, using the diabetes population age-distribution as standard. Note the overlap with the next table.*

	Calendar year							
	1995	1996	1997	1998	1999	2000	2001	2002
Australia								19.3
Canada						23.4	22.6	21.8
Denmark		41.4	39.7	38.0	36.4	34.8	33.4	31.9
Hong Kong								
Hungary								
Israel(CHS)								
Israel(MHS)							18.6	18.0
Italy								27.0
Latvia						42.1	41.5	40.8
Lithuania								
Norway								
Scotland								
Singapore								
South Korea								
Spain								
Taiwan								24.5
USA(KPNW)	27.5	27.2	27.0	26.7	26.4	26.2	26.0	25.8
USA(Medicare)							28.4	28.2
USA(NHIS)	31.9	31.8	31.8	31.7	31.6	31.3	30.8	29.7

Table A6: *Standardized rates (per 1000 PY) of mortality among persons with diabetes by data source 2001–2009, using the diabetes population age-distribution as standard. Note the overlap with the previous and next tables.*

	Calendar year								
	2001	2002	2003	2004	2005	2006	2007	2008	2009
Australia		19.3	18.7	18.2	17.6	17.1	16.6	16.2	15.8
Canada	22.6	21.8	21.0	20.3	19.6	18.9	18.2	17.6	17.0
Denmark	33.4	31.9	30.6	29.3	28.0	26.9	25.8	24.8	23.9
Hong Kong			26.3	24.5	22.8	21.2	19.8	18.5	17.5
Hungary									28.0
Israel(CHS)				31.4	29.8	28.3	26.8	25.5	24.4
Israel(MHS)	18.6	18.0	17.5	16.9	16.3	15.8	15.3	14.8	14.4
Italy		27.0	26.3	25.5	24.8	24.2	23.6	23.1	22.8
Latvia	41.5	40.8	40.1	39.3	38.5	37.6	36.4	35.0	33.4
Lithuania			41.6	40.1	38.7	37.3	36.0	34.9	34.1
Norway									18.2
Scotland				25.5	24.7	24.0	23.2	22.6	22.0
Singapore									
South Korea								22.6	21.6
Spain							14.2	13.9	13.7
Taiwan		24.5	23.7	22.9	22.1	21.3	20.5	19.6	18.7
USA(KPNW)	26.0	25.8	25.6	25.5	25.1	24.5	23.5	22.4	21.2
USA(Medicare)	28.4	28.2	28.1	28.0	27.7	27.4	26.8	26.1	25.4
USA(NHIS)	30.8	29.7	28.3	26.6	24.9	23.5	22.4	21.7	21.2

Table A7: *Standardized rates (per 1000 PY) of mortality among persons with diabetes by data source 2008–2016, using the diabetes population age-distribution as standard. Note the overlap with the previous table.*

	Calendar year								
	2008	2009	2010	2011	2012	2013	2014	2015	2016
Australia	16.2	15.8	15.5	15.3	15.1	15.0	15.0	15.0	
Canada	17.6	17.0	16.5	16.1	15.8	15.7	15.6	15.4	
Denmark	24.8	23.9	23.1	22.5	22.1	21.8	21.6	21.6	21.5
Hong Kong	18.5	17.5	16.7	16.1	15.6	15.1	14.6	14.2	13.7
Hungary		28.0	27.9	27.9	27.8	27.8	27.8	27.8	27.8
Israel(CHS)	25.5	24.4	23.4	22.7	22.3	22.0	21.9	21.9	21.8
Israel(MHS)	14.8	14.4	14.0	13.7	13.5	13.4	13.4	13.4	
Italy	23.1	22.8	22.5	22.3	22.0				
Latvia	35.0	33.4	31.7	30.1	28.9	28.1	27.6	27.2	26.8
Lithuania	34.9	34.1	33.5	33.2	32.9	32.6	32.3	31.9	31.5
Norway		18.2	18.0	17.7	17.5	17.2	17.0		
Scotland	22.6	22.0	21.6	21.3	21.2	21.1	21.1	21.0	
Singapore					20.1	19.2	18.4	17.6	16.8
South Korea	22.6	21.6	20.6	19.6	18.6	17.7	16.8	16.0	
Spain	13.9	13.7	13.4	13.3	13.3	13.7	14.2	14.9	15.6
Taiwan	19.6	18.7	17.9	17.1					
USA(KPNW)	22.4	21.2	20.0	19.1	18.4	18.0	18.0	18.3	18.6
USA(Medicare)	26.1	25.4	24.9	24.5	24.4	24.3	24.3	24.3	
USA(NHIS)	21.7	21.2	20.8	20.5	20.2	19.9	19.7	19.5	

Table A8: *Overall trends in mortality and SMR in % per year; men & women together. These are estimates from a main effects model with age (as spline) and (linear) calendar time. A graphical representation of estimates from the extension with age by calendar time interaction can be found in figures A47 and A48.*

	Mortality						SMR		
	No diabetes			Diabetes					
	Trend	95% c.i.		Trend	95% c.i.		Trend	95% c.i.	
Australia	−1.8	−1.8	−1.7	−2.0	−2.1	−1.9	−0.1	−0.2	0.0
Canada	−1.9	−2.0	−1.9	−2.9	−3.0	−2.9	−0.9	−1.0	−0.9
Denmark	−2.2	−2.2	−2.1	−3.2	−3.3	−3.1	−1.0	−1.0	−0.9
Hong Kong	−2.2	−2.3	−2.1	−4.2	−4.3	−4.1	−2.0	−2.1	−1.8
Hungary	−1.7	−1.8	−1.6	−0.5	−0.7	−0.3	1.2	1.0	1.4
Israel(CHS)	−3.7	−3.8	−3.6	−3.0	−3.1	−2.8	0.9	0.7	1.0
Israel(MHS)	−3.5	−3.7	−3.3	−2.2	−2.5	−1.9	1.4	1.0	1.8
Italy	−2.7	−2.8	−2.6	−1.2	−1.3	−1.0	1.6	1.4	1.7
Latvia	−2.2	−2.3	−2.2	−3.0	−3.2	−2.8	−0.7	−0.9	−0.5
Lithuania	−2.0	−2.0	−1.9	−1.7	−1.9	−1.5	0.2	−0.0	0.4
Norway	−1.9	−2.1	−1.6	−0.6	−1.2	0.0	1.3	0.7	2.0
Scotland	−2.0	−2.0	−1.9	−1.5	−1.7	−1.3	0.5	0.3	0.7
Singapore	−2.6	−3.1	−2.0	−3.6	−4.2	−2.9	−1.2	−2.1	−0.3
South Korea	−3.8	−4.3	−3.4	−4.0	−4.8	−3.2	0.0	−0.9	1.0
Spain	1.9	1.8	2.0	1.1	0.9	1.3	−0.9	−1.2	−0.7
Taiwan	−2.9	−3.2	−2.5	−3.5	−4.0	−3.0	−0.4	−1.0	0.3
USA(KPNW)	−1.5	−1.7	−1.4	−2.3	−2.5	−2.0	−0.3	−0.6	−0.0
USA(Medicare)	1.3	1.3	1.3	−1.5	−1.6	−1.5	−3.0	−3.0	−2.9
USA(NHIS)	−1.2	−1.2	−1.2	−2.8	−2.8	−2.8	−1.3	−1.4	−1.3

Note that 0.0 means between 0 and 0.05, while −0.0 means between 0 and −0.05.

Table A9: *Overall trends in mortality and SMR in % per year for men.*

	Mortality								
	No diabetes			Diabetes			SMR		
	Trend	95% c.i.		Trend	95% c.i.		Trend	95% c.i.	
Australia	−2.2	−2.2	−2.1	−2.2	−2.4	−2.1	0.1	−0.0	0.2
Canada	−2.3	−2.4	−2.3	−3.1	−3.2	−3.1	−0.7	−0.8	−0.6
Denmark	−2.6	−2.6	−2.5	−3.5	−3.6	−3.3	−0.8	−0.9	−0.7
Hong Kong	−2.2	−2.3	−2.1	−4.2	−4.3	−4.0	−2.0	−2.2	−1.8
Hungary	−2.3	−2.5	−2.2	−0.6	−0.8	−0.3	1.7	1.4	2.0
Israel(CHS)	−3.7	−3.8	−3.5	−2.8	−3.0	−2.6	1.0	0.7	1.2
Israel(MHS)	−3.6	−3.9	−3.4	−2.1	−2.5	−1.7	1.5	1.0	2.0
Italy	−3.4	−3.5	−3.3	−1.9	−2.1	−1.7	1.6	1.4	1.8
Latvia	−2.2	−2.3	−2.1	−2.9	−3.2	−2.6	−0.8	−1.2	−0.5
Lithuania	−1.9	−2.0	−1.8	−1.6	−1.9	−1.3	0.1	−0.2	0.5
Norway	−2.5	−2.8	−2.1	−1.2	−2.0	−0.4	1.3	0.4	2.2
Scotland	−2.4	−2.5	−2.3	−1.9	−2.1	−1.6	0.5	0.3	0.8
Singapore	−2.5	−3.3	−1.7	−3.3	−4.3	−2.4	−1.0	−2.3	0.3
South Korea	−4.0	−4.6	−3.4	−3.9	−5.0	−2.8	0.2	−1.1	1.5
Spain	1.7	1.5	1.9	1.1	0.8	1.4	−0.7	−1.0	−0.4
Taiwan	−2.4	−2.9	−2.0	−3.2	−3.9	−2.5	−0.5	−1.4	0.4
USA(KPNW)	−2.0	−2.2	−1.8	−2.4	−2.7	−2.0	0.2	−0.2	0.6
USA(Medicare)	0.8	0.8	0.9	−2.1	−2.1	−2.0	−3.1	−3.1	−3.0
USA(NHIS)	−1.5	−1.5	−1.5	−2.9	−2.9	−2.8	−1.1	−1.2	−1.1

Note that 0.0 means between 0 and 0.05, while −0.0 means between 0 and −0.05.

Table A10: *Overall trends in mortality and SMR in % per year for women.*

	Mortality								
	No diabetes			Diabetes			SMR		
	Trend	95% c.i.		Trend	95% c.i.		Trend	95% c.i.	
Australia	−1.4	−1.4	−1.3	−1.7	−1.9	−1.6	−0.2	−0.4	−0.1
Canada	−1.6	−1.6	−1.5	−2.7	−2.8	−2.6	−1.1	−1.2	−1.1
Denmark	−1.8	−1.9	−1.8	−2.9	−3.0	−2.8	−1.1	−1.2	−1.0
Hong Kong	−2.2	−2.3	−2.1	−4.2	−4.4	−4.1	−1.8	−2.0	−1.6
Hungary	−1.1	−1.2	−0.9	−0.4	−0.7	−0.2	0.8	0.5	1.1
Israel(CHS)	−3.7	−3.9	−3.6	−3.1	−3.3	−2.9	0.8	0.5	1.0
Israel(MHS)	−3.3	−3.6	−3.0	−2.3	−2.8	−1.9	1.2	0.7	1.7
Italy	−2.1	−2.2	−2.0	−0.4	−0.6	−0.2	1.7	1.4	1.9
Latvia	−2.3	−2.4	−2.2	−3.1	−3.4	−2.9	−0.6	−0.9	−0.3
Lithuania	−2.0	−2.1	−1.9	−1.8	−2.1	−1.6	0.3	−0.0	0.6
Norway	−1.4	−1.7	−1.0	0.2	−0.7	1.0	1.5	0.5	2.4
Scotland	−1.6	−1.7	−1.5	−1.1	−1.4	−0.9	0.5	0.2	0.8
Singapore	−2.6	−3.5	−1.7	−3.8	−4.8	−2.8	−1.4	−2.8	−0.0
South Korea	−3.6	−4.3	−2.9	−4.1	−5.3	−2.8	−0.0	−1.5	1.5
Spain	2.1	2.0	2.3	1.1	0.8	1.4	−1.1	−1.5	−0.8
Taiwan	−3.7	−4.3	−3.0	−4.0	−4.7	−3.2	−0.1	−1.1	1.0
USA(KPNW)	−1.0	−1.2	−0.9	−2.2	−2.5	−1.8	−0.8	−1.2	−0.4
USA(Medicare)	1.6	1.6	1.6	−1.1	−1.1	−1.1	−2.9	−2.9	−2.8
USA(NHIS)	−0.9	−1.0	−0.9	−2.7	−2.7	−2.7	−1.6	−1.6	−1.6

Note that 0.0 means between 0 and 0.05, while −0.0 means between 0 and −0.05.

4 Figures

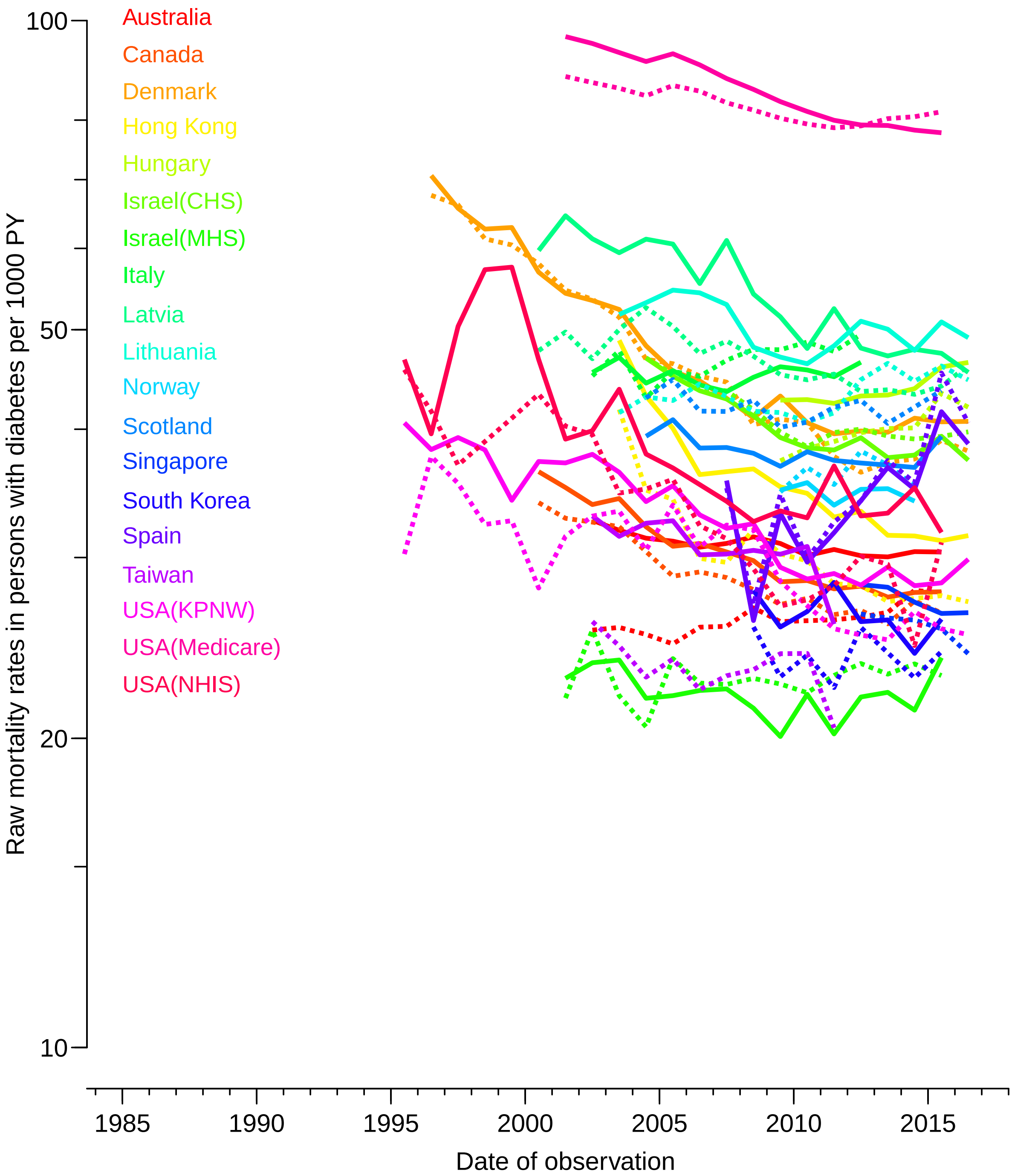

Figure A1: *Raw mortality in persons with diabetes by data source and sex. Men in full lines, women in broken lines.*

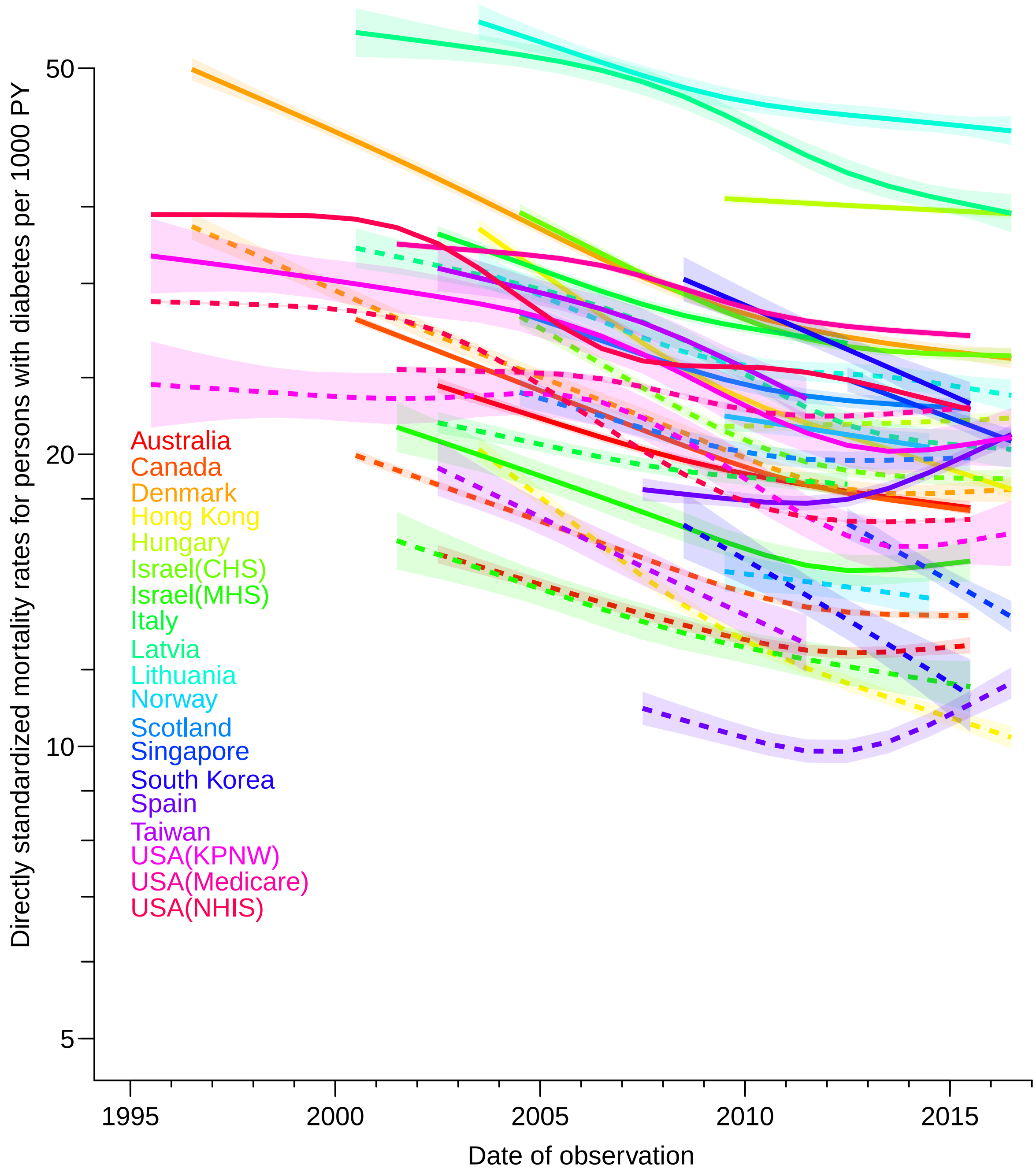

Figure A2: *Age-standardized mortality rates using the total risk time across all studies as standard, separately for men and women. Smoothing is based on separate age-period-cohort models for men and women. Men are shown in full lines, women in broken lines.*

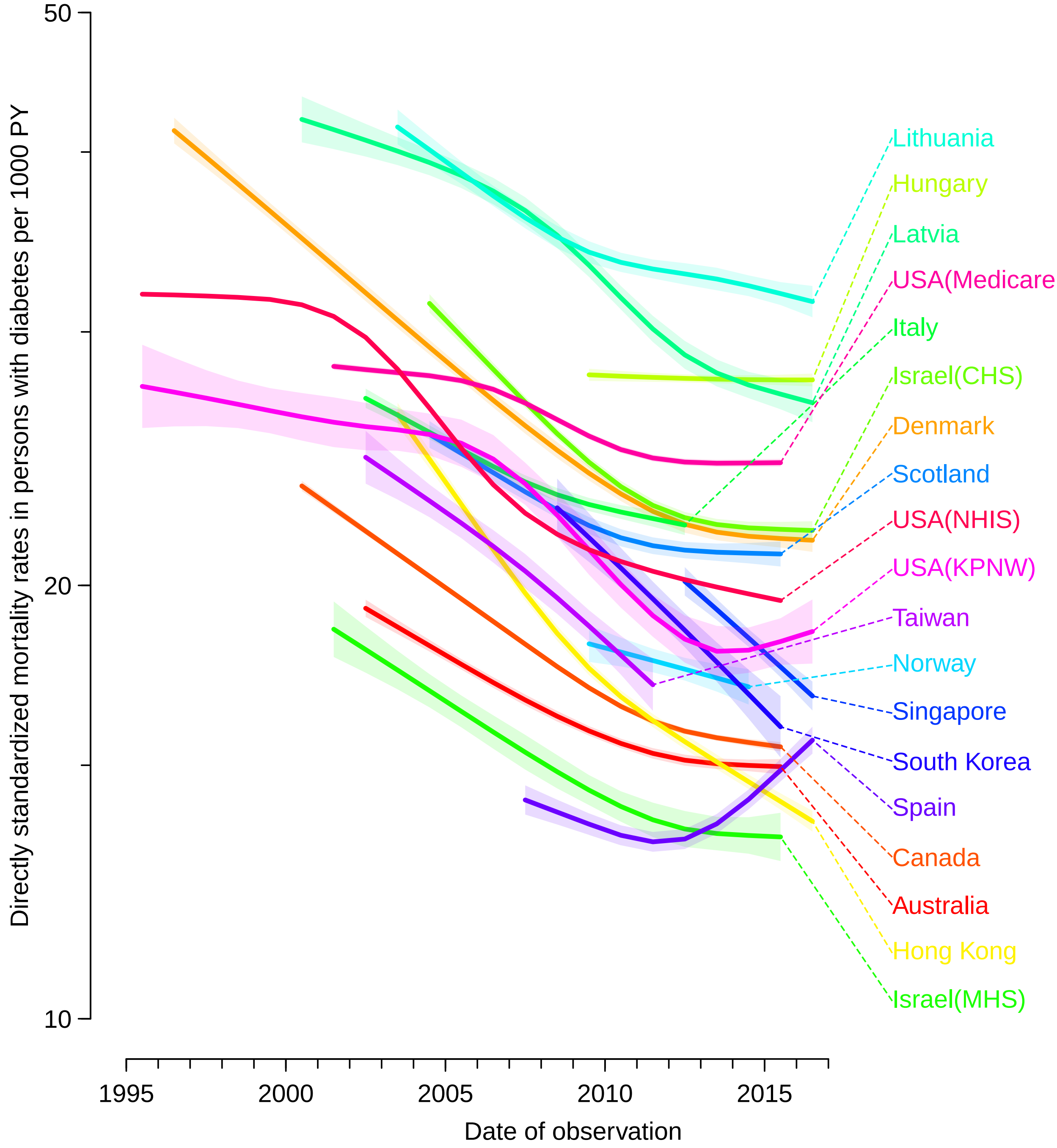

Figure A3: *Age- and sex-standardized mortality rates using the total risk time across all studies as standard with equal weights for men and women. Smoothing is based on separate age-period-cohort models for men and women.*

