Prevalence, incidence and mortality of type 1 and type 2 diabetes in Denmark 1996–2016

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1 Material and methods

This section provides further details on the underlying register and the statistical methods used in the analysis.

A complete documentation of the construction of the register and the analysis files of prevalence and follow-up can be found in
http://BendixCarstensen.com/DMreg/Reg2016.pdf , and a complete account of all statistical analyses based on these is available in
http://BendixCarstensen.com/DMreg/Ana2016.pdf. Both documents are approximately 300 pages, as they contain a complete code documentation and extensive tabulations of results.

1.1 Register data

The Danish national health care system (NHS) is run by the state (through 5 health care regions) and covers all Danish citizens free of charge. Thus all citizens are in the *same* system.

Furthermore, in Denmark (as in all Nordic Countries) there are population-wide registers covering virtually all aspects of life, including heath care. All registers are linkable by a unique person id [1], so residents of Denmark can be followed with respect to disease occurrence, medicine purchase, health care use, migration etc.

The registers are available for research purposes at a secure server at Statistics Denmark in anonymized, linkable form; Statistics Denmark generates an id which can be used for linkage across the registers at our disposal, but not to identify a person. Thus, linkage is exact, not probabilistic.

1.1.1 Diabetes data

We constructed a Danish diabetes register from existing Danish health care registers. The five registers are considered to be those where diabetes patients will appear, so our approach has been to maximize sensitivity. We included persons as diabetes patients using the *earliest* of the following dates from the registers as inclusion date (all registers may have multiple records per person):

- first diagnosis of diabetes (ICD-8: 249, 250; ICD-10: E10, E11) in the National Patient Register [2] (NPR; 1977–). The NPR is a register of all contacts with the hospital system, from 1990 also including visits to out-patient clinics.

- first use of "podiatry for diabetes patients" as recorded in the National Health Services Register [3] (NHSR, 1990–). The NHSR includes all billings for health services paid to health care providers, and "podiatry for diabetes patients" are only available for persons with a referral from physician. Hence everyone in this database is a verified diabetes patient.

- first date of purchase of any anti-diabetic medication (ATC A10xxx) in the Medicines Products Register [4] ("Prescription register") (MPR, 1995–). The MPR includes all filled prescriptions since 1995-01-01 with detailed information on product and amount, linked to the person-id.

- first date of diagnosis mentioned in the Danish Adult Diabetes Database [5] (DADD, 2005–). The DADD is a database for quality monitoring where clinical information on diabetes patients is reported annually by GPs and outpatient clinics. The reports include information on type of diabetes (as T1D, T2D or other type). Hence everyone in this database is a verified diabetes patient. The information from outpatient clinics is complete, but that from general practice is currently incomplete. But since all T1D patients are seen in outpatient clinics, this data base will identify all T1D patients, in the period of coverage.

  The dates of diagnosis are inaccurate (83% are either 1 Jan or 15 Jul), so the date from DADD is only used if DADD is the only source for a given person. Thus DADD is mainly used for classification of patients as T1D/T2D.

- first date of eye examination recorded in the diaBase [6] (diaB, 2009–). The diaBase is a data base for quality monitoring of retinopathy screening, where eye-screenings of diabetes patients are reported. Hence everyone in this database is a verified diabetes patient.

In order to increase specificity of the recording we included only persons from the second date of either NPR or MPR recording; we extracted the two first dates of NPR recordings and the dates of two first MPR recording, and used the second of these four dates as the inclusion date.

Dates within 30 days prior and 365 days after a recorded diagnosis of gestational diabetes in the NPR were disregarded. Dates of metformin purchase between a date of polycystic ovary syndrome (PCOS) and the woman's 40^{th} birthday were disregarded. Purchase of metformin in women between 18 and 40 were disregarded because purchase of metformin alone was considered most likely to be part of treatment of infertility in a PCOS patient.

Type of diabetes: A person was classified as T1D from DADD if the majority of the person's records classified the person as T1D, and similarly for T2D. Persons not meeting any of these criteria were left unclassified by the DADD — this would be persons classified as other type of DM or with an equal number of classifications as T1D and T2D.

A person was classified as T1D from NPR if the majority of the person's records classified the person as T1D, and similarly for T2D. Persons not meeting any of these criteria were left unclassified by the NPR — this would be persons with an equal number of records with classification as T1D and T2D.

Persons were classified as T1D in the diabetes register if any of the following criteria were met (and otherwise as T2D):

- Purchase of oral anti-diabetic drugs (OAD) before age 15
- Purchase of insulin before age 30
- DADD classification as T1D.
- Unclassified from DADD, but classified as T1D from NPR.

Finally, persons without a recorded insulin purchase in the MPR, will always be classified a T2D regardless of the above. Persons not classified as T1D are classified as T2D.

The main source of T1D status was the DADD, which however only comprises persons alive at 2005 or later, so the sensitivity of the T1D classification is declining backwards in time prior to 2005, particularly for persons who died before 2005.