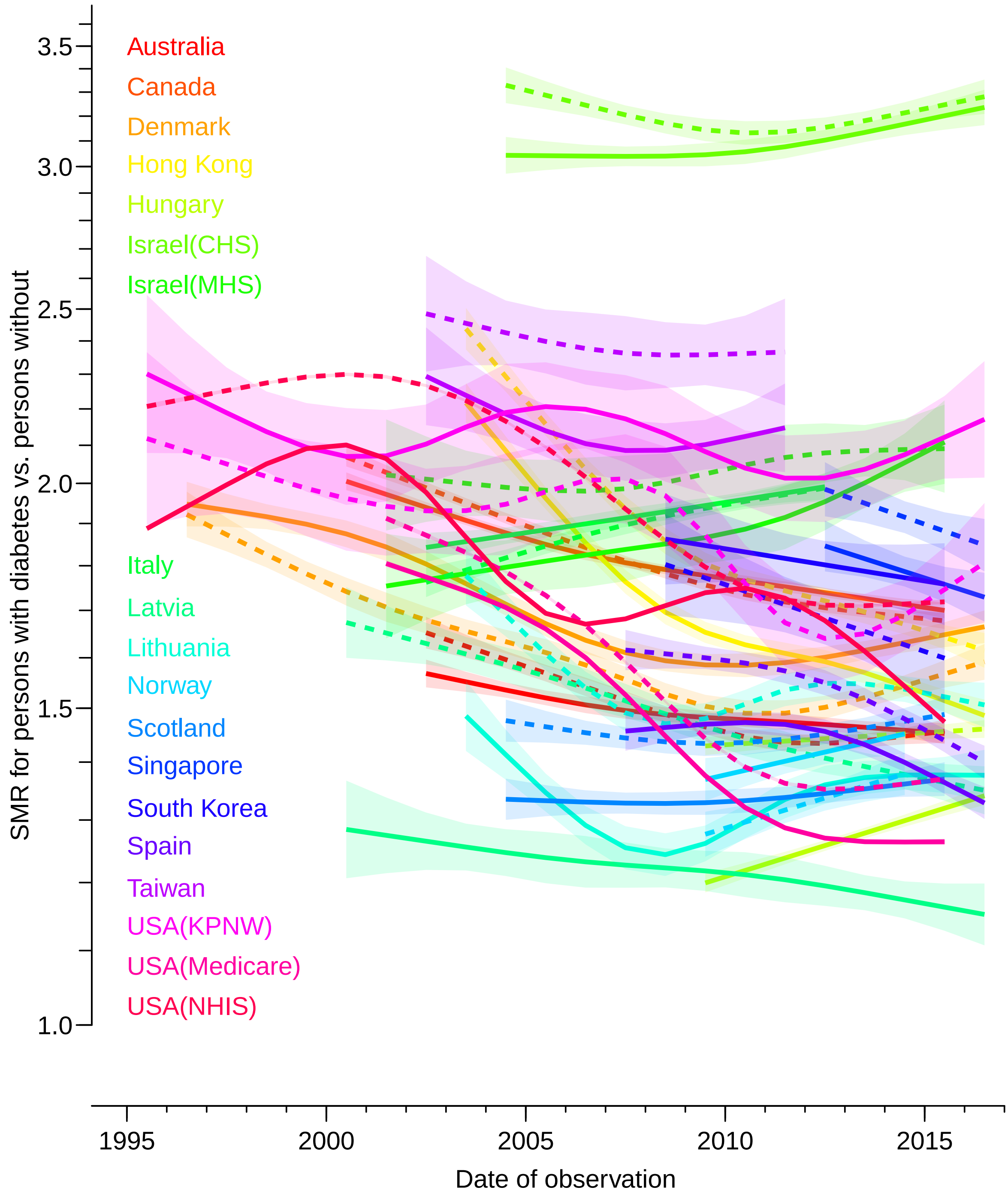

Figure A4: *SMR for persons with diabetes versus persons without. Smoothing is based on a model with SMR constant over age.*

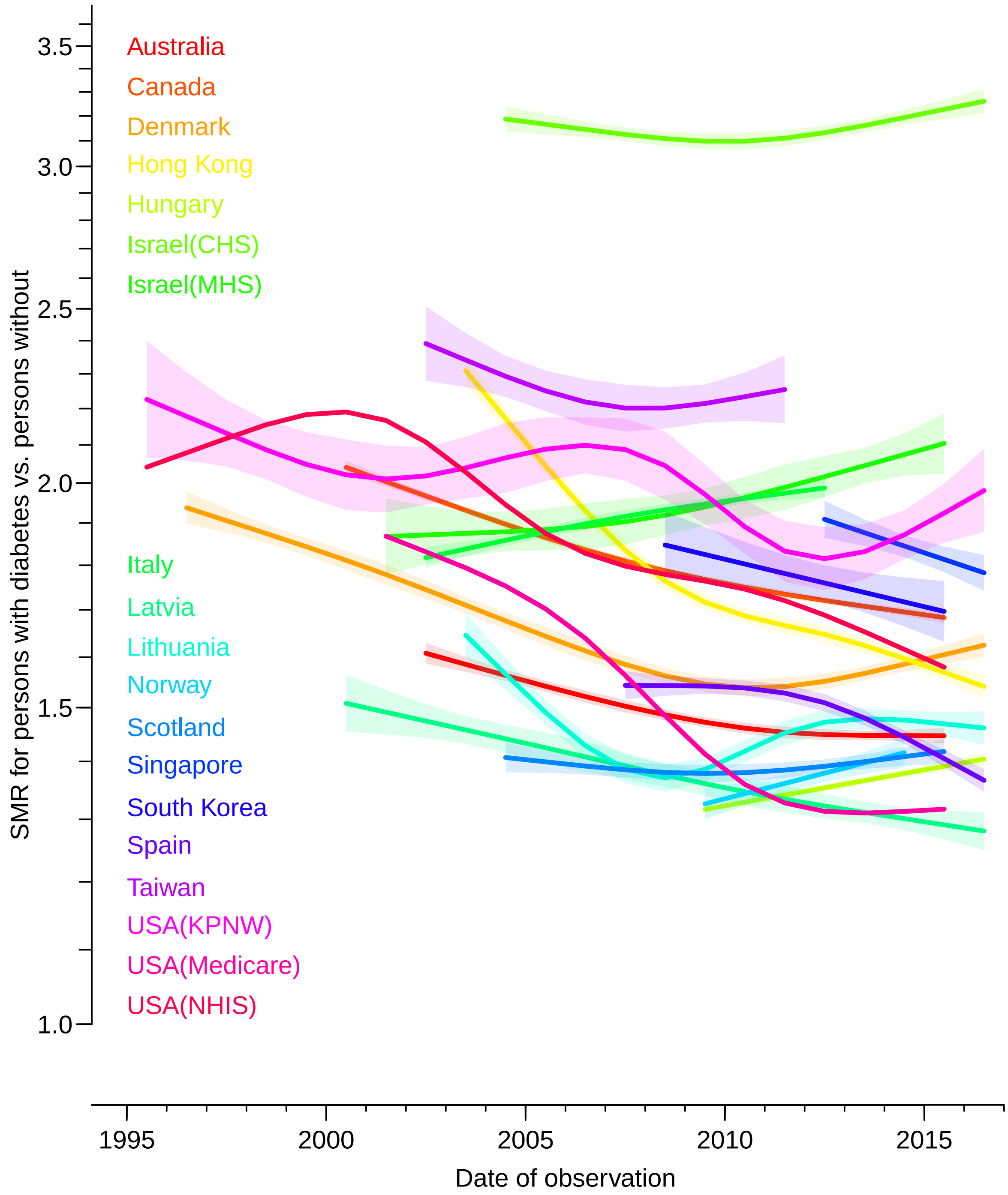

Figure A5: *SMR for persons with diabetes versus persons without. Smoothing is based on a model with SMR constant over age and sex.*

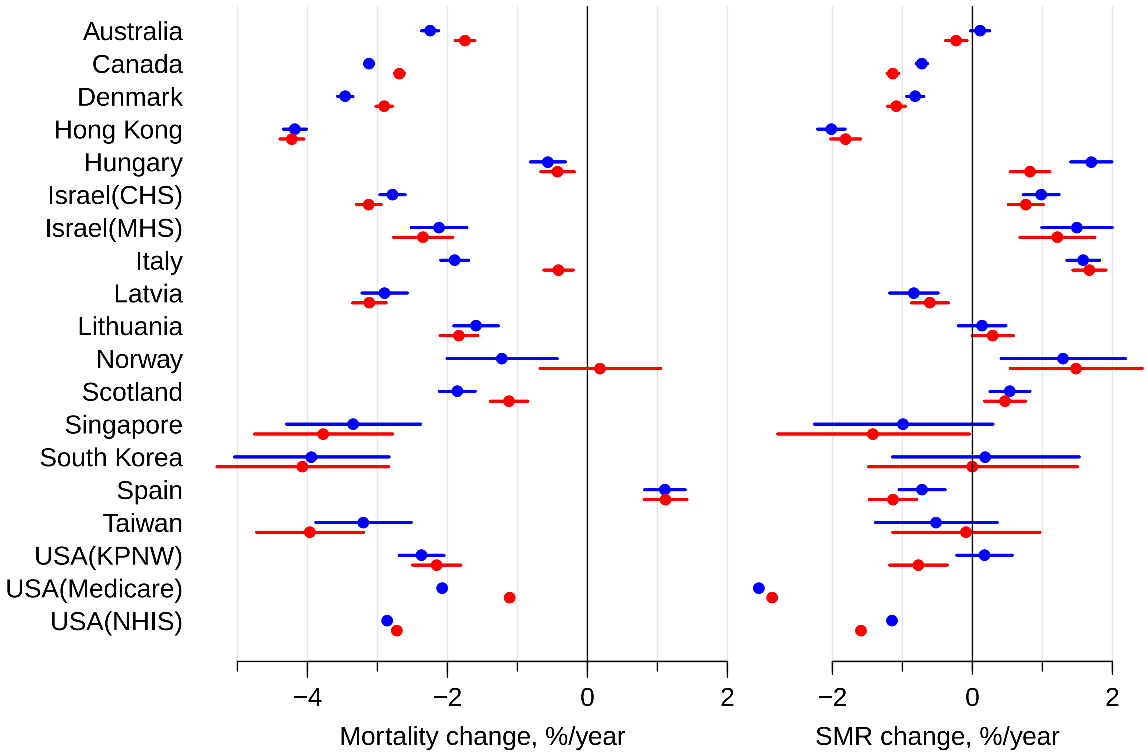

Figure A6: *Time-trends in mortality and SMR by country, estimates and 95% confidence intervals. Men in blue; women in red.*

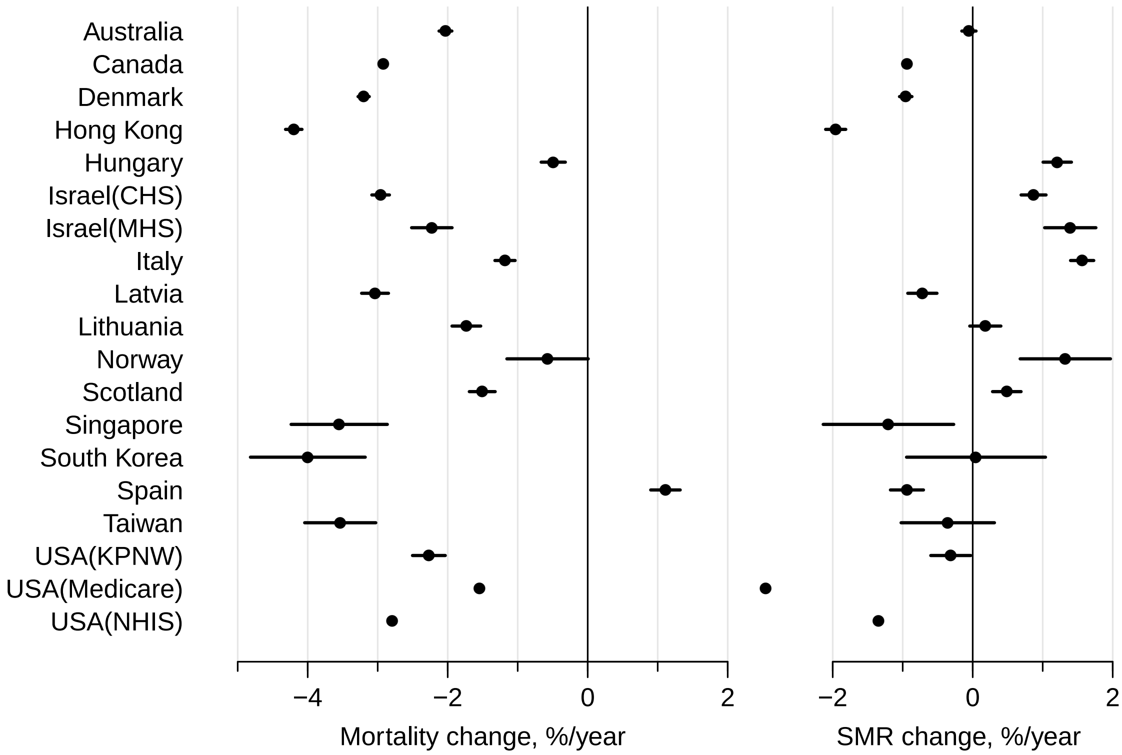

Figure A7: *Time-trends in mortality and SMR by country for men and women together. Estimates of mortality trends are from a model with separate smooth effects of age for each sex and a common linear trend by calendar time. Estimates of trends in SMR are from a model with smooth effects of age, period and cohort and separate smooth age interaction with diabetes status (Y/N) and a linear interaction between period and diabetes status.*

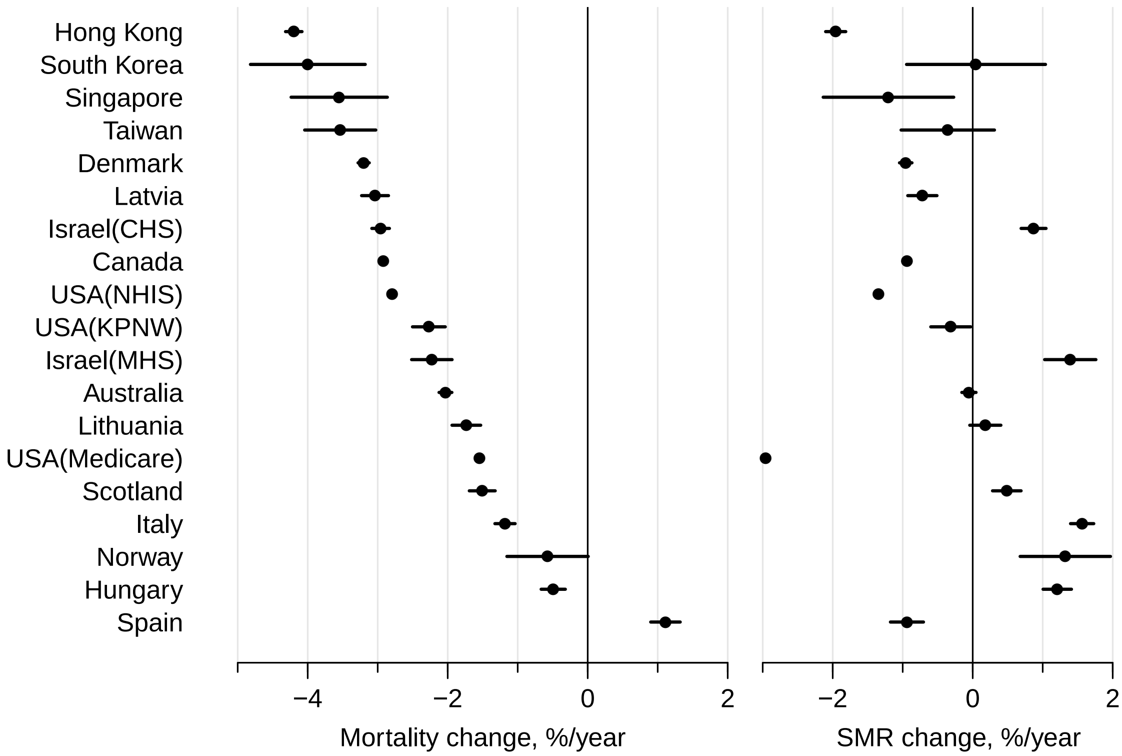

Figure A8: *Time-trends in mortality and SMR by country for men and women together, ordered by mortality trend. Estimates of mortality trends are from a model with separate smooth effects of age for each sex and a common linear trend by calendar time. Estimates of trends in SMR are from a model with smooth effects of age, period and cohort and separate smooth age interaction with diabetes status (Y/N) and a linear interaction between period and diabetes status.*

4.1 Mortality by age and period

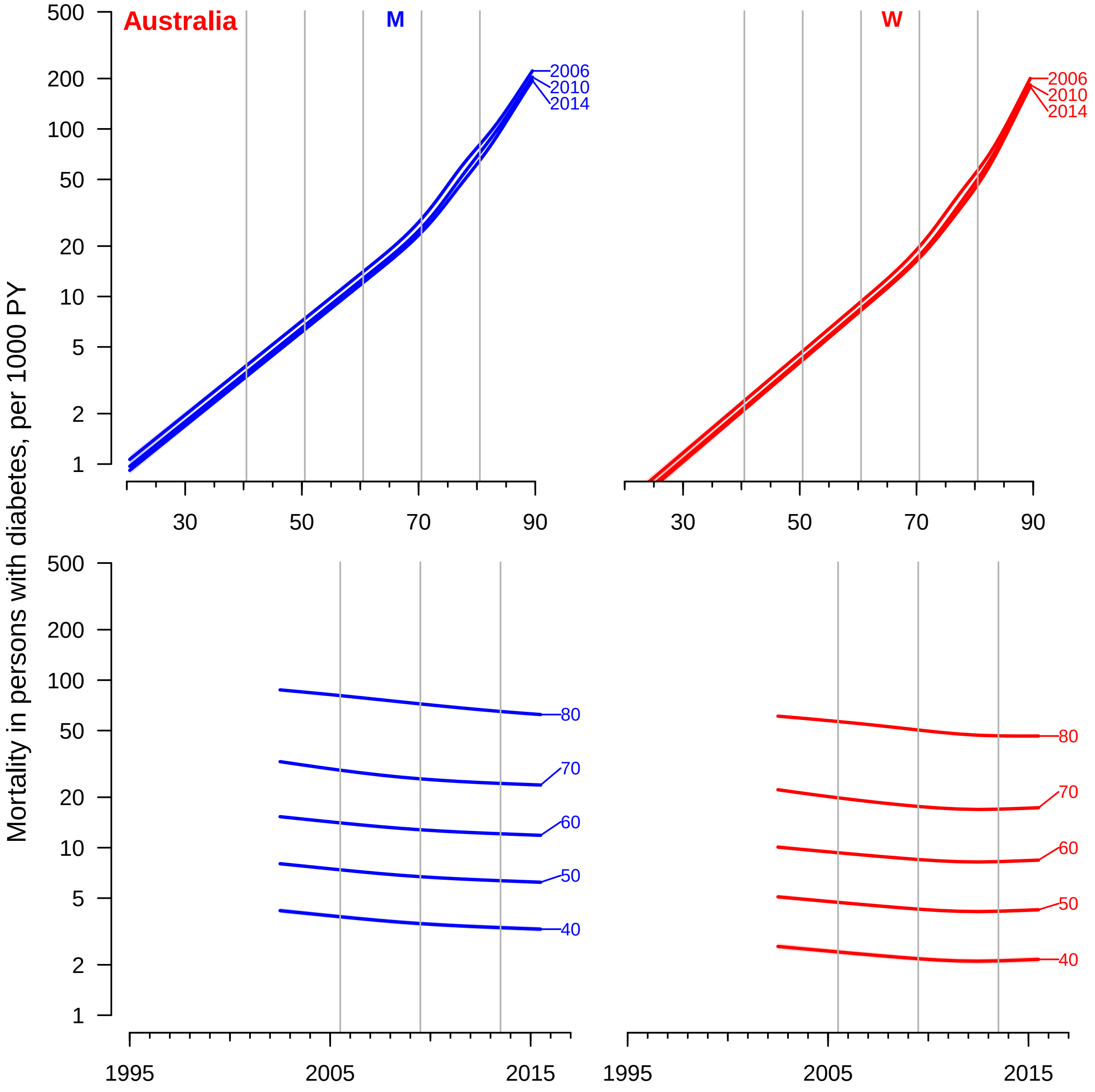

Figure A9: *Estimated mortality rates of diabetes by age and period in Australia. Estimates of mortality rates are from age-period-cohort models, fitted separately for men and women. Upper panels show age-specific rates at different dates, as indicated by vertical lines in the lower panels. Lower panels show period-specific rates at different ages, as indicated by vertical lines in the upper panels. Left panels (blue curves) are men, right panels (red curves) are women.*

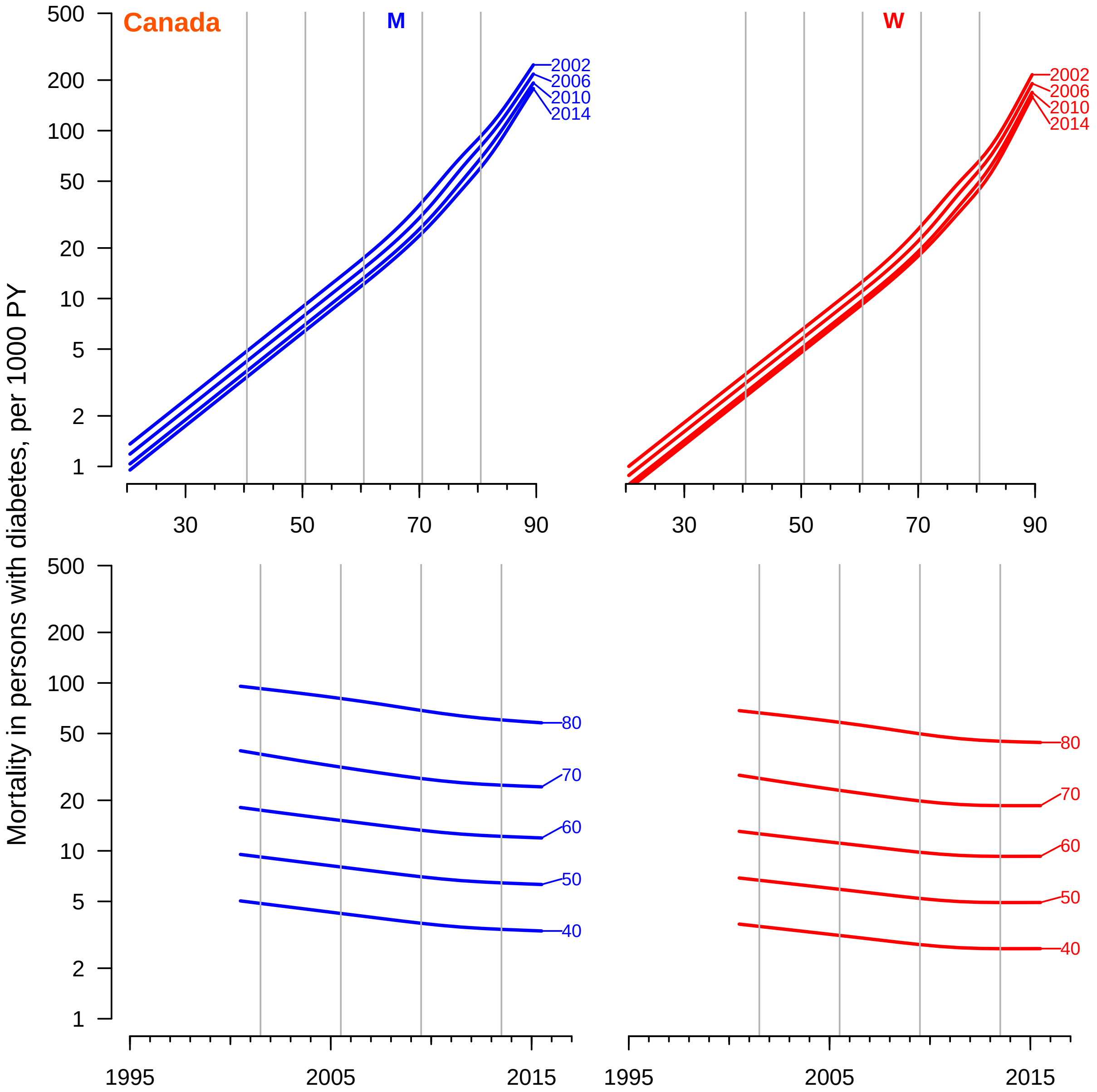

Figure A10: *Estimated mortality rates of diabetes by age and period in Canada. Estimates of mortality rates are from age-period-cohort models, fitted separately for men and women. Upper panels show age-specific rates at different dates, as indicated by vertical lines in the lower panels. Lower panels show period-specific rates at different ages, as indicated by vertical lines in the upper panels. Left panels (blue curves) are men, right panels (red curves) are women.*

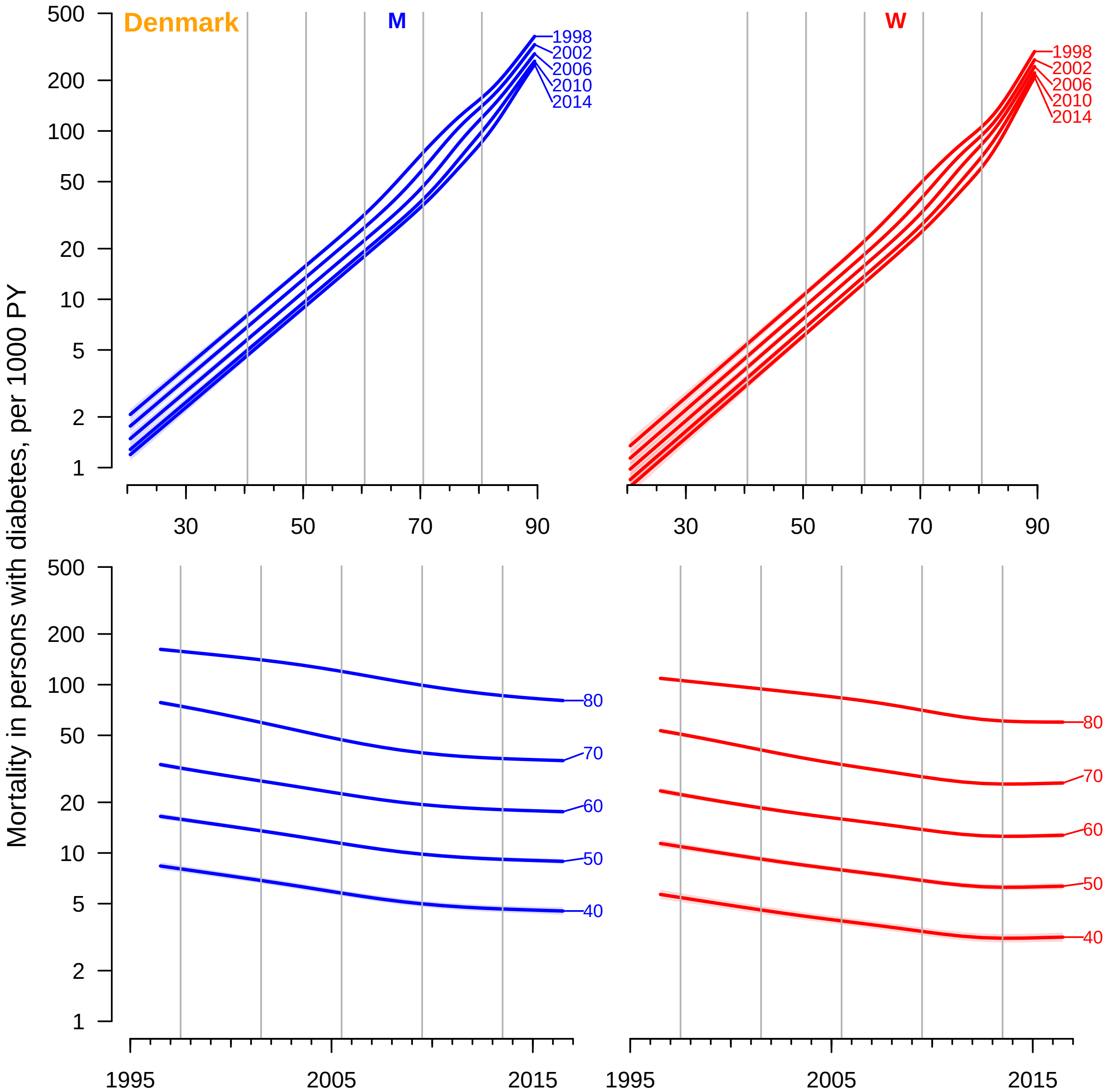

Figure A11: *Estimated mortality rates of diabetes by age and period in Denmark. Estimates of mortality rates are from age-period-cohort models, fitted separately for men and women. Upper panels show age-specific rates at different dates, as indicated by vertical lines in the lower panels. Lower panels show period-specific rates at different ages, as indicated by vertical lines in the upper panels. Left panels (blue curves) are men, right panels (red curves) are women.*

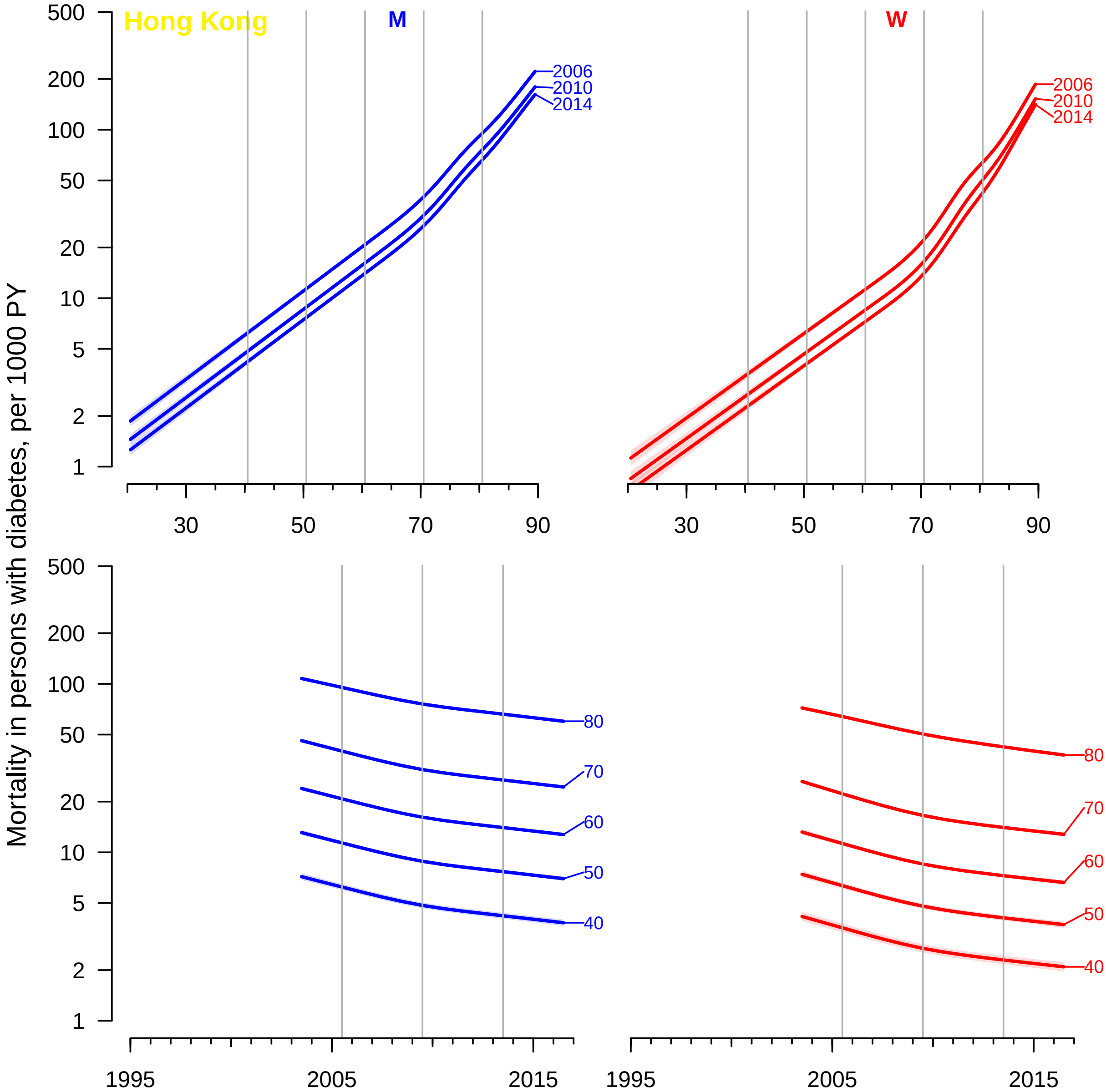

Figure A12: *Estimated mortality rates of diabetes by age and period in HongKong. Estimates of mortality rates are from age-period-cohort models, fitted separately for men and women. Upper panels show age-specific rates at different dates, as indicated by vertical lines in the lower panels. Lower panels show period-specific rates at different ages, as indicated by vertical lines in the upper panels. Left panels (blue curves) are men, right panels (red curves) are women.*

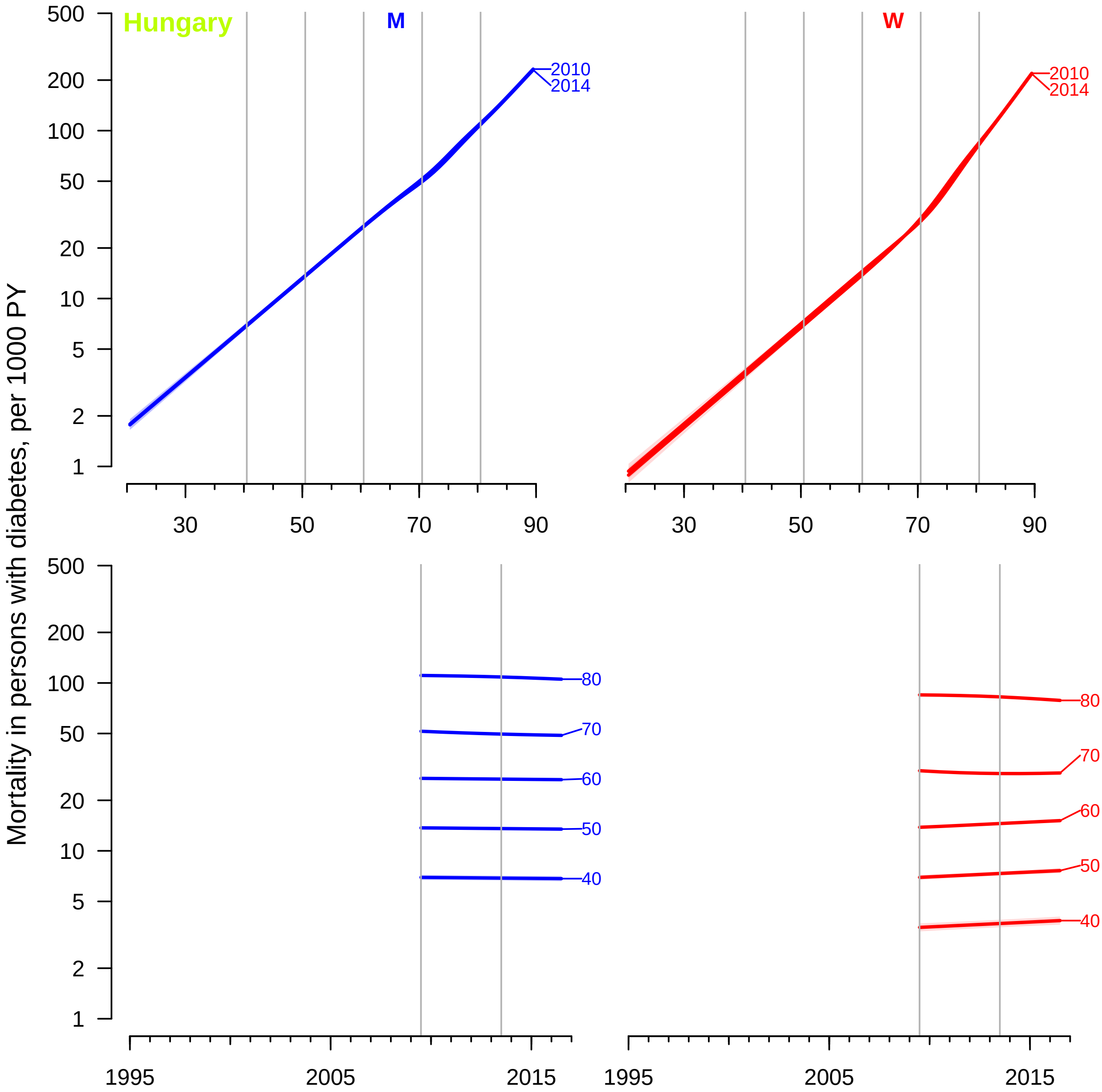

Figure A13: *Estimated mortality rates of diabetes by age and period in Hungary. Estimates of mortality rates are from age-period-cohort models, fitted separately for men and women. Upper panels show age-specific rates at different dates, as indicated by vertical lines in the lower panels. Lower panels show period-specific rates at different ages, as indicated by vertical lines in the upper panels. Left panels (blue curves) are men, right panels (red curves) are women.*

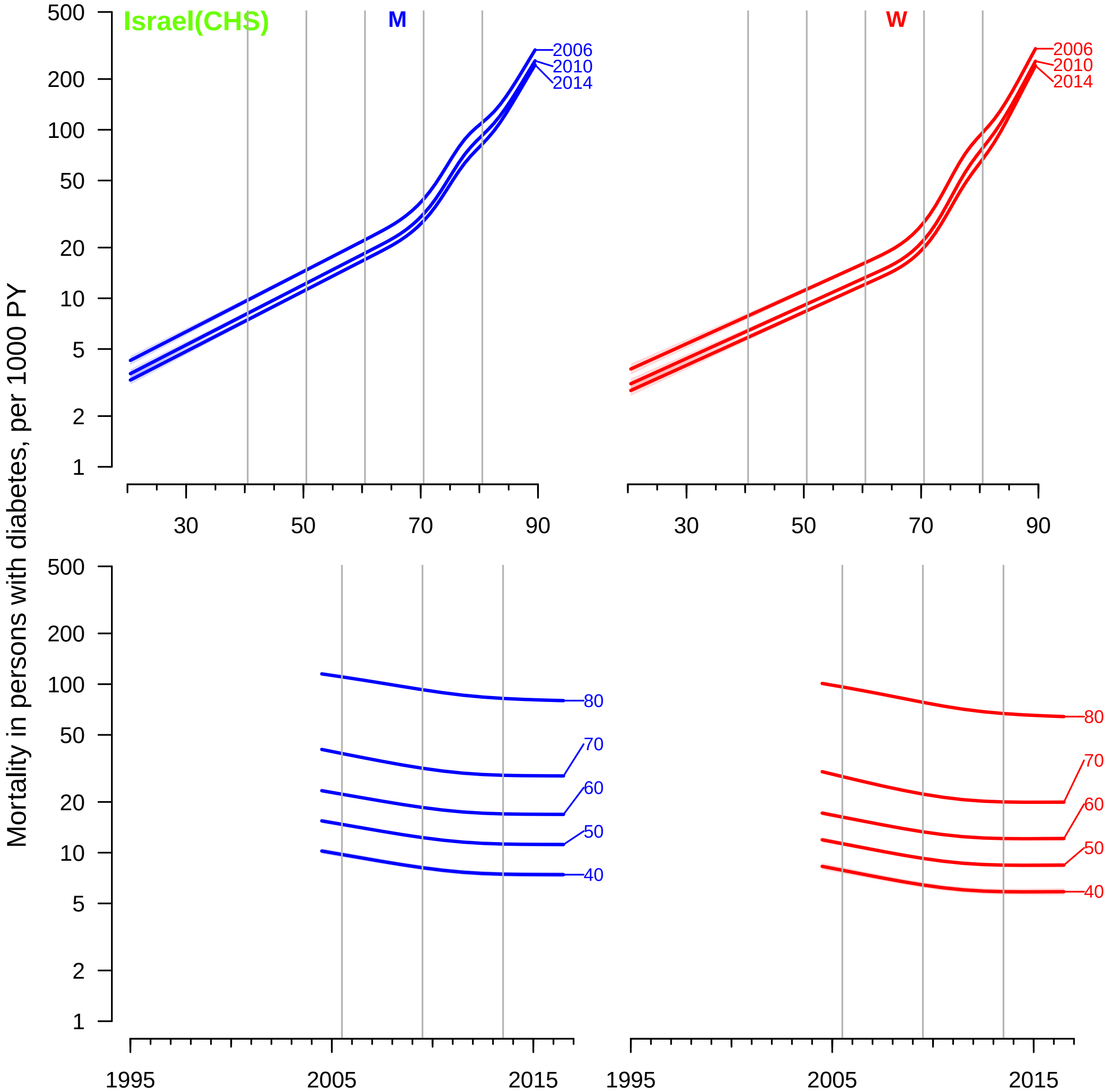

Figure A14: *Estimated mortality rates of diabetes by age and period in Israel(CHS). Estimates of mortality rates are from age-period-cohort models, fitted separately for men and women. Upper panels show age-specific rates at different dates, as indicated by vertical lines in the lower panels. Lower panels show period-specific rates at different ages, as indicated by vertical lines in the upper panels. Left panels (blue curves) are men, right panels (red curves) are women.*

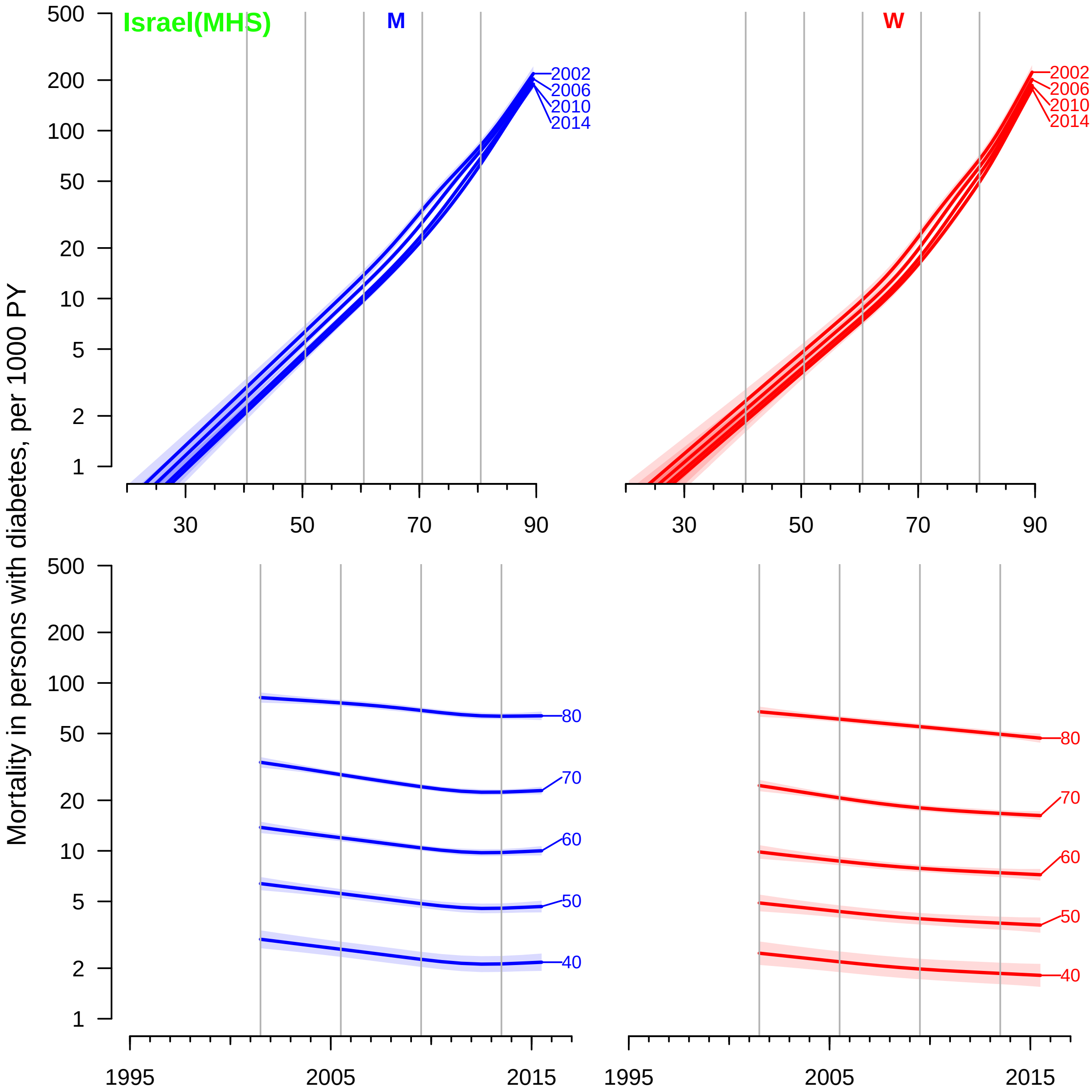

Figure A15: *Estimated mortality rates of diabetes by age and period in Israel(MHS). Estimates of mortality rates are from age-period-cohort models, fitted separately for men and women. Upper panels show age-specific rates at different dates, as indicated by vertical lines in the lower panels. Lower panels show period-specific rates at different ages, as indicated by vertical lines in the upper panels. Left panels (blue curves) are men, right panels (red curves) are women.*

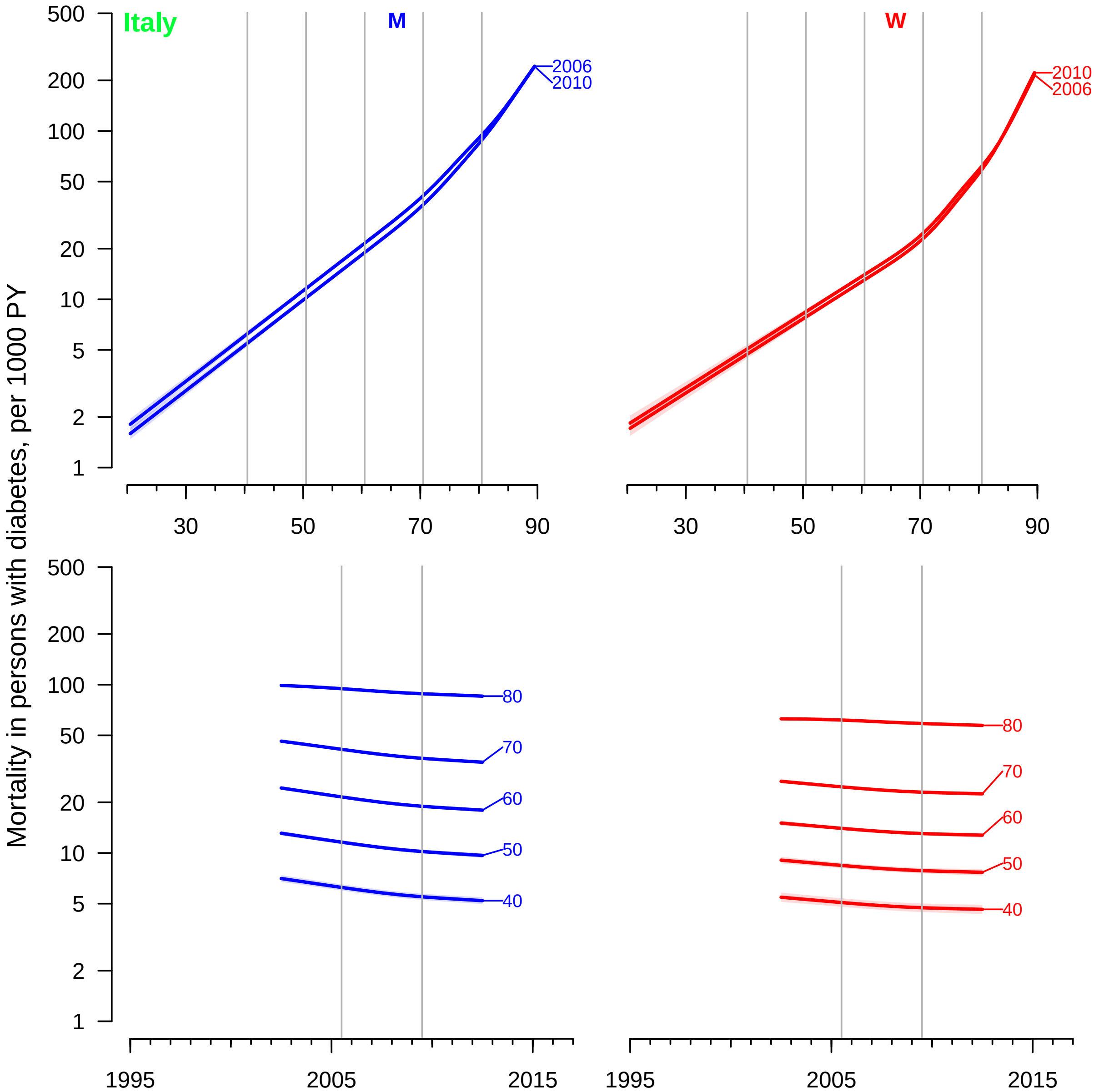

Figure A16: *Estimated mortality rates of diabetes by age and period in Italy. Estimates of mortality rates are from age-period-cohort models, fitted separately for men and women. Upper panels show age-specific rates at different dates, as indicated by vertical lines in the lower panels. Lower panels show period-specific rates at different ages, as indicated by vertical lines in the upper panels. Left panels (blue curves) are men, right panels (red curves) are women.*

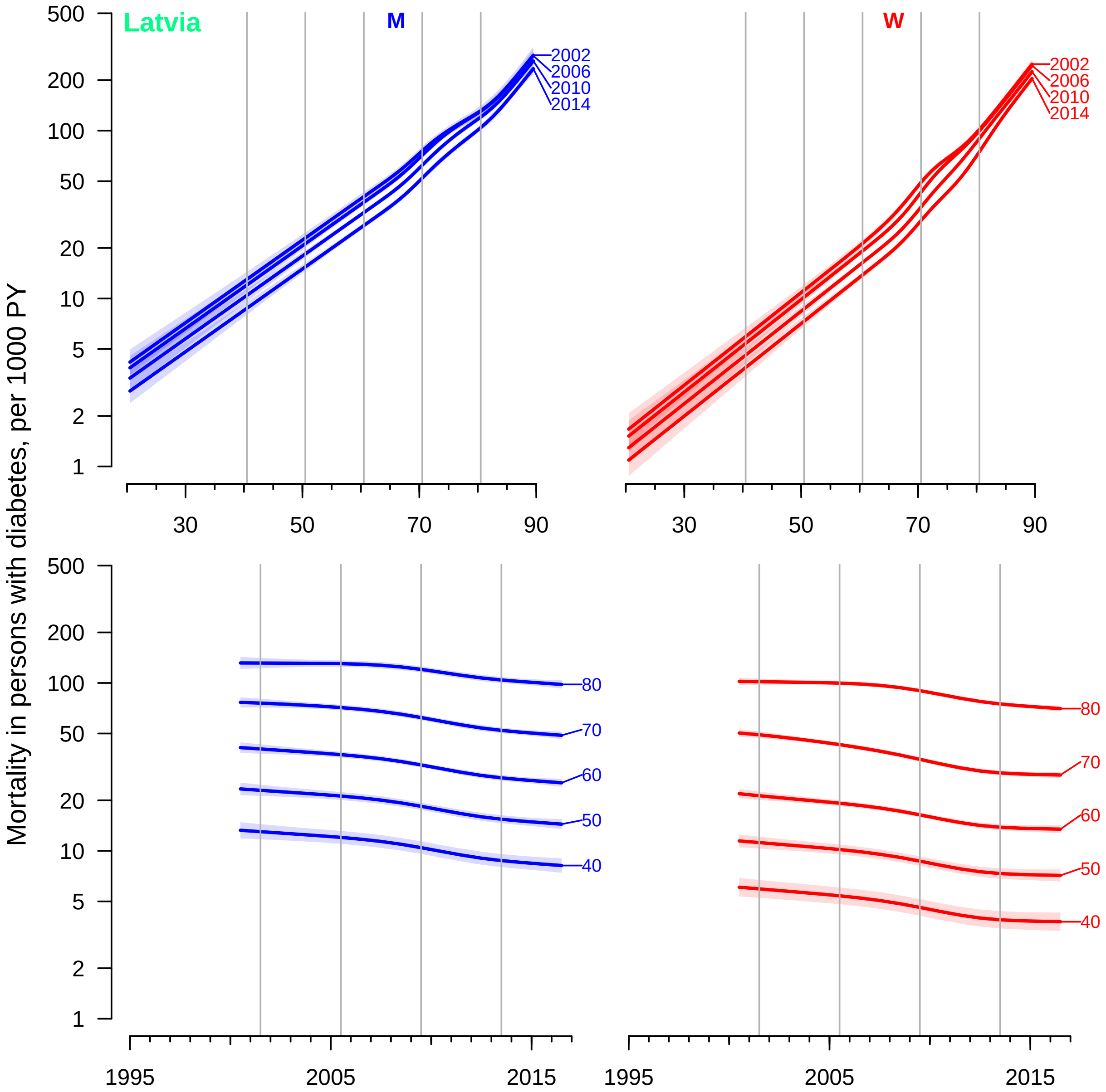

Figure A17: *Estimated mortality rates of diabetes by age and period in Latvia. Estimates of mortality rates are from age-period-cohort models, fitted separately for men and women. Upper panels show age-specific rates at different dates, as indicated by vertical lines in the lower panels. Lower panels show period-specific rates at different ages, as indicated by vertical lines in the upper panels. Left panels (blue curves) are men, right panels (red curves) are women.*

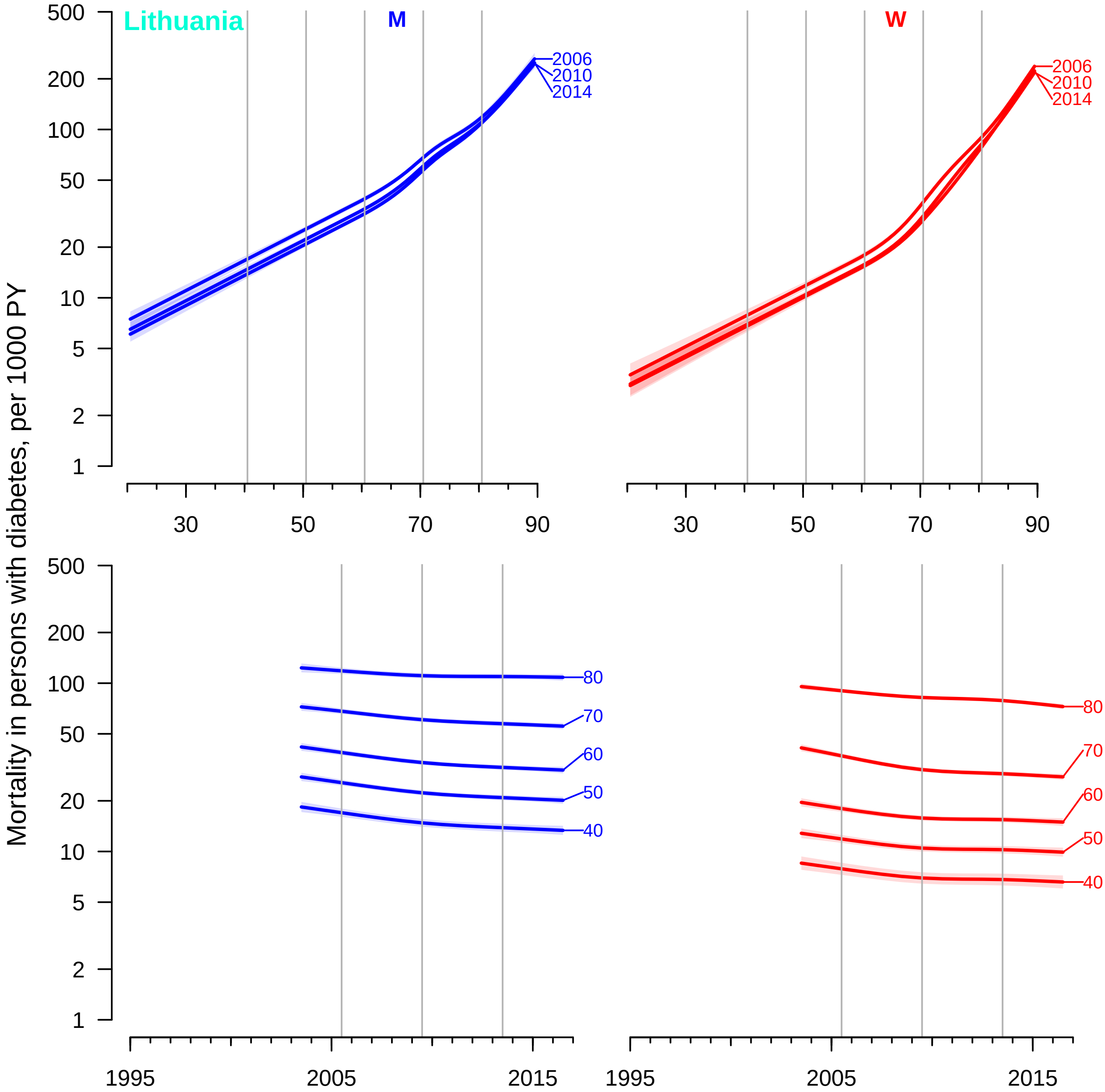

Figure A18: *Estimated mortality rates of diabetes by age and period in Lithuania. Estimates of mortality rates are from age-period-cohort models, fitted separately for men and women. Upper panels show age-specific rates at different dates, as indicated by vertical lines in the lower panels. Lower panels show period-specific rates at different ages, as indicated by vertical lines in the upper panels. Left panels (blue curves) are men, right panels (red curves) are women.*

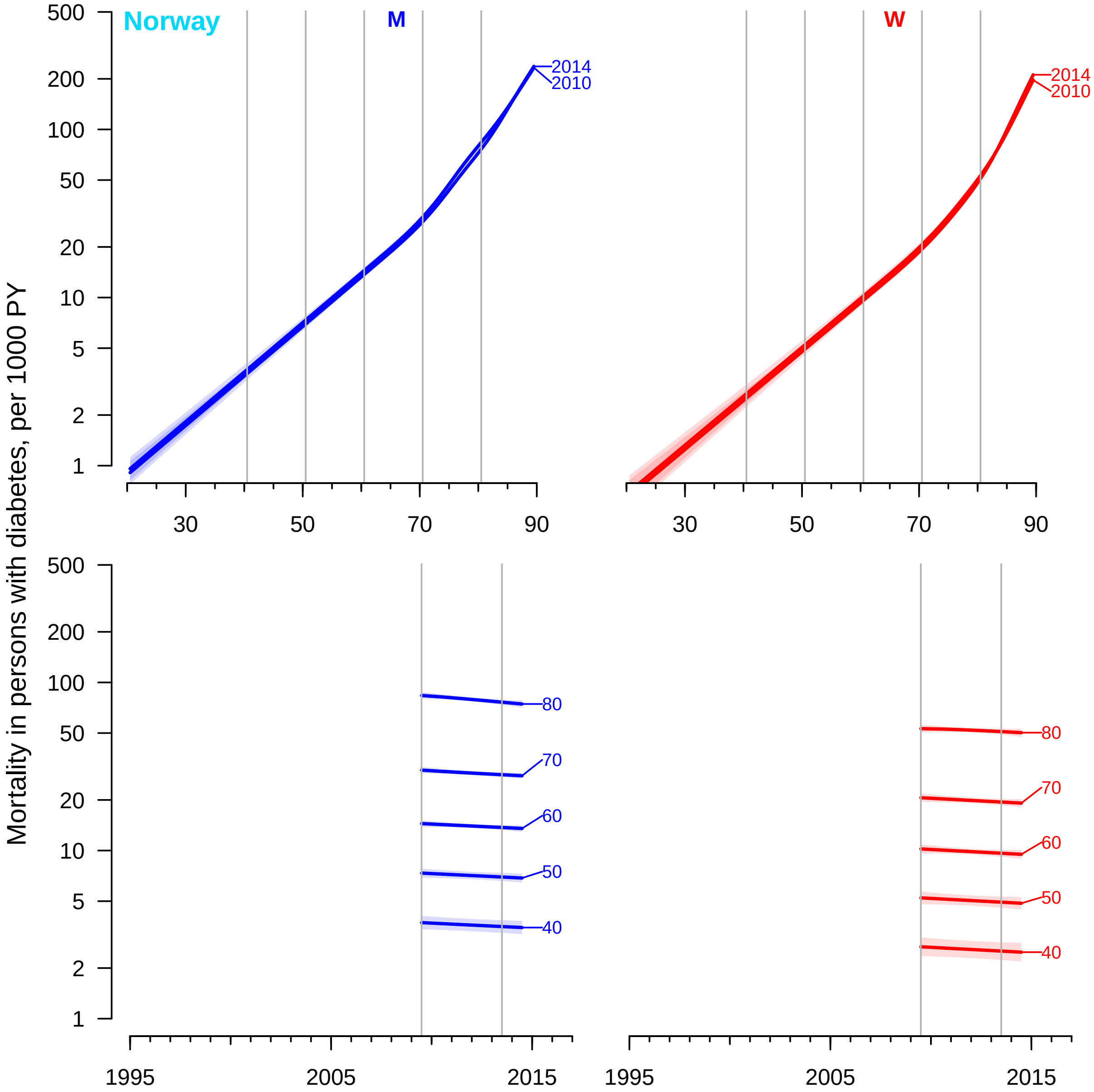

Figure A19: *Estimated mortality rates of diabetes by age and period in Norway. Estimates of mortality rates are from age-period-cohort models, fitted separately for men and women. Upper panels show age-specific rates at different dates, as indicated by vertical lines in the lower panels. Lower panels show period-specific rates at different ages, as indicated by vertical lines in the upper panels. Left panels (blue curves) are men, right panels (red curves) are women.*

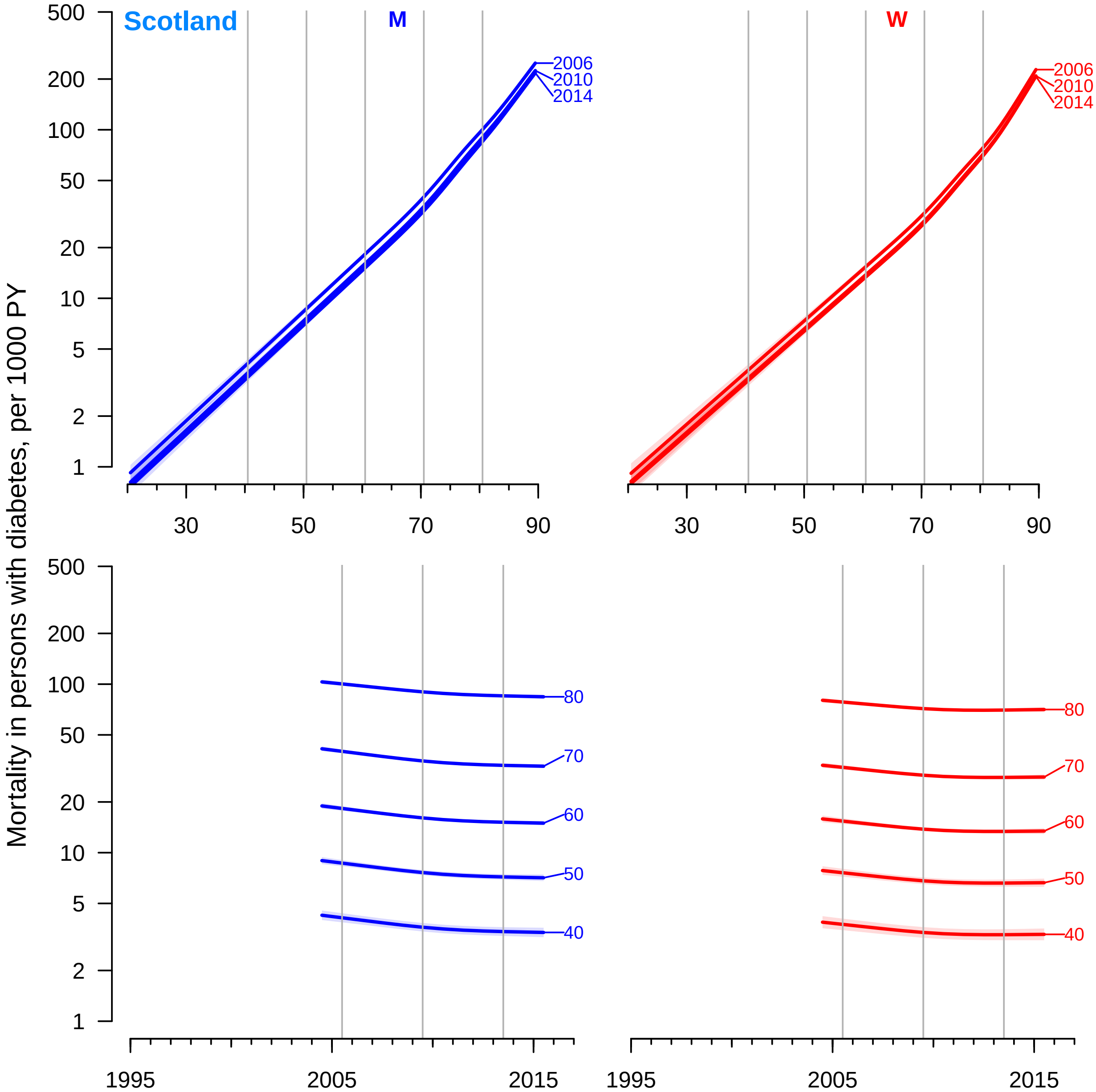

Figure A20: *Estimated mortality rates of diabetes by age and period in Scotland. Estimates of mortality rates are from age-period-cohort models, fitted separately for men and women. Upper panels show age-specific rates at different dates, as indicated by vertical lines in the lower panels. Lower panels show period-specific rates at different ages, as indicated by vertical lines in the upper panels. Left panels (blue curves) are men, right panels (red curves) are women.*

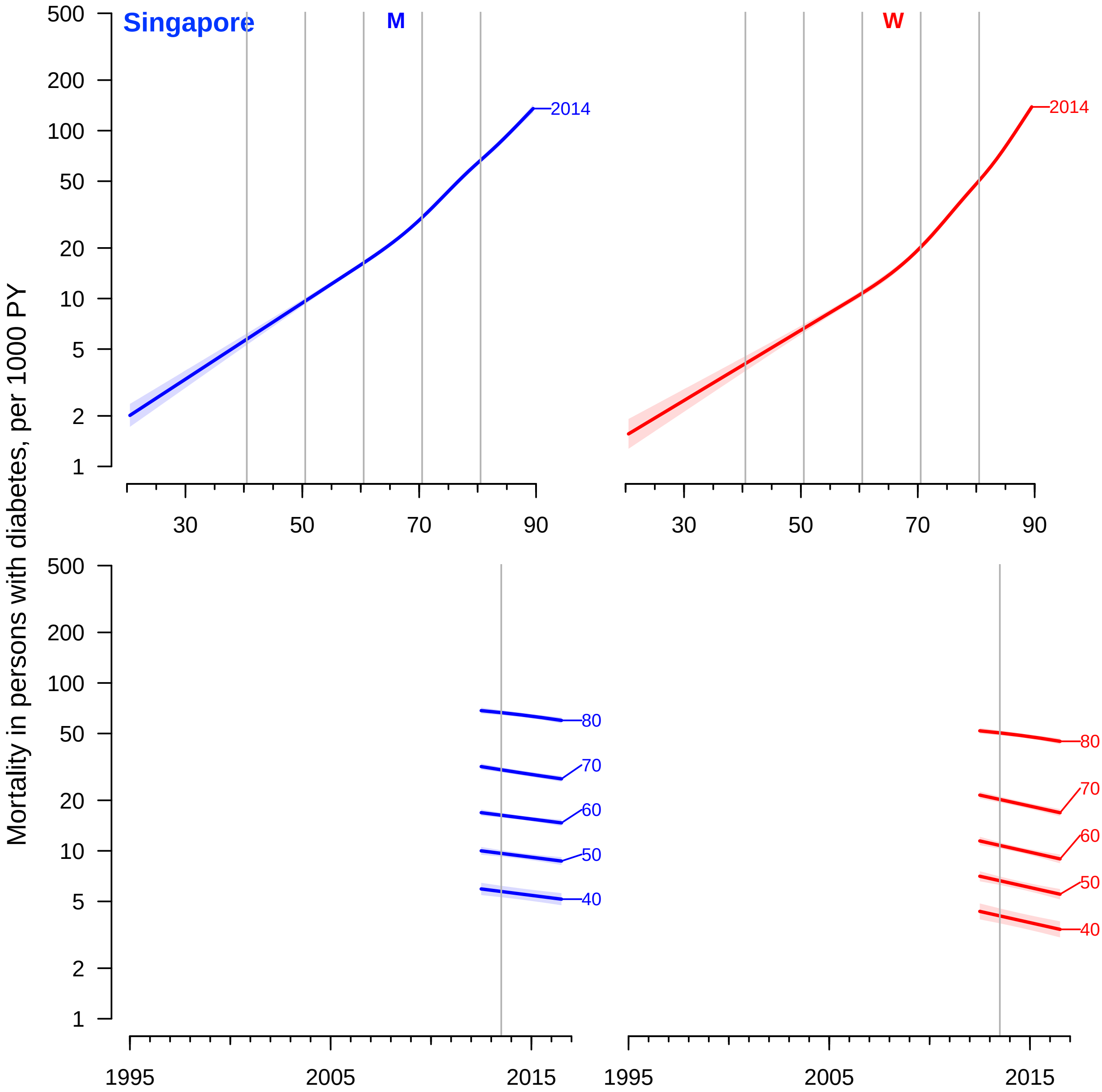

Figure A21: *Estimated mortality rates of diabetes by age and period in Singapore. Estimates of mortality rates are from age-period-cohort models, fitted separately for men and women. Upper panels show age-specific rates at different dates, as indicated by vertical lines in the lower panels. Lower panels show period-specific rates at different ages, as indicated by vertical lines in the upper panels. Left panels (blue curves) are men, right panels (red curves) are women.*

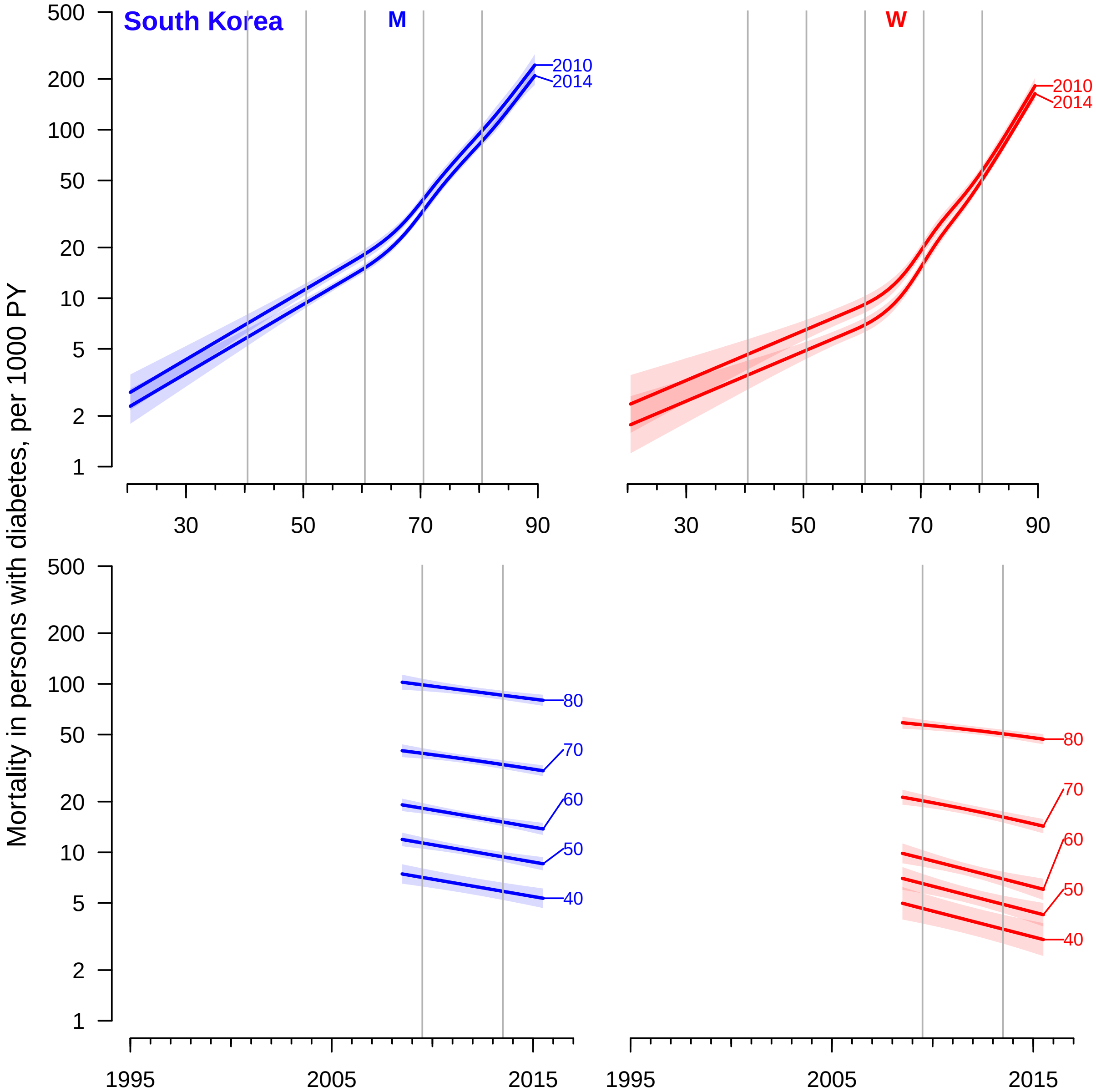

Figure A22: *Estimated mortality rates of diabetes by age and period in SouthKorea. Estimates of mortality rates are from age-period-cohort models, fitted separately for men and women. Upper panels show age-specific rates at different dates, as indicated by vertical lines in the lower panels. Lower panels show period-specific rates at different ages, as indicated by vertical lines in the upper panels. Left panels (blue curves) are men, right panels (red curves) are women.*

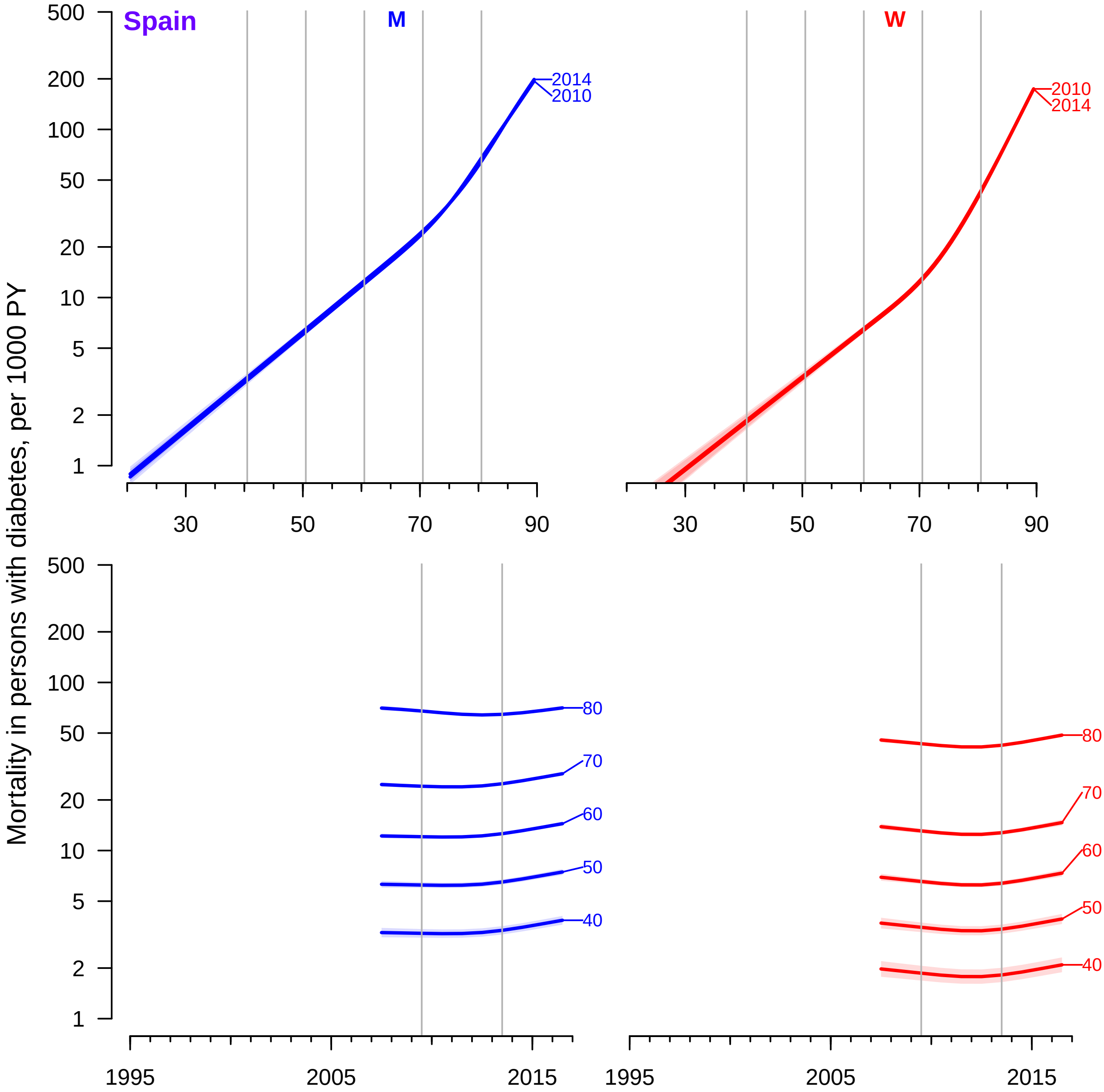

Figure A23: *Estimated mortality rates of diabetes by age and period in Spain. Estimates of mortality rates are from age-period-cohort models, fitted separately for men and women. Upper panels show age-specific rates at different dates, as indicated by vertical lines in the lower panels. Lower panels show period-specific rates at different ages, as indicated by vertical lines in the upper panels. Left panels (blue curves) are men, right panels (red curves) are women.*

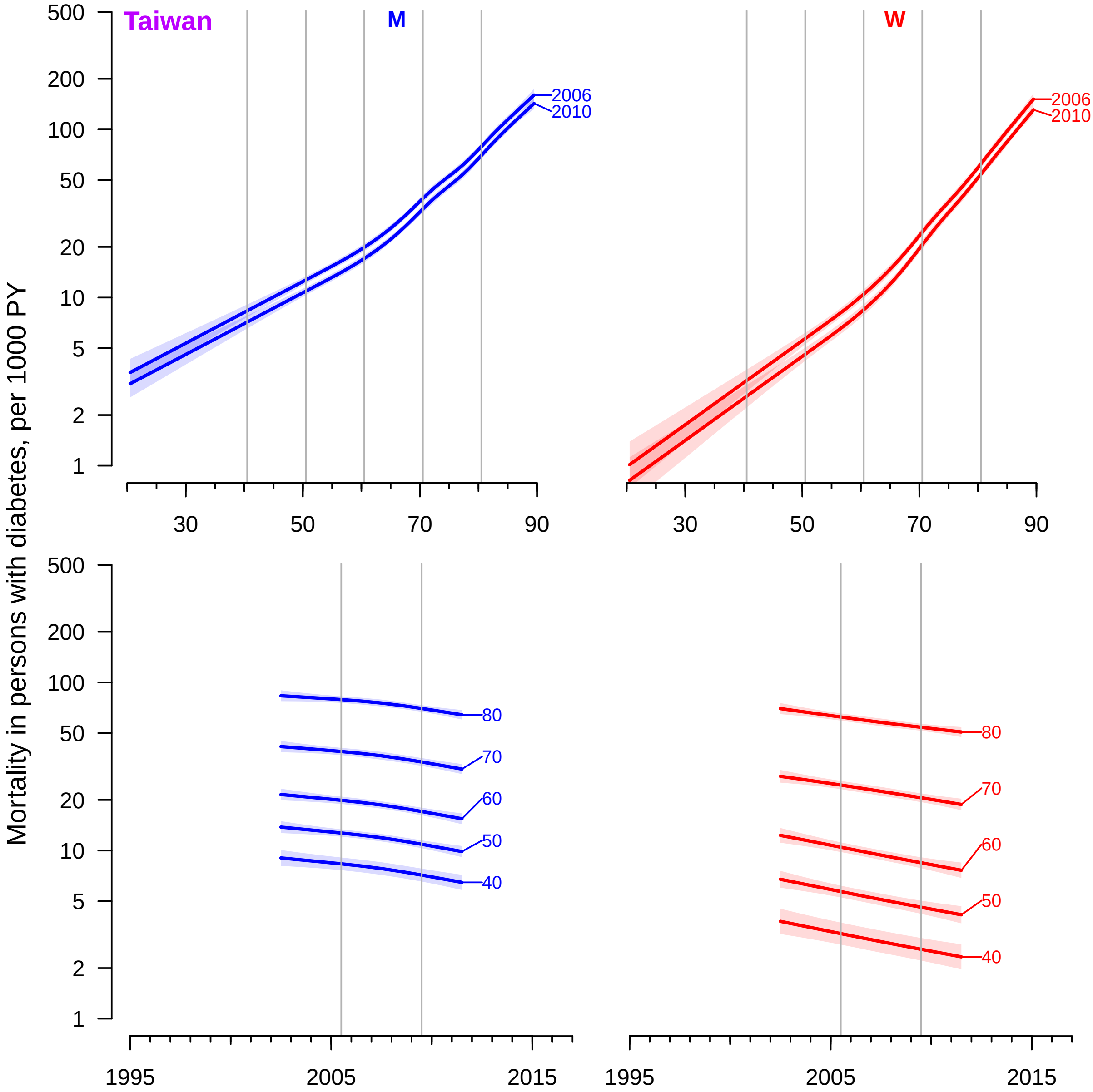

Figure A24: *Estimated mortality rates of diabetes by age and period in Taiwan. Estimates of mortality rates are from age-period-cohort models, fitted separately for men and women. Upper panels show age-specific rates at different dates, as indicated by vertical lines in the lower panels. Lower panels show period-specific rates at different ages, as indicated by vertical lines in the upper panels. Left panels (blue curves) are men, right panels (red curves) are women.*

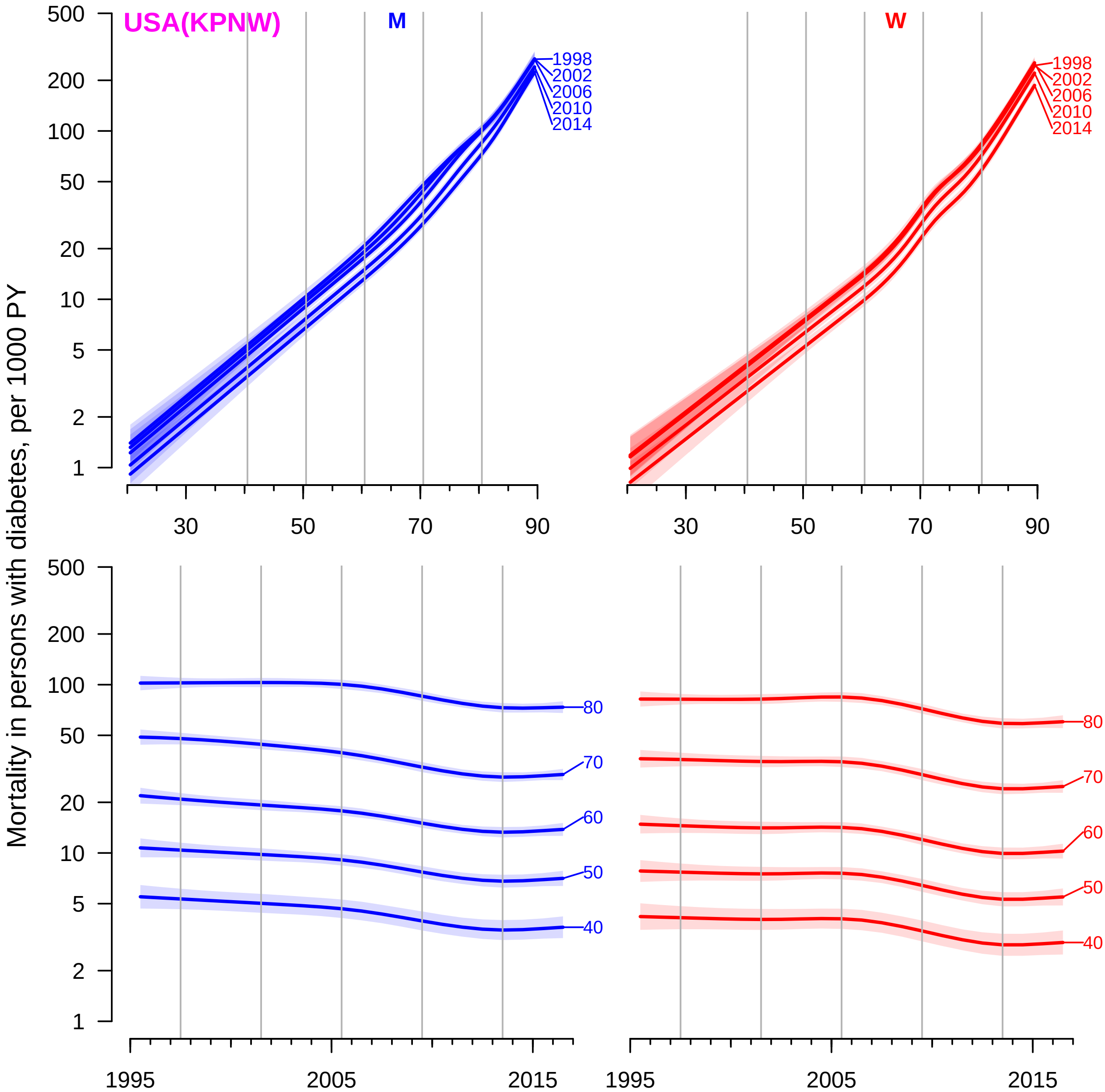

Figure A25: *Estimated mortality rates of diabetes by age and period in USA(KPNW). Estimates of mortality rates are from age-period-cohort models, fitted separately for men and women. Upper panels show age-specific rates at different dates, as indicated by vertical lines in the lower panels. Lower panels show period-specific rates at different ages, as indicated by vertical lines in the upper panels. Left panels (blue curves) are men, right panels (red curves) are women.*

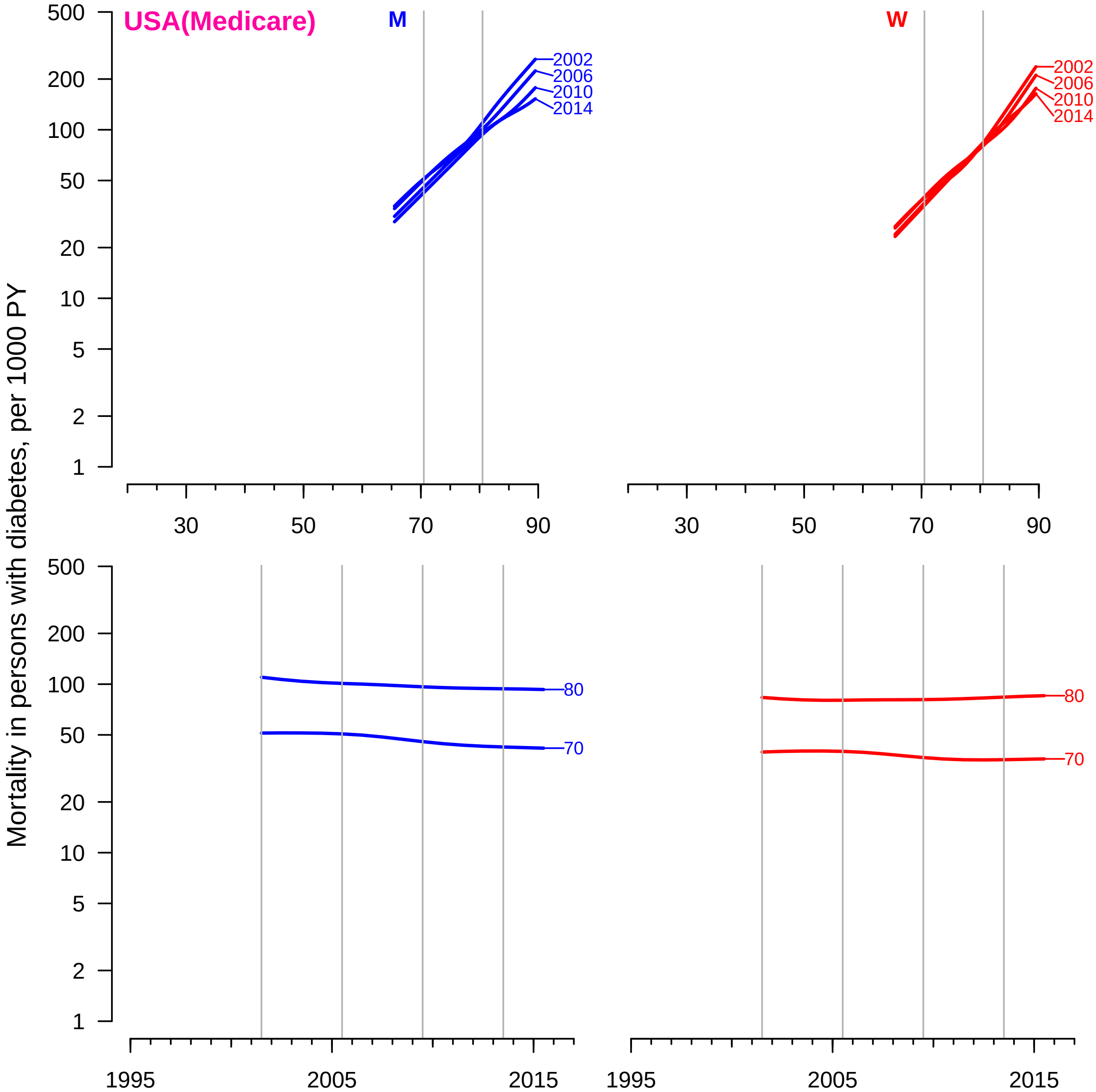

Figure A 26: *Estimated mortality rates of diabetes by age and period in USA(Medicare). Estimates of mortality rates are from age-period-cohort models, fitted separately for men and women. Upper panels show age-specific rates at different dates, as indicated by vertical lines in the lower panels. Lower panels show period-specific rates at different ages, as indicated by vertical lines in the upper panels. Left panels (blue curves) are men, right panels (red curves) are women.*

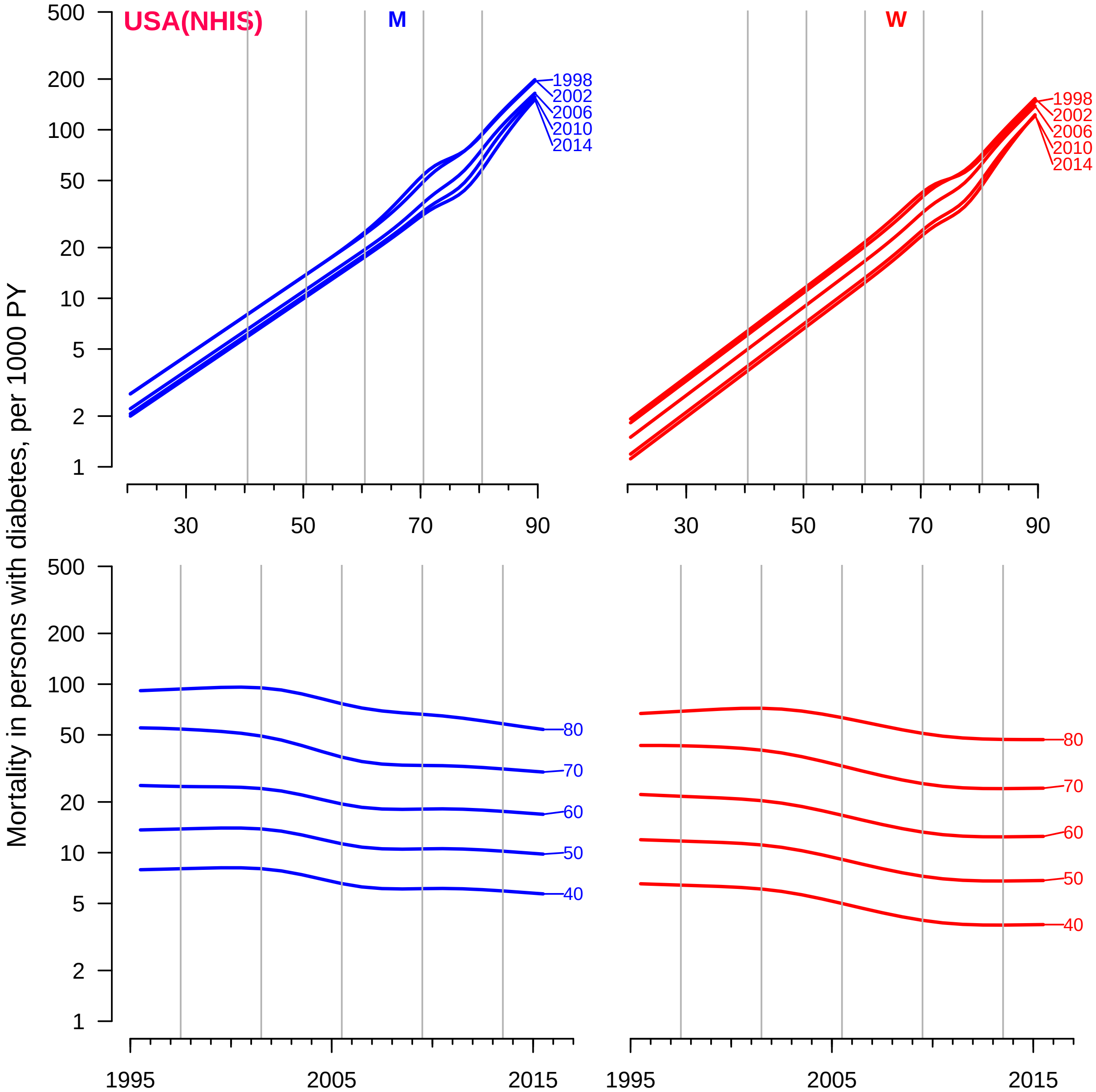

Figure A27: *Estimated mortality rates of diabetes by age and period in USA(NHIS). Estimates of mortality rates are from age-period-cohort models, fitted separately for men and women. Upper panels show age-specific rates at different dates, as indicated by vertical lines in the lower panels. Lower panels show period-specific rates at different ages, as indicated by vertical lines in the upper panels. Left panels (blue curves) are men, right panels (red curves) are women.*

4.2 SMR by age and period

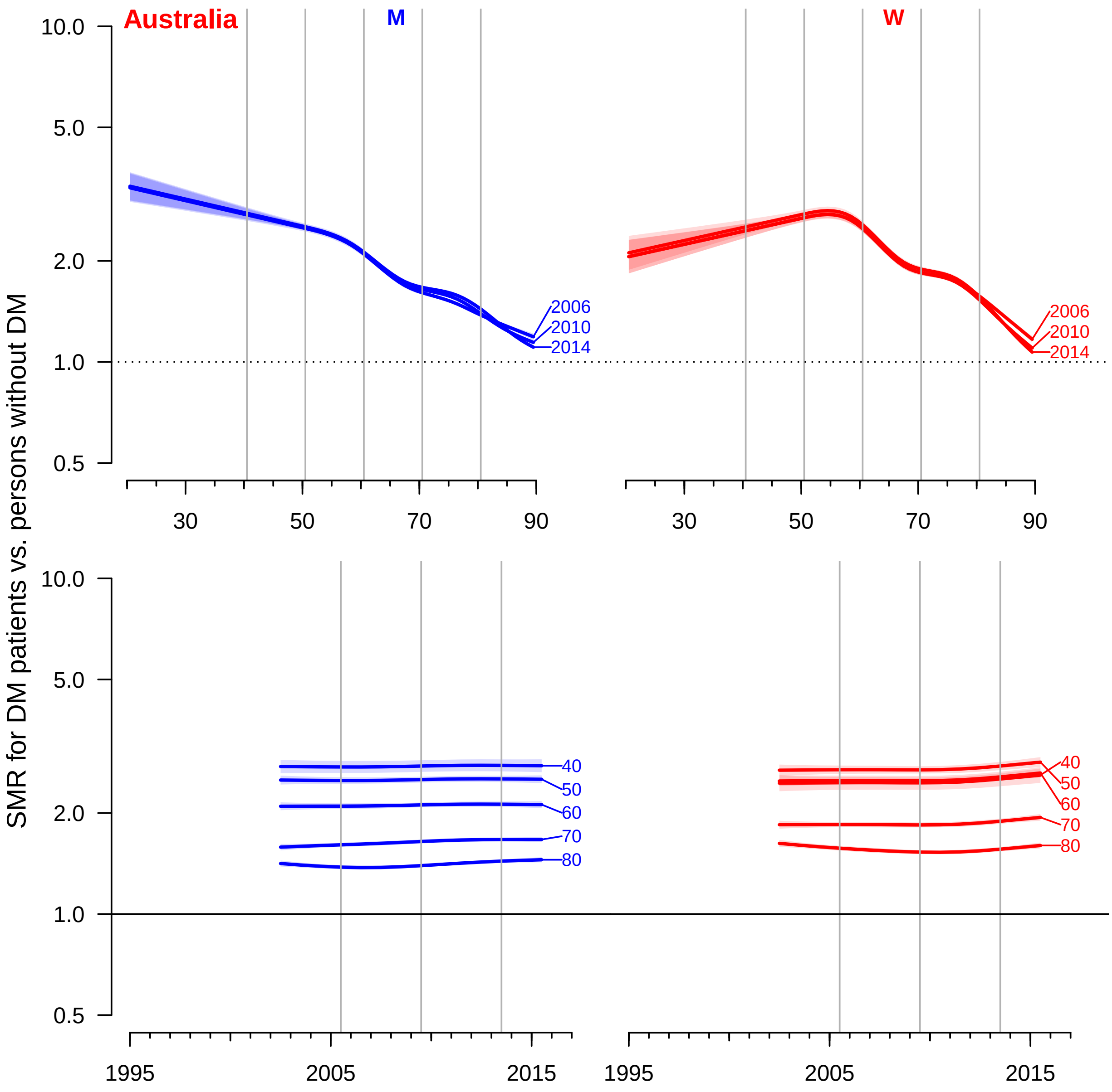

Figure A28: *Estimated SMR relative to the non-diabetes by age and period in Australia. Estimates of the SMRs are from age-period-cohort models, fitted separately for men and women. Upper panels show age-specific SMRs at different dates, as indicated by vertical lines in the lower panels. Lower panels show period-specific SMRs at different ages, as indicated by vertical lines in the upper panels. Left panels (blue curves) are men, right panels (red curves) are women.*

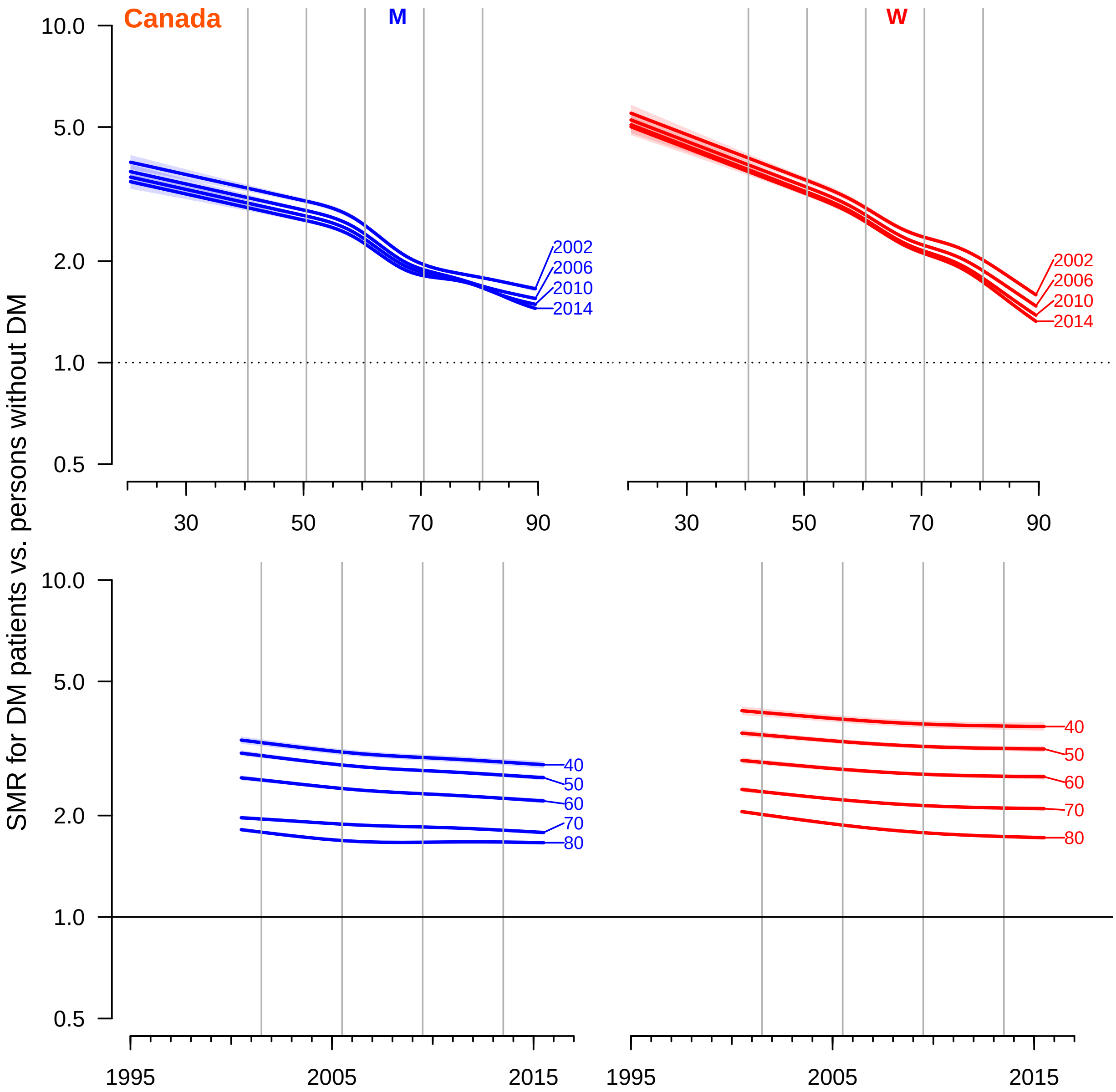

Figure A 29: *Estimated SMR relative to the non-diabetes by age and period in Canada. Estimates of the SMRs are from age-period-cohort models, fitted separately for men and women. Upper panels show age-specific SMRs at different dates, as indicated by vertical lines in the lower panels. Lower panels show period-specific SMRs at different ages, as indicated by vertical lines in the upper panels. Left panels (blue curves) are men, right panels (red curves) are women.*

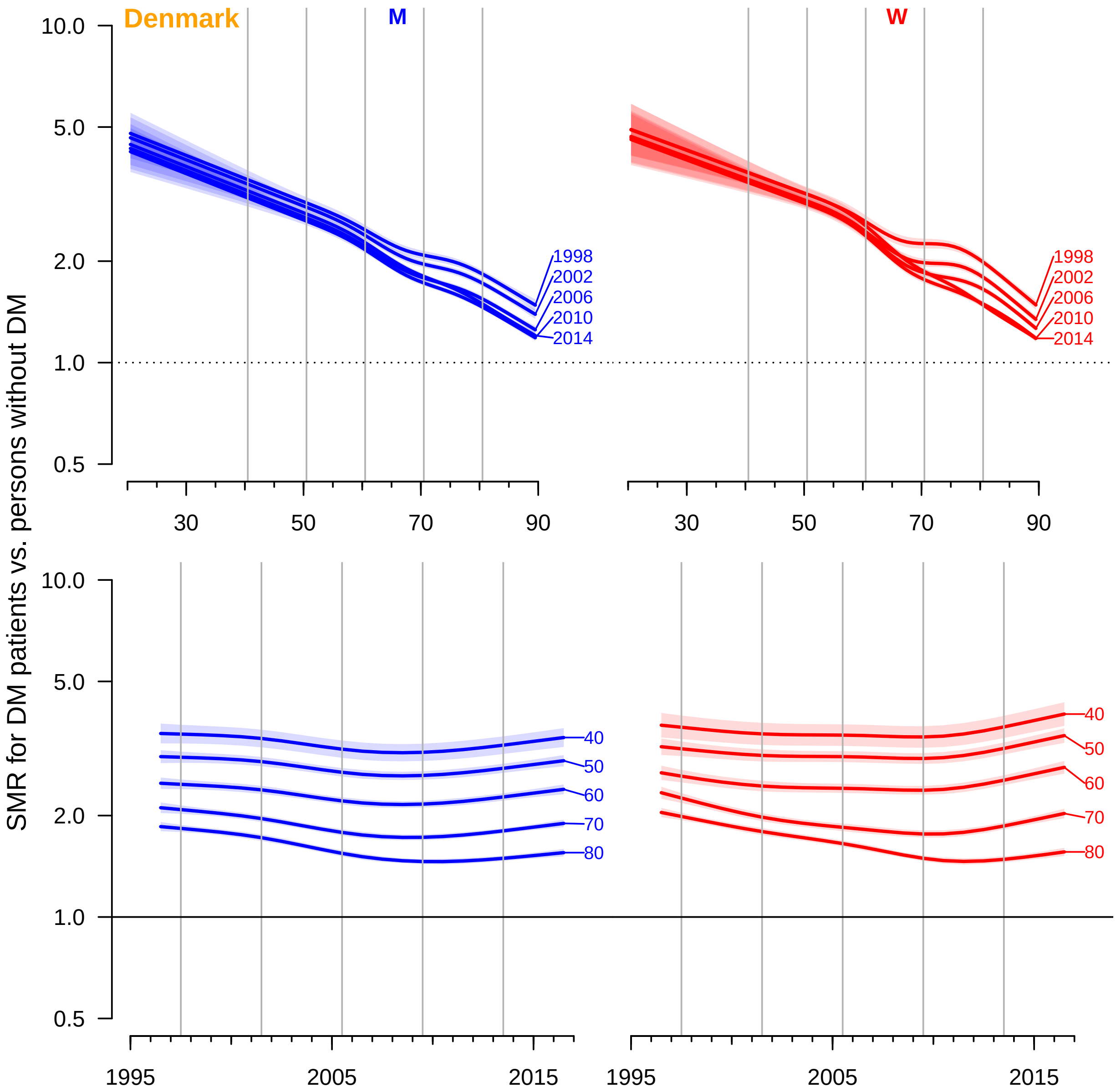

Figure A30: *Estimated SMR relative to the non-diabetes by age and period in Denmark. Estimates of the SMRs are from age-period-cohort models, fitted separately for men and women. Upper panels show age-specific SMRs at different dates, as indicated by vertical lines in the lower panels. Lower panels show period-specific SMRs at different ages, as indicated by vertical lines in the upper panels. Left panels (blue curves) are men, right panels (red curves) are women.*

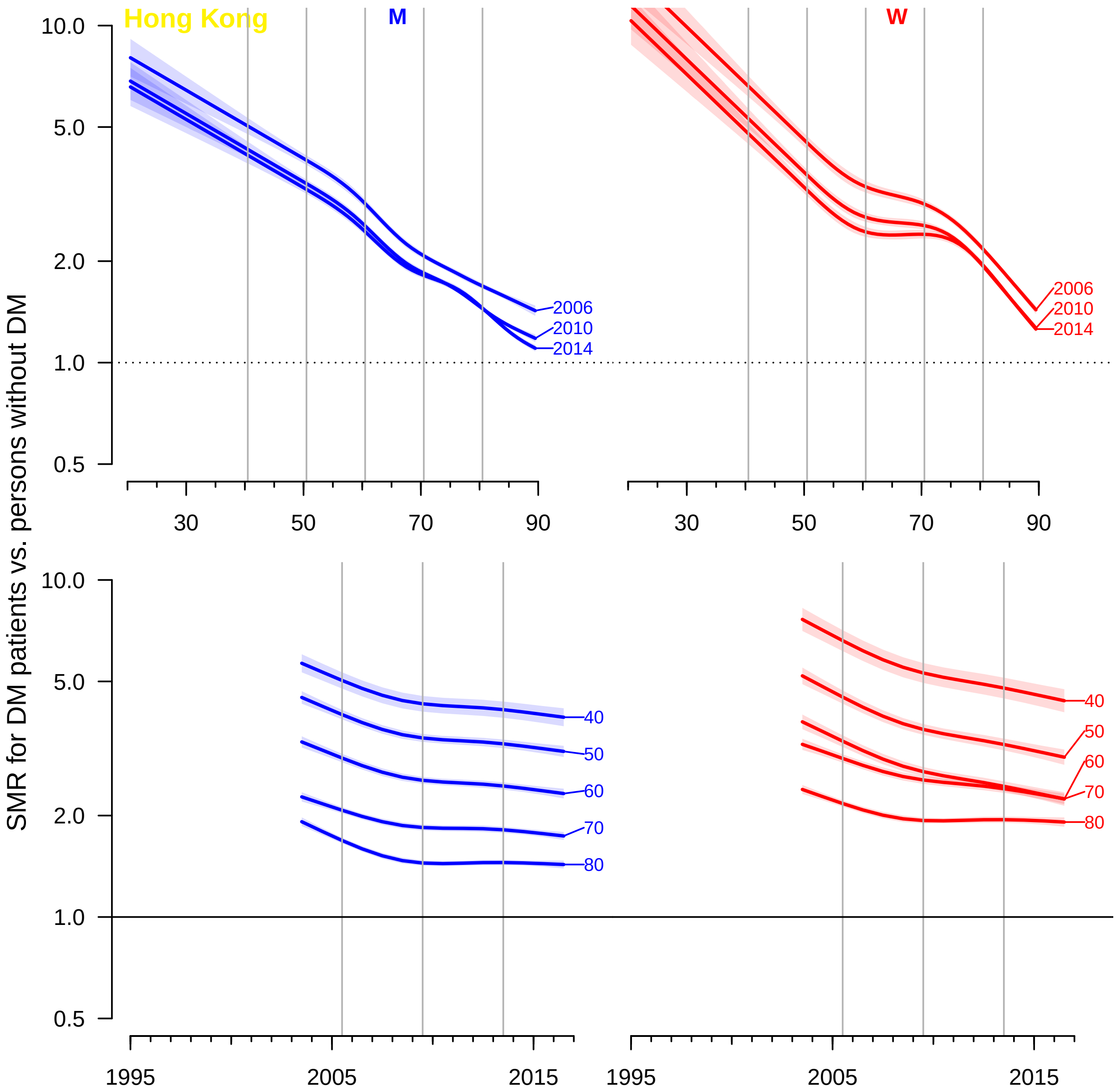

Figure A31: *Estimated SMR relative to the non-diabetes by age and period in HongKong. Estimates of the SMRs are from age-period-cohort models, fitted separately for men and women. Upper panels show age-specific SMRs at different dates, as indicated by vertical lines in the lower panels. Lower panels show period-specific SMRs at different ages, as indicated by vertical lines in the upper panels. Left panels (blue curves) are men, right panels (red curves) are women.*

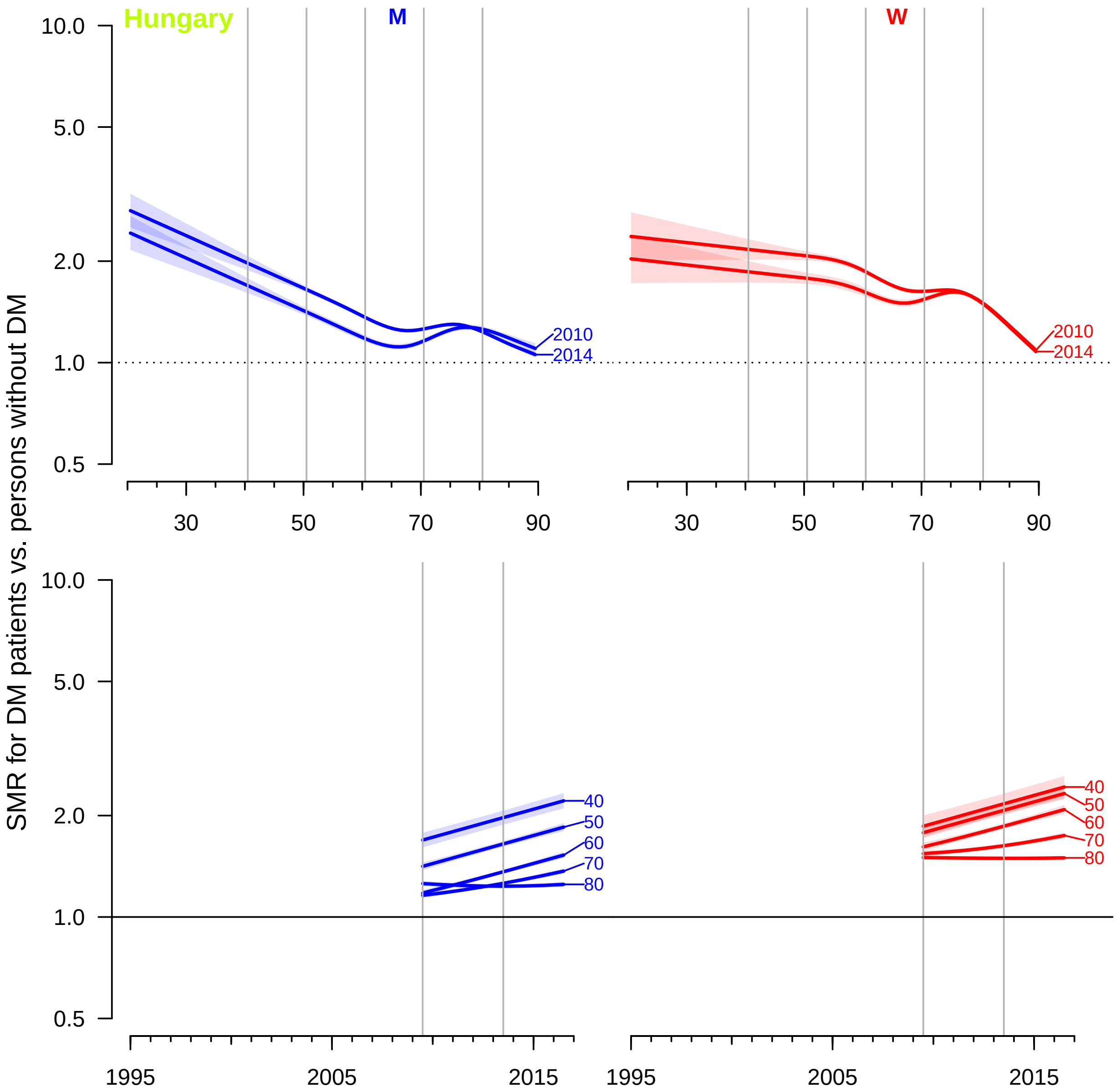

Figure A 32: *Estimated SMR relative to the non-diabetes by age and period in Hungary. Estimates of the SMRs are from age-period-cohort models, fitted separately for men and women. Upper panels show age-specific SMRs at different dates, as indicated by vertical lines in the lower panels. Lower panels show period-specific SMRs at different ages, as indicated by vertical lines in the upper panels. Left panels (blue curves) are men, right panels (red curves) are women.*

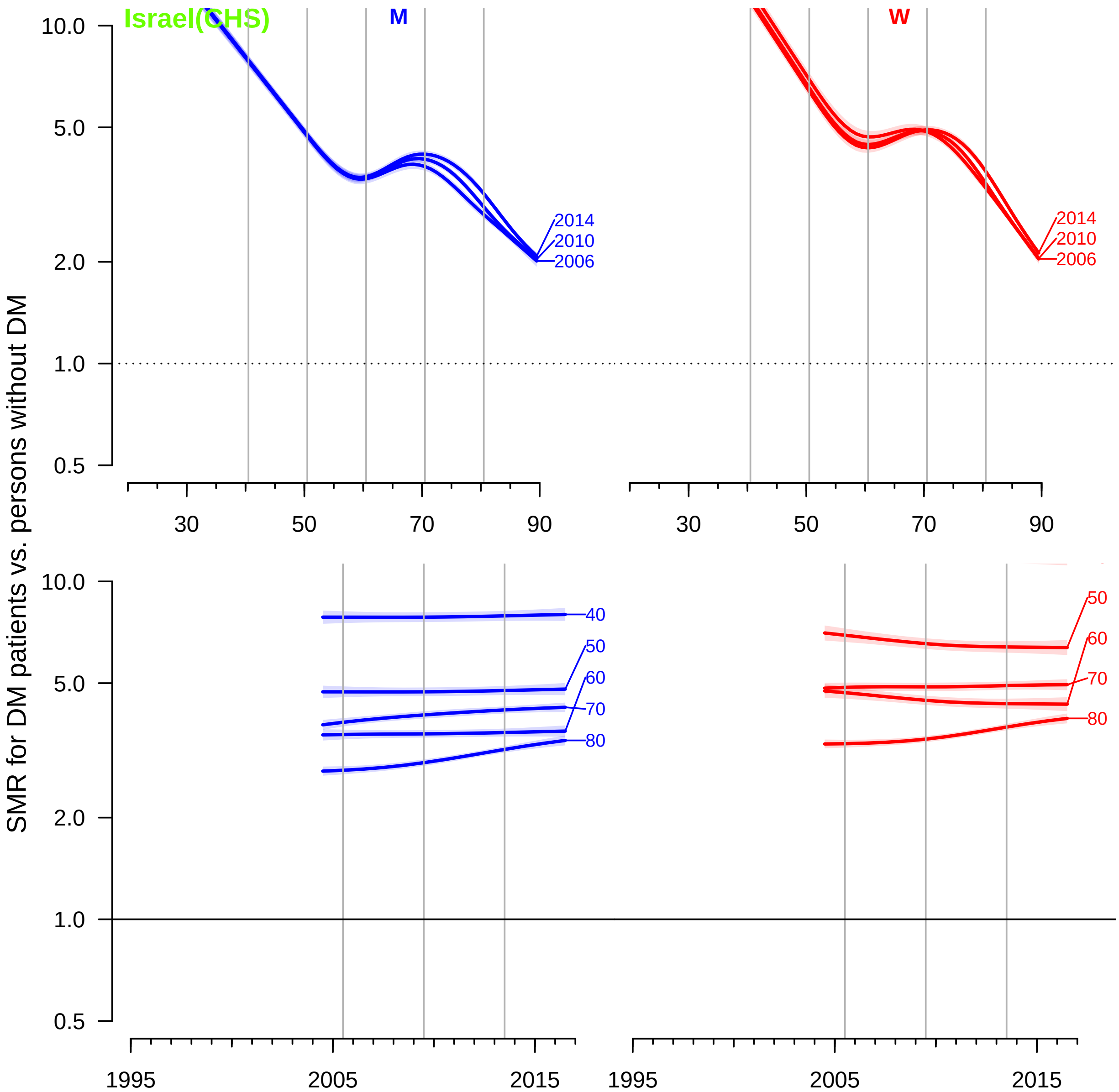

Figure A33: *Estimated SMR relative to the non-diabetes by age and period in Israel(CHS). Estimates of the SMRs are from age-period-cohort models, fitted separately for men and women. Upper panels show age-specific SMRs at different dates, as indicated by vertical lines in the lower panels. Lower panels show period-specific SMRs at different ages, as indicated by vertical lines in the upper panels. Left panels (blue curves) are men, right panels (red curves) are women.*

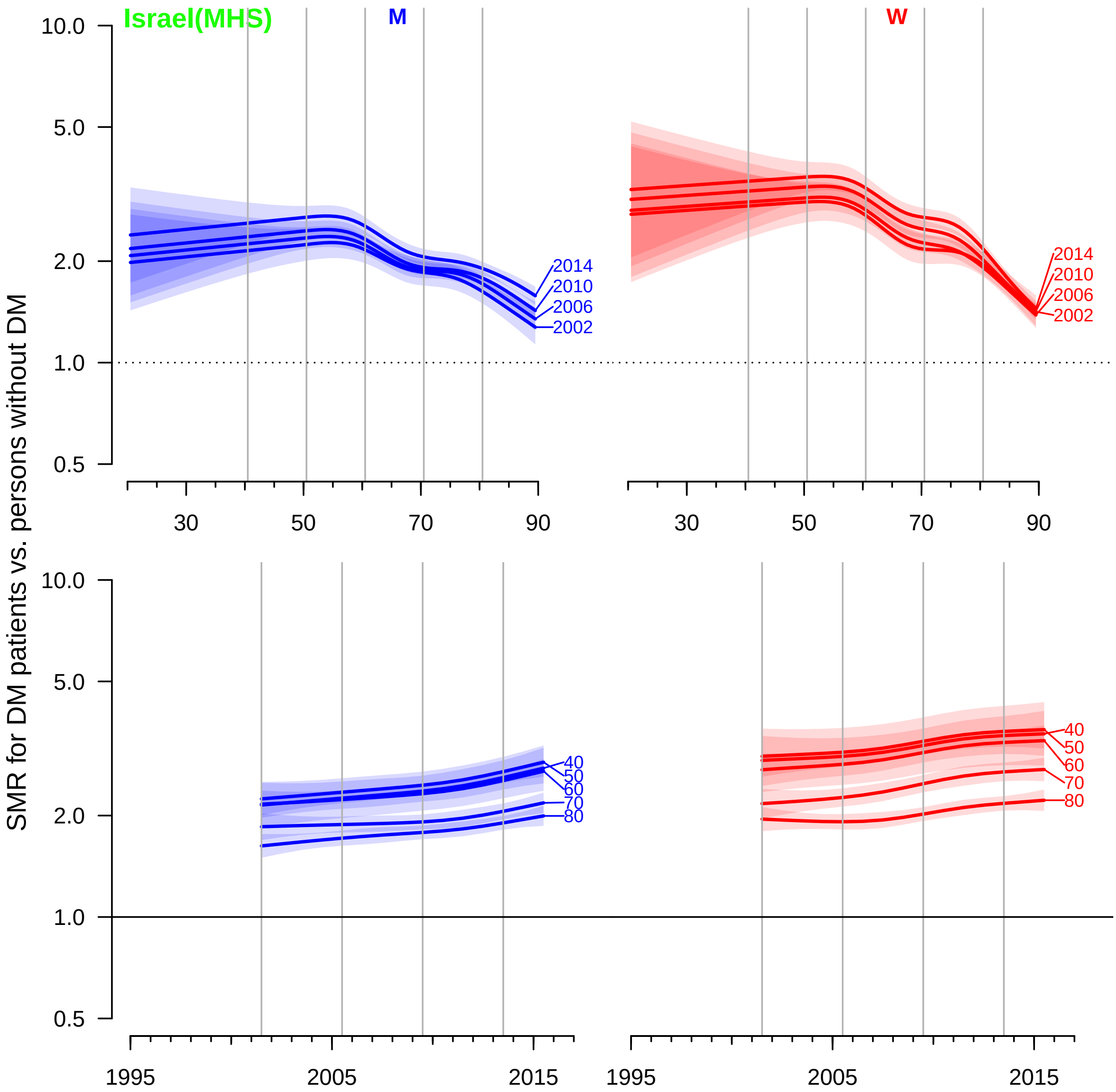

Figure A34: *Estimated SMR relative to the non-diabetes by age and period in Israel(MHS). Estimates of the SMRs are from age-period-cohort models, fitted separately for men and women. Upper panels show age-specific SMRs at different dates, as indicated by vertical lines in the lower panels. Lower panels show period-specific SMRs at different ages, as indicated by vertical lines in the upper panels. Left panels (blue curves) are men, right panels (red curves) are women.*

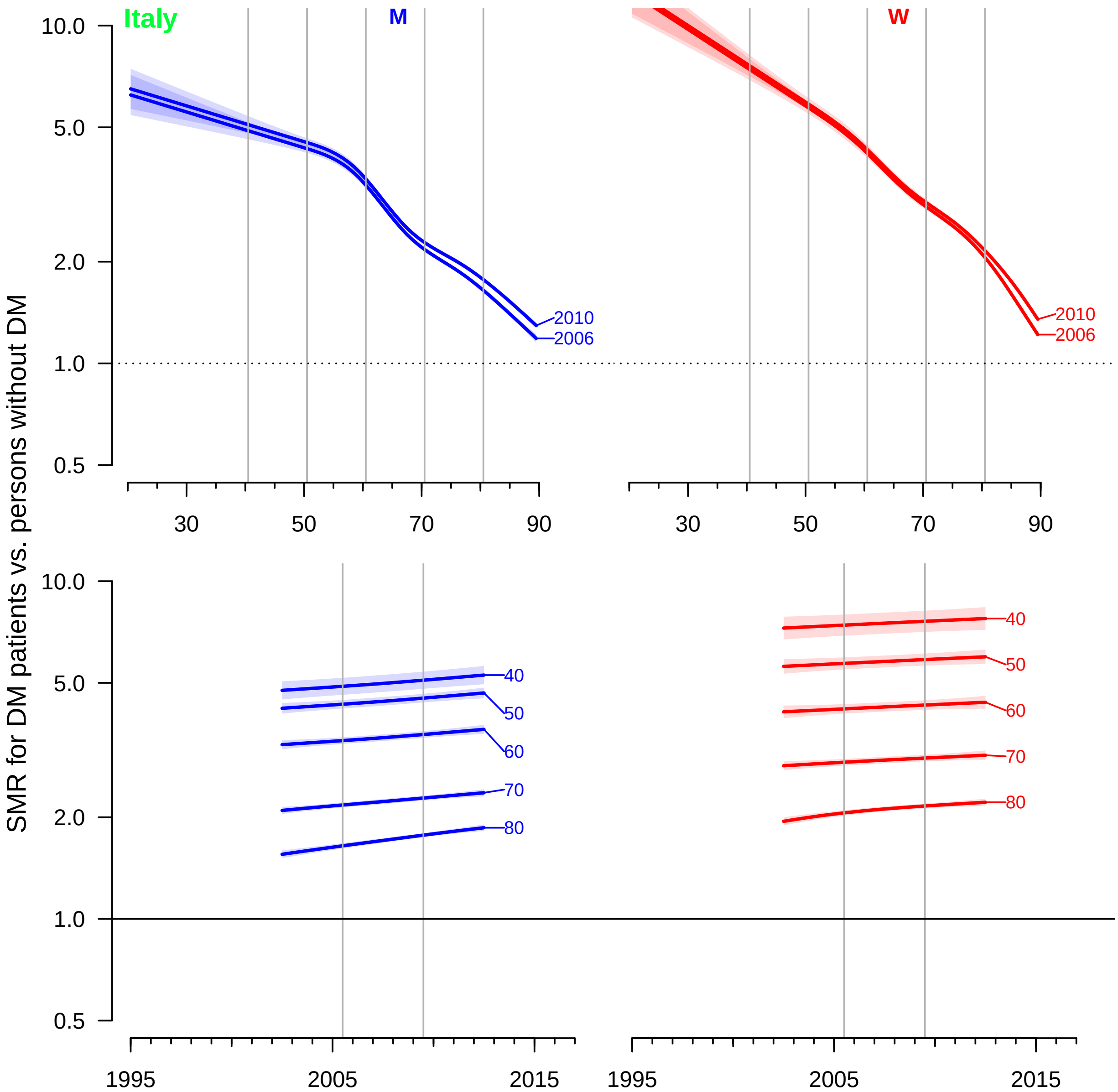

Figure A35: *Estimated SMR relative to the non-diabetes by age and period in Italy. Estimates of the SMRs are from age-period-cohort models, fitted separately for men and women. Upper panels show age-specific SMRs at different dates, as indicated by vertical lines in the lower panels. Lower panels show period-specific SMRs at different ages, as indicated by vertical lines in the upper panels. Left panels (blue curves) are men, right panels (red curves) are women.*

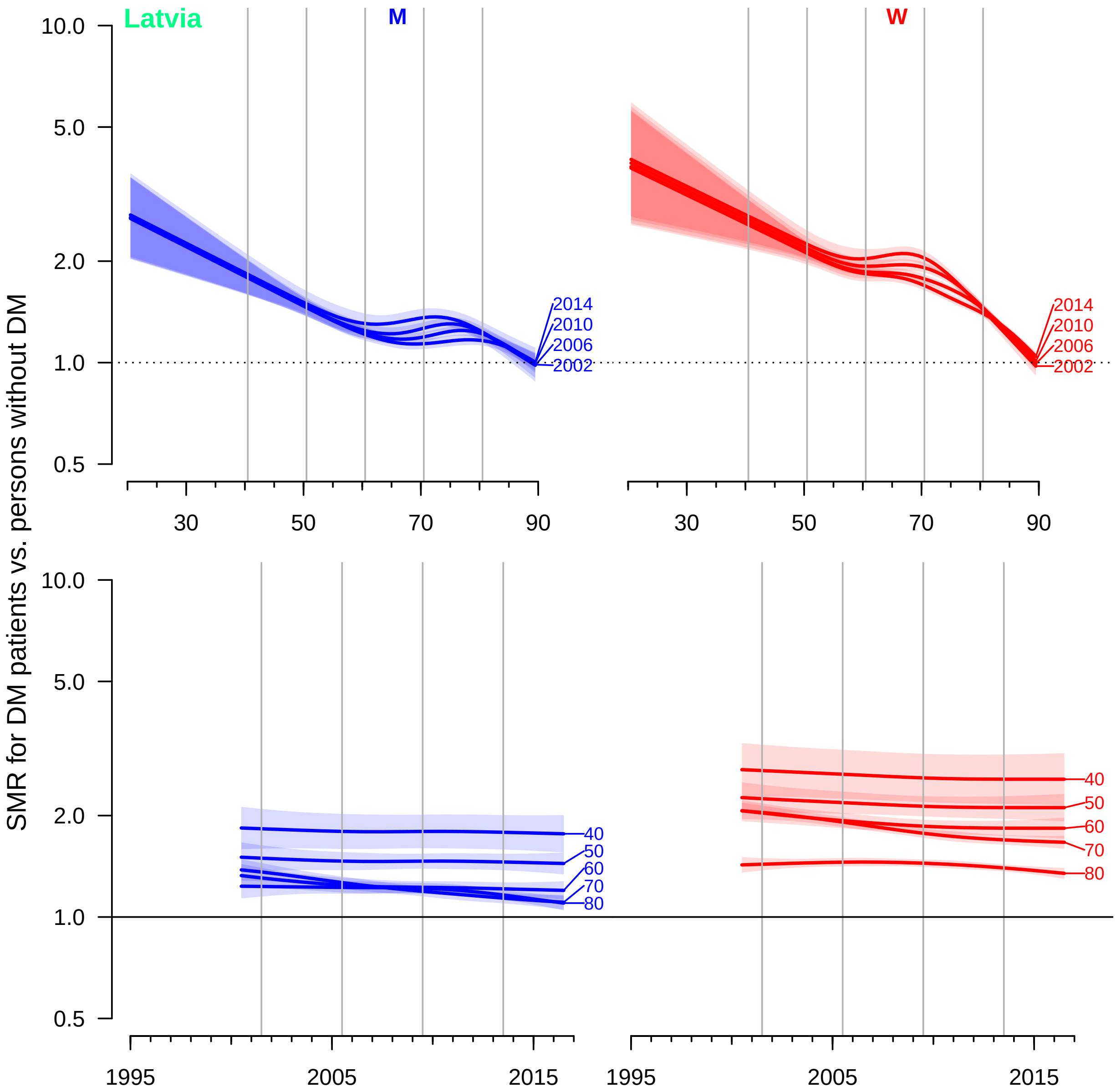

Figure A36: *Estimated SMR relative to the non-diabetes by age and period in Latvia. Estimates of the SMRs are from age-period-cohort models, fitted separately for men and women. Upper panels show age-specific SMRs at different dates, as indicated by vertical lines in the lower panels. Lower panels show period-specific SMRs at different ages, as indicated by vertical lines in the upper panels. Left panels (blue curves) are men, right panels (red curves) are women.*

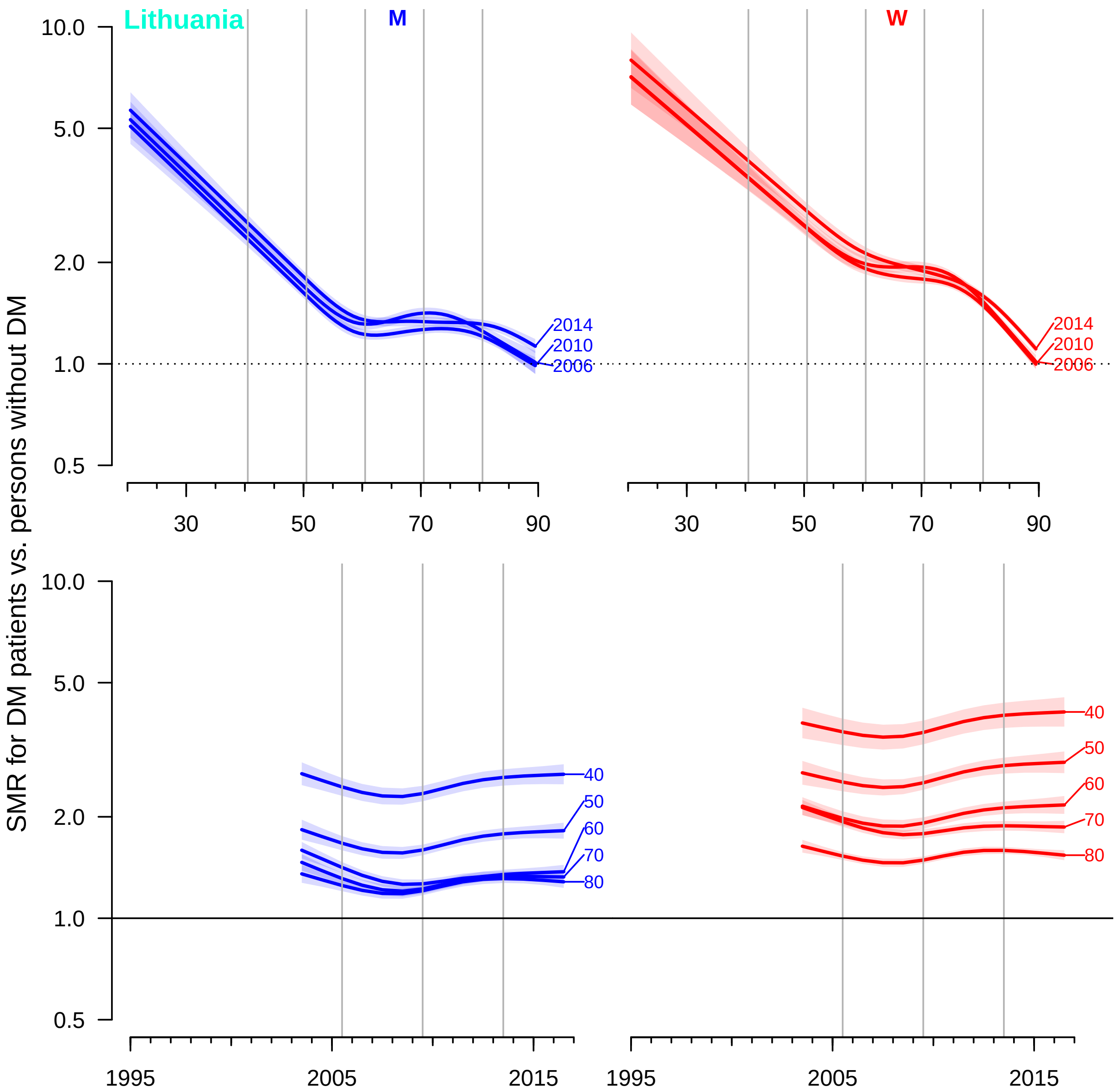

Figure A37: *Estimated SMR relative to the non-diabetes by age and period in Lithuania. Estimates of the SMRs are from age-period-cohort models, fitted separately for men and women. Upper panels show age-specific SMRs at different dates, as indicated by vertical lines in the lower panels. Lower panels show period-specific SMRs at different ages, as indicated by vertical lines in the upper panels. Left panels (blue curves) are men, right panels (red curves) are women.*

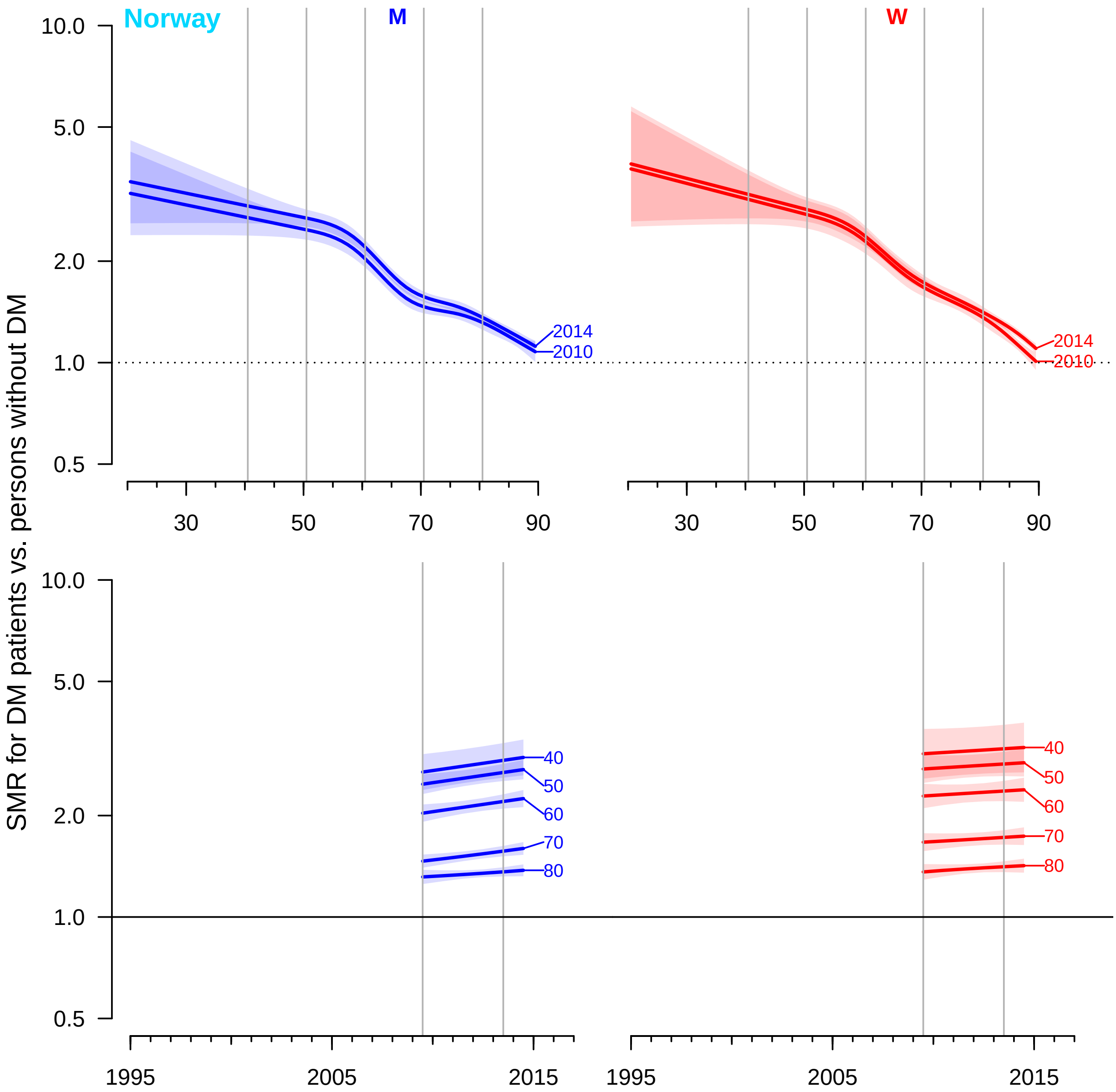

Figure A 38: *Estimated SMR relative to the non-diabetes by age and period in Norway. Estimates of the SMRs are from age-period-cohort models, fitted separately for men and women. Upper panels show age-specific SMRs at different dates, as indicated by vertical lines in the lower panels. Lower panels show period-specific SMRs at different ages, as indicated by vertical lines in the upper panels. Left panels (blue curves) are men, right panels (red curves) are women.*

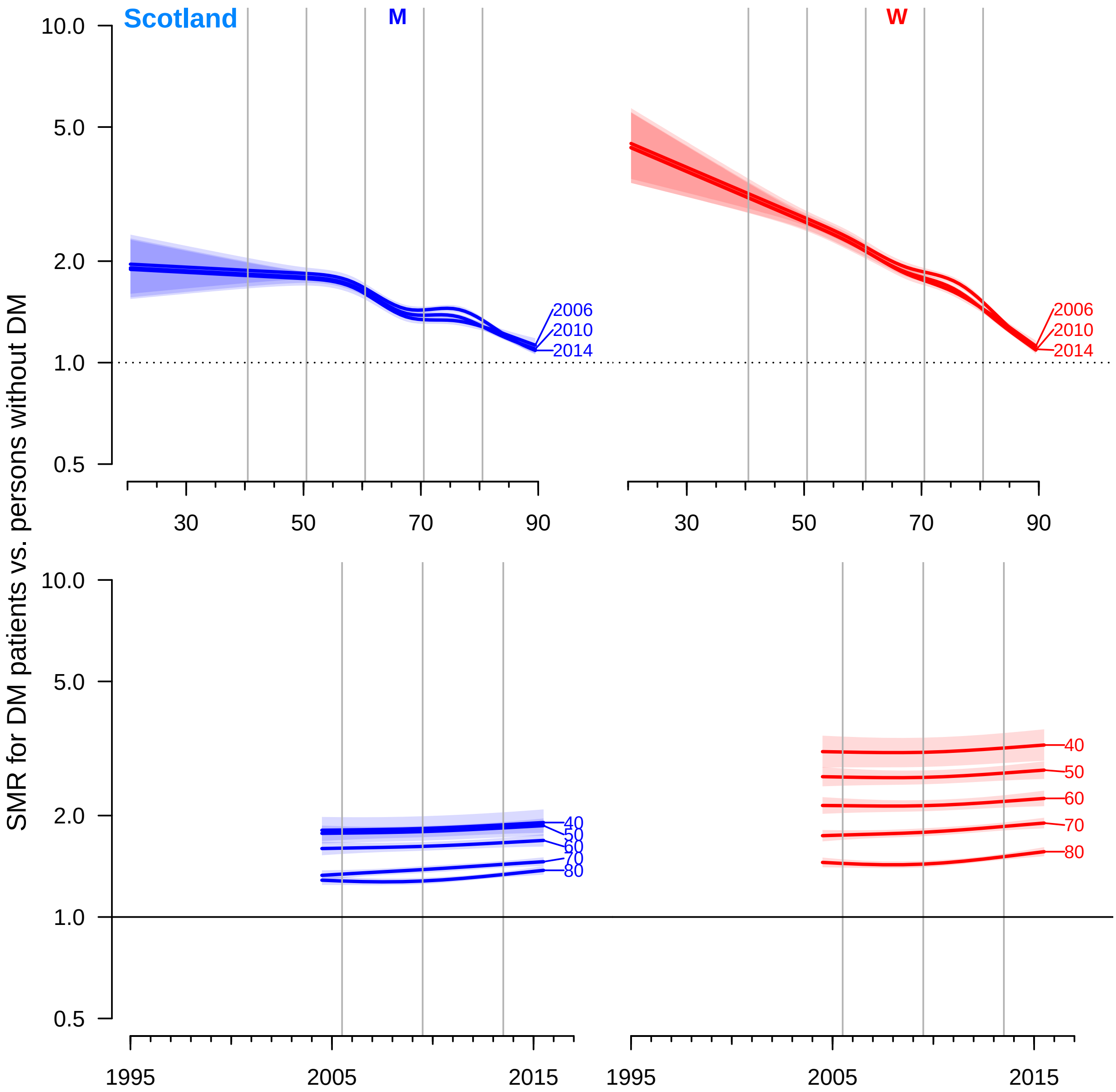

Figure A 39: *Estimated SMR relative to the non-diabetes by age and period in Scotland. Estimates of the SMRs are from age-period-cohort models, fitted separately for men and women. Upper panels show age-specific SMRs at different dates, as indicated by vertical lines in the lower panels. Lower panels show period-specific SMRs at different ages, as indicated by vertical lines in the upper panels. Left panels (blue curves) are men, right panels (red curves) are women.*

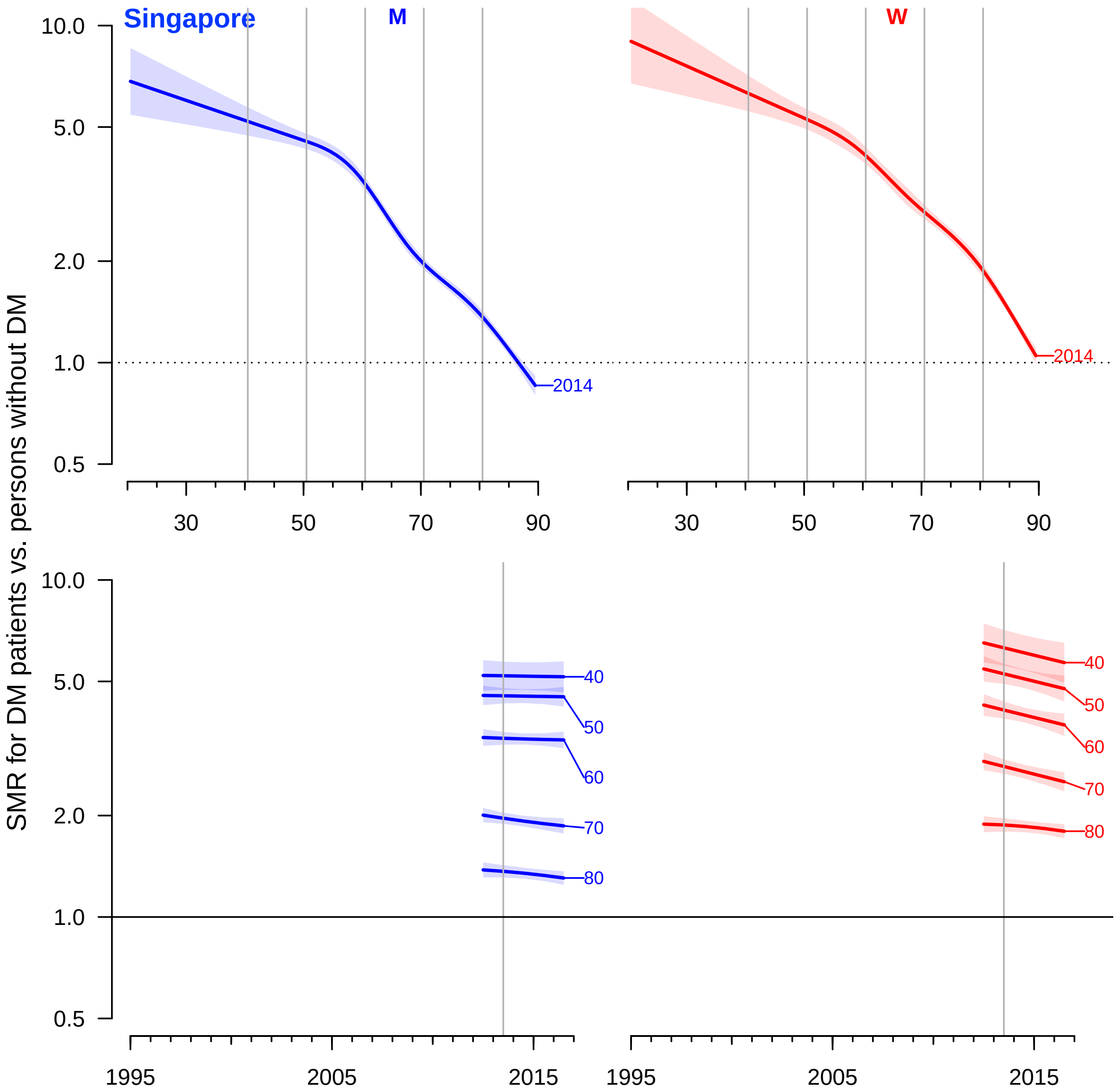

Figure A40: *Estimated SMR relative to the non-diabetes by age and period in Singapore. Estimates of the SMRs are from age-period-cohort models, fitted separately for men and women. Upper panels show age-specific SMRs at different dates, as indicated by vertical lines in the lower panels. Lower panels show period-specific SMRs at different ages, as indicated by vertical lines in the upper panels. Left panels (blue curves) are men, right panels (red curves) are women.*

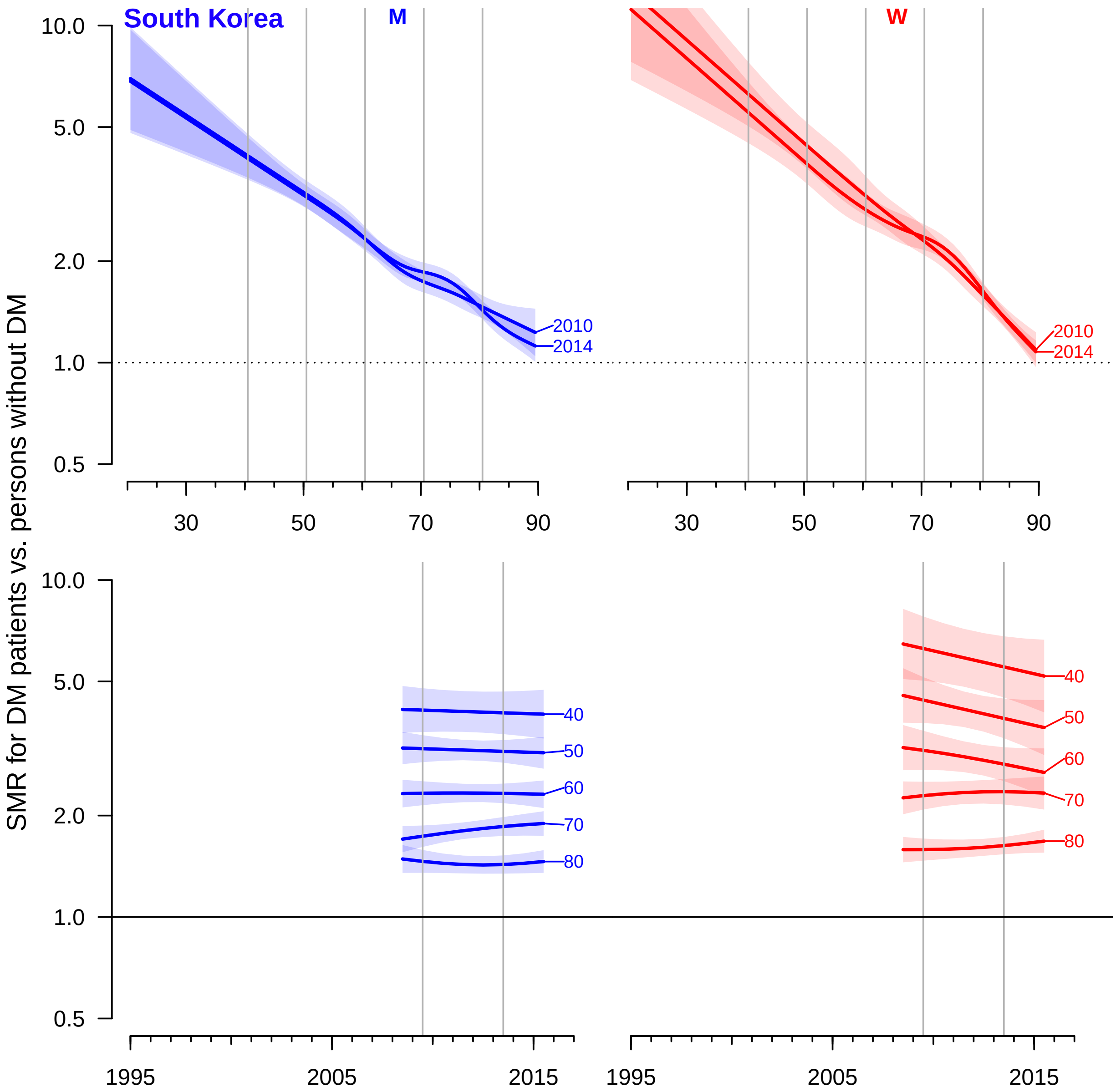

Figure A41: *Estimated SMR relative to the non-diabetes by age and period in SouthKorea. Estimates of the SMRs are from age-period-cohort models, fitted separately for men and women. Upper panels show age-specific SMRs at different dates, as indicated by vertical lines in the lower panels. Lower panels show period-specific SMRs at different ages, as indicated by vertical lines in the upper panels. Left panels (blue curves) are men, right panels (red curves) are women.*

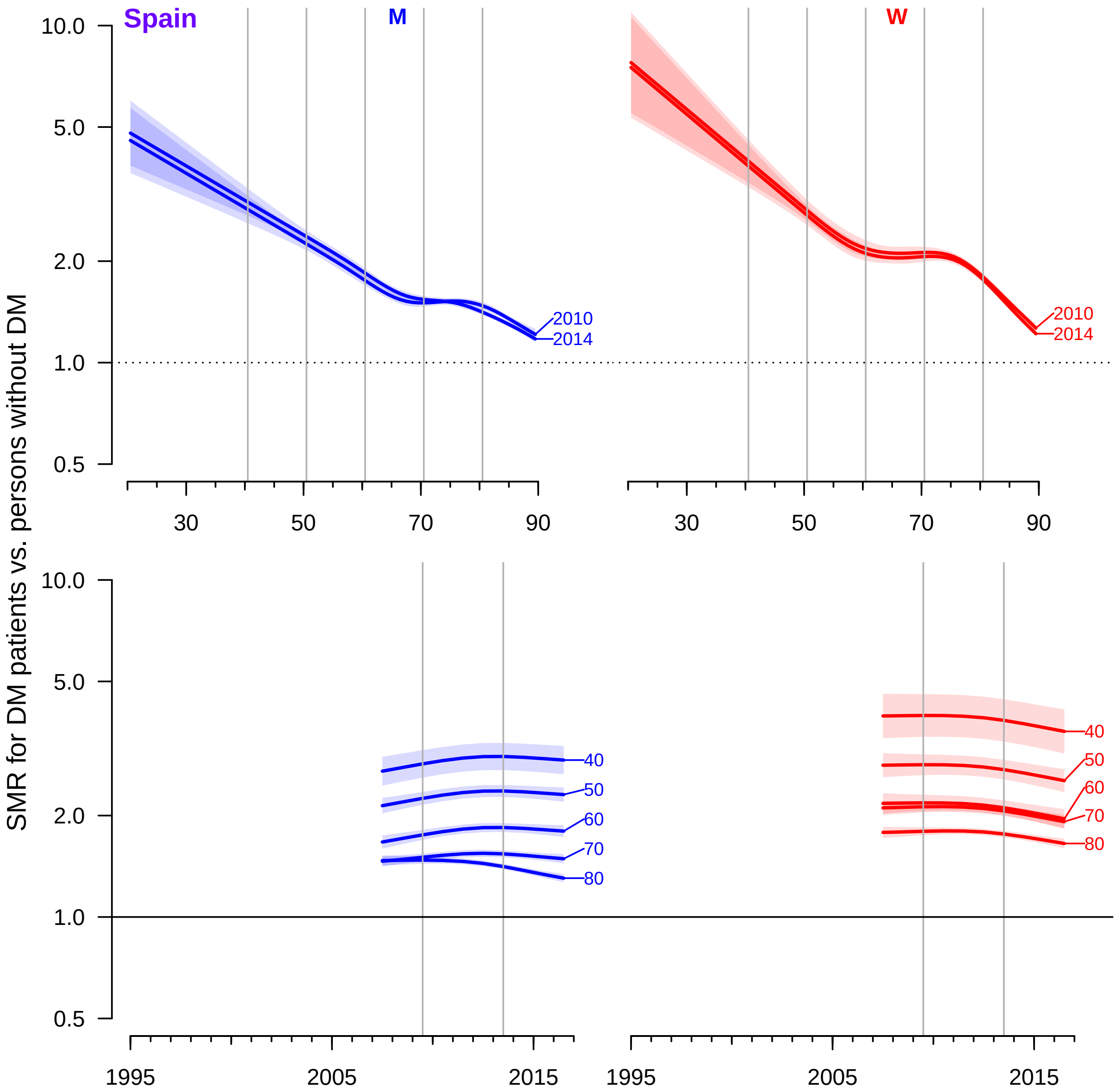

Figure A42: *Estimated SMR relative to the non-diabetes by age and period in Spain. Estimates of the SMRs are from age-period-cohort models, fitted separately for men and women. Upper panels show age-specific SMRs at different dates, as indicated by vertical lines in the lower panels. Lower panels show period-specific SMRs at different ages, as indicated by vertical lines in the upper panels. Left panels (blue curves) are men, right panels (red curves) are women.*

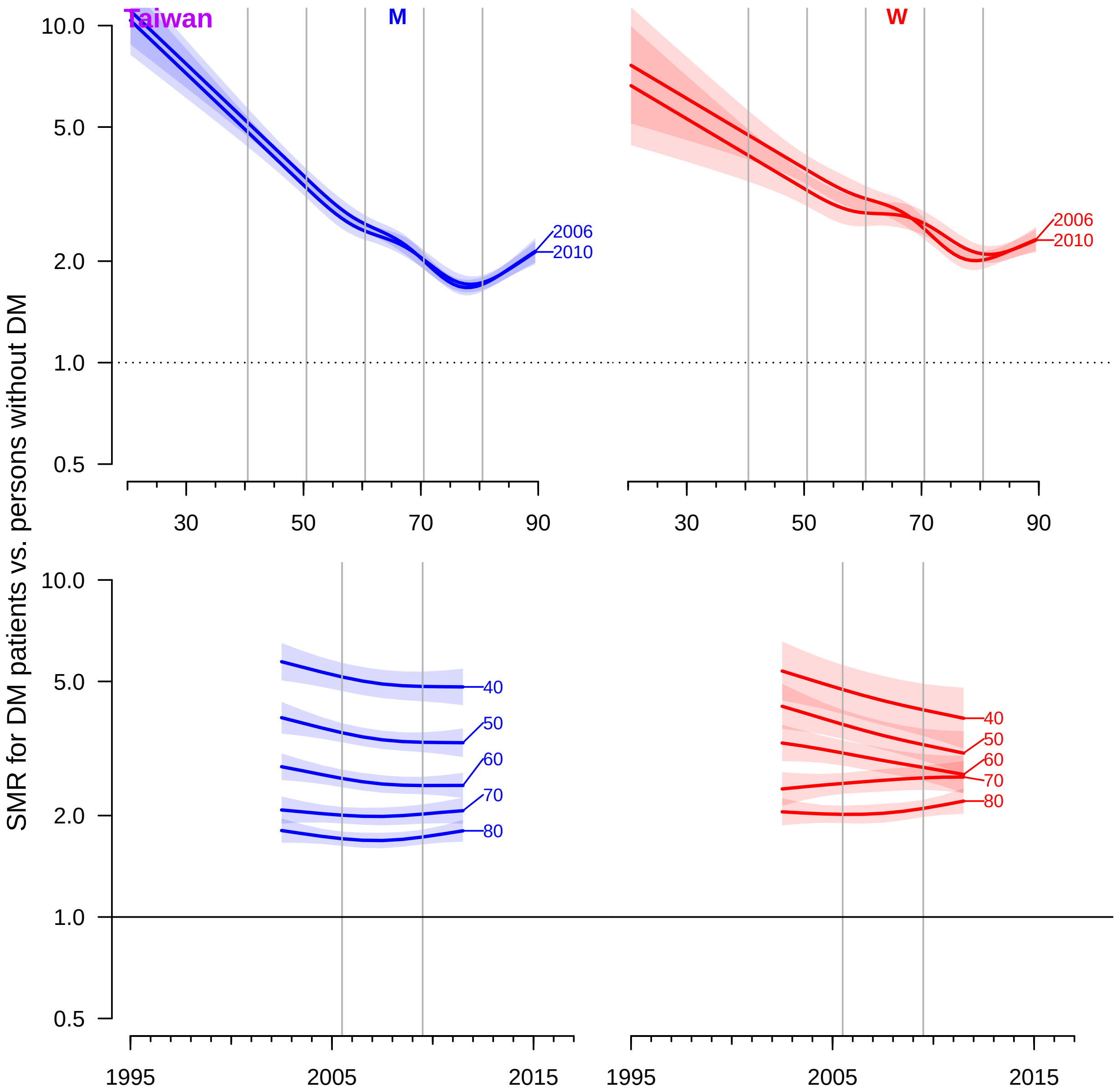

Figure A 43: *Estimated SMR relative to the non-diabetes by age and period in Taiwan. Estimates of the SMRs are from age-period-cohort models, fitted separately for men and women. Upper panels show age-specific SMRs at different dates, as indicated by vertical lines in the lower panels. Lower panels show period-specific SMRs at different ages, as indicated by vertical lines in the upper panels. Left panels (blue curves) are men, right panels (red curves) are women.*

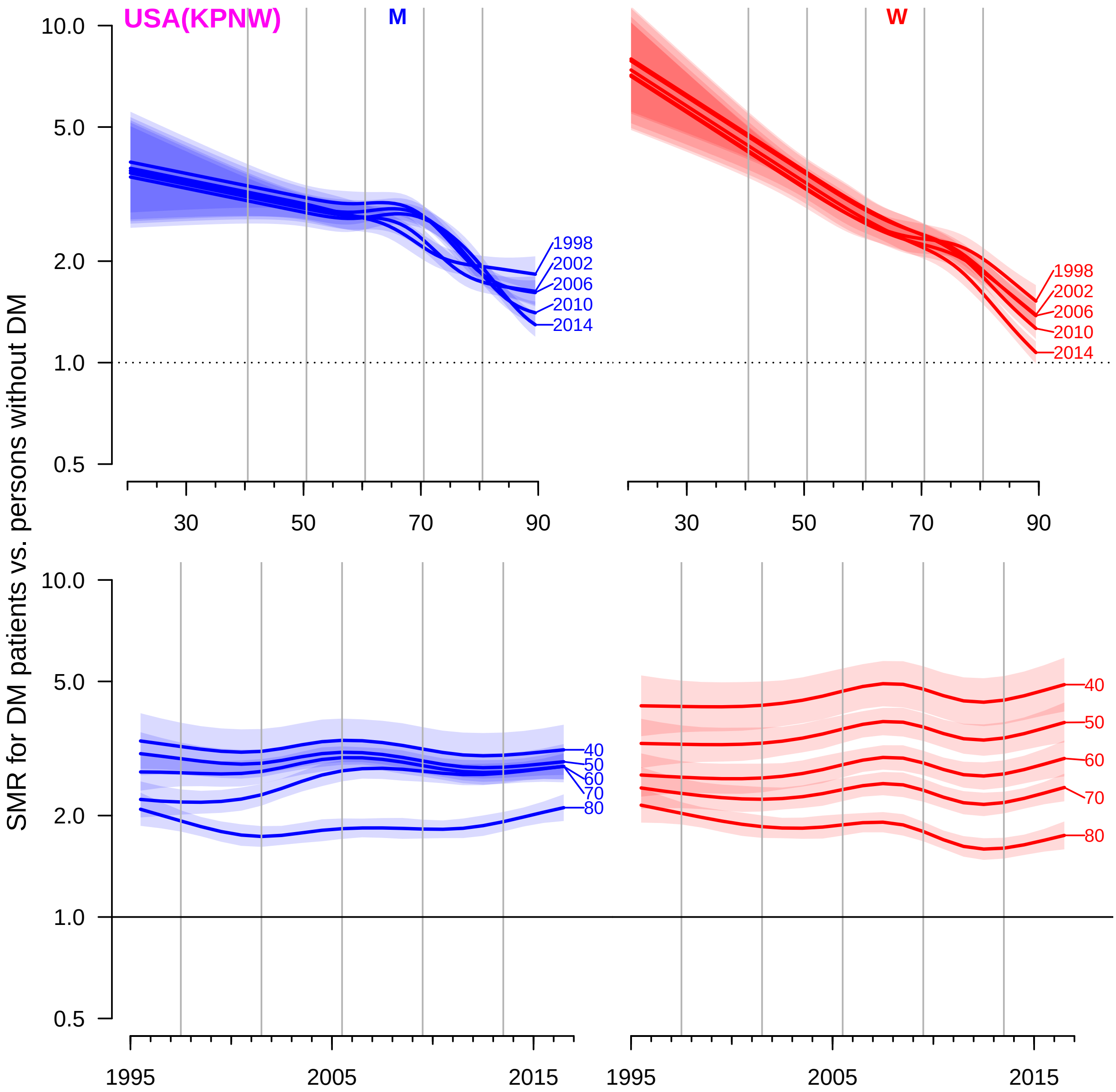

Figure A44: *Estimated SMR relative to the non-diabetes by age and period in USA(KPNW). Estimates of the SMRs are from age-period-cohort models, fitted separately for men and women. Upper panels show age-specific SMRs at different dates, as indicated by vertical lines in the lower panels. Lower panels show period-specific SMRs at different ages, as indicated by vertical lines in the upper panels. Left panels (blue curves) are men, right panels (red curves) are women.*

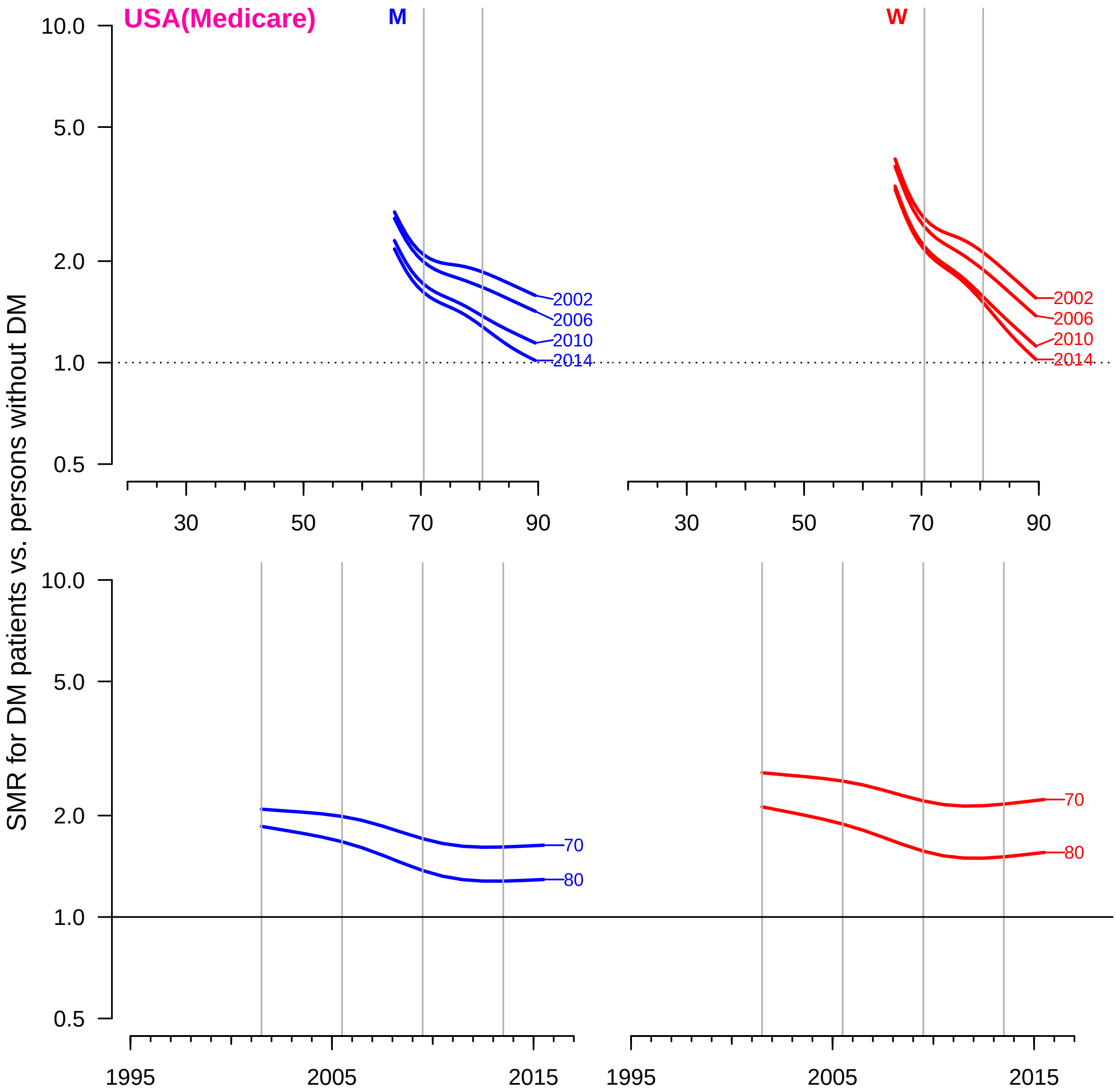

Figure A45: *Estimated SMR relative to the non-diabetes by age and period in USA(Medicare). Estimates of the SMRs are from age-period-cohort models, fitted separately for men and women. Upper panels show age-specific SMRs at different dates, as indicated by vertical lines in the lower panels. Lower panels show period-specific SMRs at different ages, as indicated by vertical lines in the upper panels. Left panels (blue curves) are men, right panels (red curves) are women.*

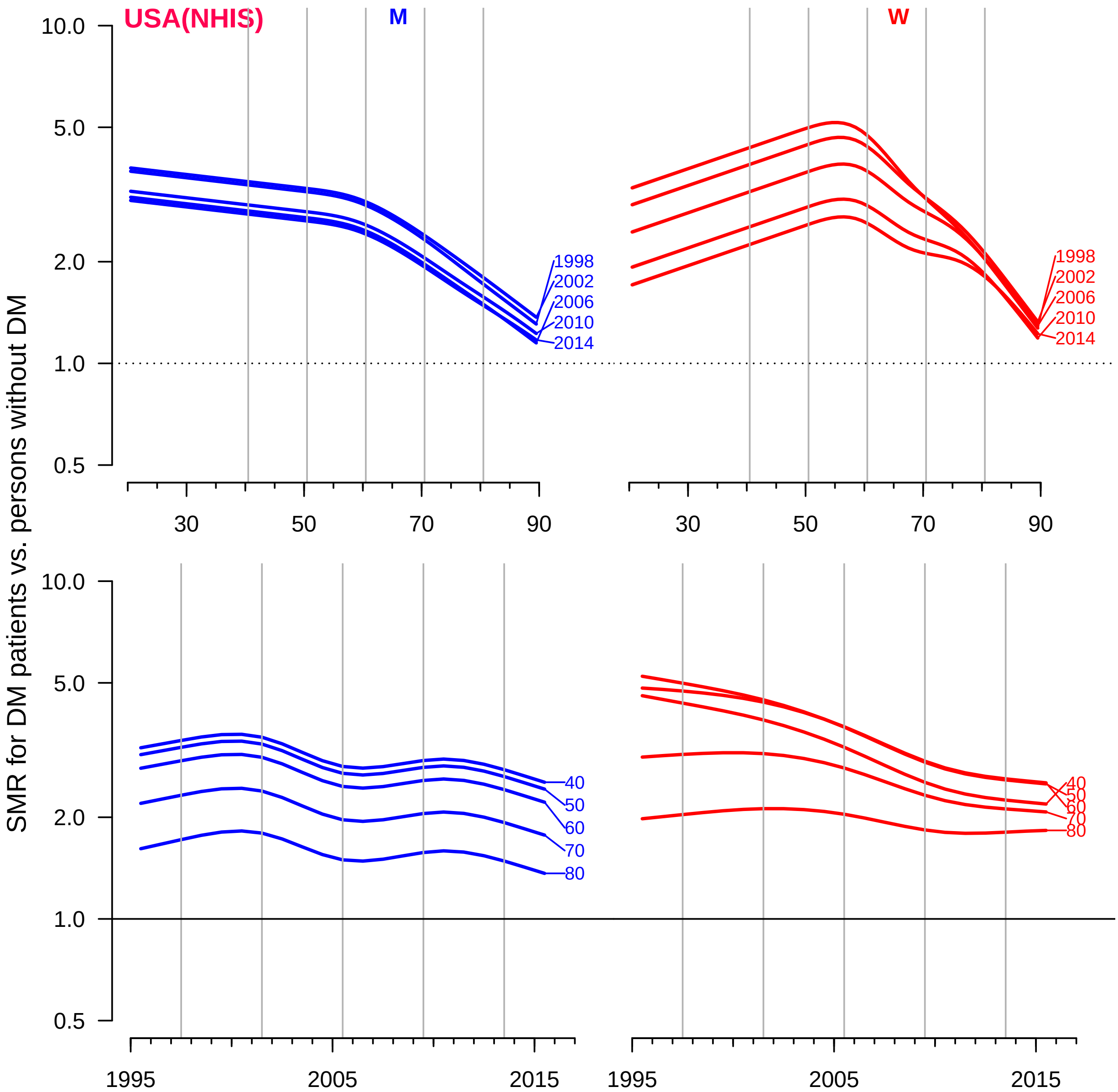

Figure A46: *Estimated SMR relative to the non-diabetes by age and period in USA(NHIS). Estimates of the SMRs are from age-period-cohort models, fitted separately for men and women. Upper panels show age-specific SMRs at different dates, as indicated by vertical lines in the lower panels. Lower panels show period-specific SMRs at different ages, as indicated by vertical lines in the upper panels. Left panels (blue curves) are men, right panels (red curves) are women.*

4.3 Age by time interaction

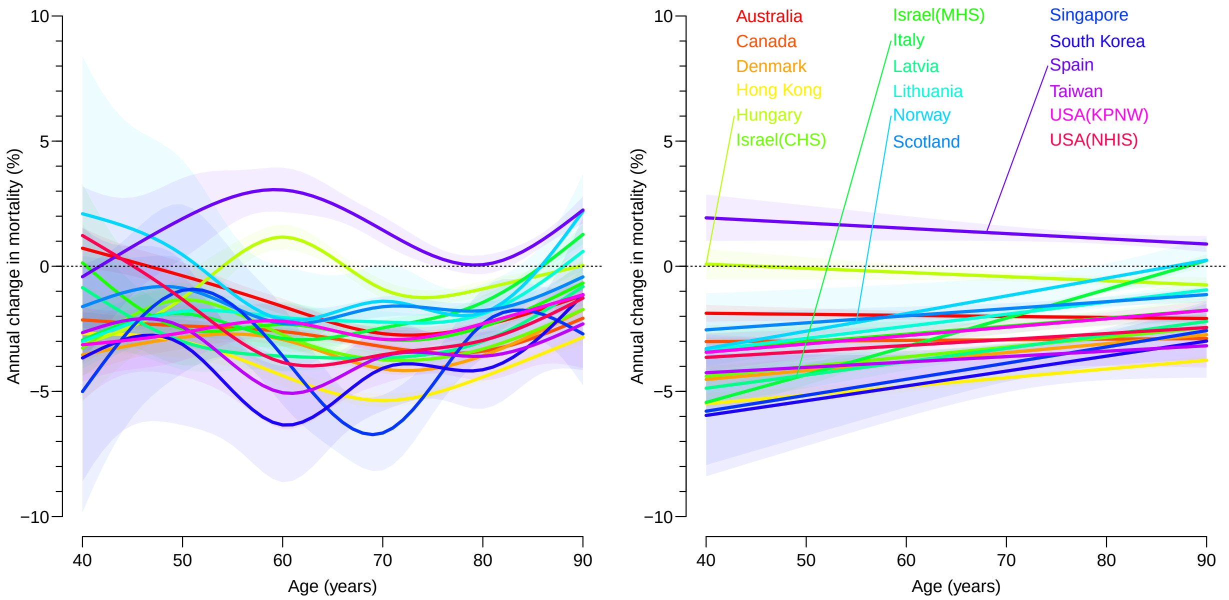

Figure A47: *Age by time interaction of mortality rates as estimated annual change in mortality by age. USA(Medicare) is excluded because of the limited age-range (65+) in the study. Estimates are From a model with calendar time trend varying by age. The left panel is from using a spline for age (a varying coefficients model), the right panel just using the product of age and calendar time.*
12 of the formal tests for interaction were significant, but there is no systematic pattern. Except possibly that the between-centres variation is smaller in older ages, but this is most likely attributable to the larger uncertainty in time-trends of mortality in the younger ages (where there are much fewer deaths).
The absolute sizes of the estimates (i.e. where the lines are located), are consistent with the overall picture of mortality rates among diabetes patients declining some 3–5 % per year.

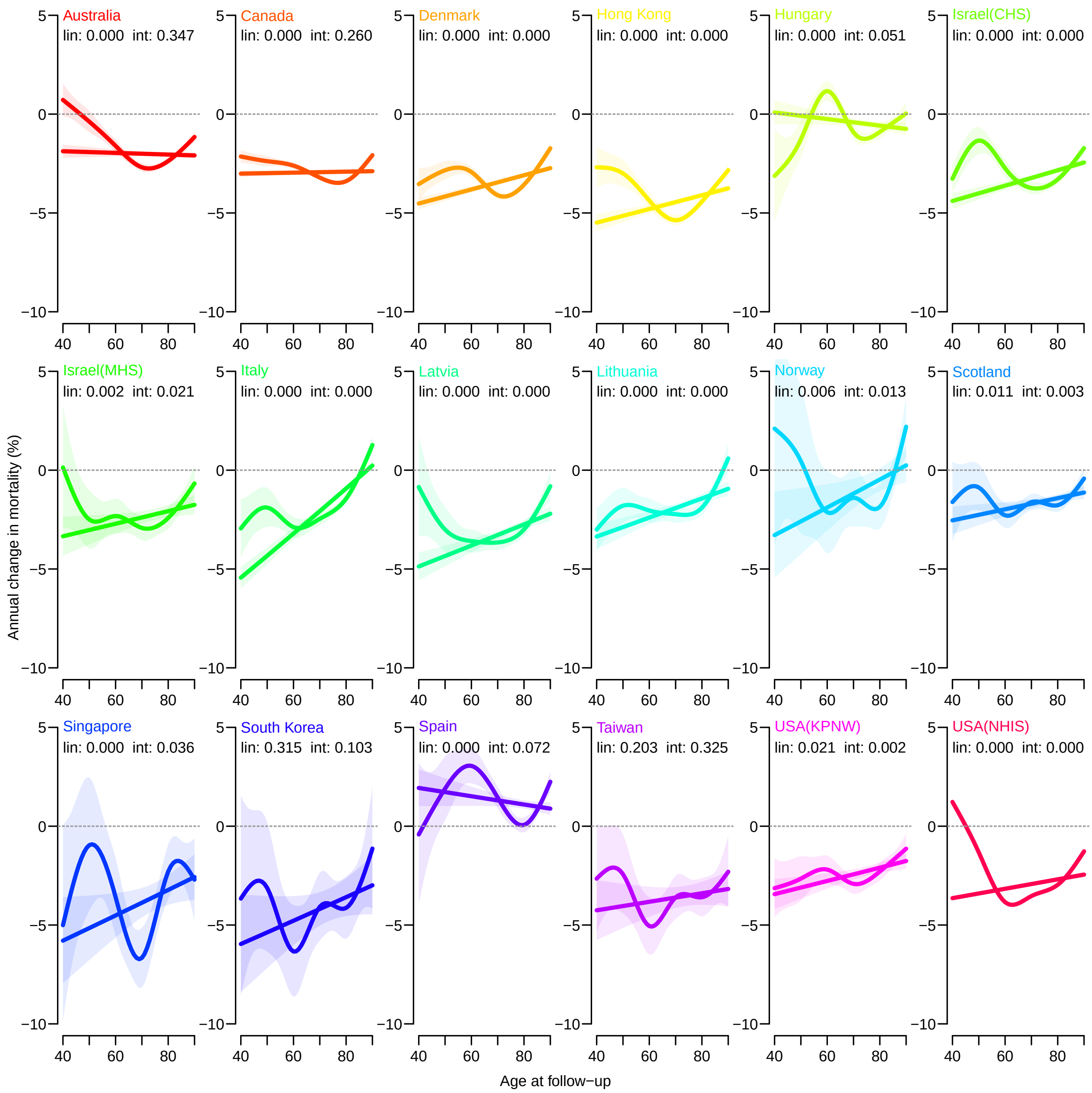

Figure A48: *Age by time interaction of mortality rates as estimated annual change in mortality by age. USA(Medicare) is excluded because of the limited age-range (65+) in the study. Estimates are from models with calendar time trend varying by age, either by smooth splines or linearly; both plotted in each panel. The curves here are the same as in figure A47, just arranged differently. The numbers in the plots are p-values for the hypotheses of linear interaction (*`lin`*—smooth curve not different from linear) and no linear interaction (*`int`*—line has slope 0).*
The absolute sizes of the estimates (i.e. where the curves are located), are consistent with the overall picture of mortality rates among diabetes patients declining some 3–5 % per year.