Strictly speaking, the classification of persons by type (as of the date of inclusion) depends on recordings *later* than the date of inclusion, and so we are formally conditioning on the future in the definition of diabetes type.

Time-range of the constructed register: The MPR is complete from 1995-01-01, so if the first recorded anti-diabetic drug purchase was after 1996-01-01, *i.e.* after at least one year with no recorded purchase, we assumed that it was actually a first drug purchase for that person. Since the other major sources of information predates 1996, we assume the constructed register to be reliable as incidence register from 1996-01-01, with the persons in the register alive as of that date to be a reliable recording of prevalent cases. This implies that dates of entry to the register before 1996-01-01 are unreliable as dates of diagnosis of diabetes, and these persons are only included as prevalent cases of diabetes as of 1996-01-01. The latter limits analyses involving duration of diabetes to persons included in the register after 1996-01-01.

1.1.2 Population data

In addition to the registers mentioned above, we had access to complete individual level register information on the entire Danish population, including sex and dates of birth, emigration, immigration and death as well as cause of death.

1.2 Tabulation of data

With the described register information we were able to classify all follow-up time (person-years and events of diabetes and death) in the entire Danish resident population as being either without diabetes or with T1D or T2D. We have observations from the registers for the 21 calendar years 1996 through 2016, so the last date of observation is 2016-12-31, which we for convenience in connection with dates of prevalence will label as 2017-01-01 (or just 2017).

1.2.1 Prevalence

The number of prevalent cases of T1D and T2D separately, alive at 1 January 1996–2017 were tabulated by sex and 1-year age group. The corresponding total population counts at each date were derived from our total register of the Danish population.

1.2.2 Follow-up

Periods after emigration and before immigration were excluded from the tabulation of follow-up. The follow-up (time at risk, events of diabetes by type and death by cause) in the Danish population 1996–2016 incl. was tabulated by current diabetes status (no DM, T1D, T2D), sex, age and date of follow-up and date of birth in 1-year classes (Lexis triangles, [7]). As an example, persons who contribute follow-up in the age class 66 during the year 2006 are classified by date of birth in one of two groups: those born in 1939 (who are 66 years of age as of 2006-01-01), and those born in 1940 (who turn 66 during 2006).

Among those born in 1939 the mean age at follow-up is $66\frac{2}{3}$, and the mean date of follow-up is $2006\frac{1}{3}$, and consequently the mean date of birth $1939\frac{2}{3}$. Among those born in 1940 the mean age at follow-up is $66\frac{1}{3}$, and the mean date of follow-up is $2006\frac{2}{3}$, and consequently the mean date of birth is $1940\frac{1}{3}$.

Further, the follow-up among diabetes patients diagnosed after 1996-01-01 (for whom date of diagnosis was known) were further classified by duration of diabetes in intervals divided at 0, 0.2, 0.5, 1, 2,... years, *i.e.* with means 0.1, 0.35, 0.75, 1.5, 2.5,... years.

These mean values are used as *quantitative* variables in the modeling of age, calender time, birth cohort and duration effects on incidence and mortality rates, as well as duration effects on mortality.

1.3 Statistical methods

All statistical models were fitted separately for men and women and for no DM (where relevant), T1D and T2D. For each tabulation unit (Lexis triangle) we used the mean of current age (occasionally termed attained age or age at follow-up), date and duration of diabetes and date of birth, as *quantitative* explanatory variables. The effect of these were modeled by natural splines (restricted cubic splines).

1.3.1 Prevalence

We modeled prevalence separately for each of the dates 1 January 1996–2017 by restricted cubic splines for age, using a binomial model with log-link. The resulting age-curves were shown for each of the 22 dates. We also fitted models jointly for all dates with a linear effect of date in order to devise an overall annual relative change in prevalence.

1.3.2 Incidence rates

Incidence rates were modeled using Poisson models with log person time as offset and natural cubic spline effects of current age and date of follow-up and date of birth (age-period-cohort (APC) model [7]). We used 2015-01-01 as reference point for calendar time, thus rendering the age-specific rates estimates of the rates as of this date, the period effects as estimates of RR relative to 2015-01-01 and the cohort effects as residual effects relative to this. We extracted the overall linear trend (drift) from the APC models. Finally, we also show the non-linear time-trends evaluated at different ages derived from these models.

1.3.3 Mortality rates

Mortality rates were modeled using Poisson models with log person time as offset and natural cubic spine effects of calendar time, current age, duration of diabetes, age at diagnosis (calculated as current age minus duration).

We used 2015-01-01 as reference point for the calendar time, thus rendering the age-specific mortality rates estimates of the rates as of this date. As model check we also show the residuals by date of birth as RRs from this model.

1.3.4 Age, duration and age at diagnosis

Since the variables current age, duration and age at diagnosis are linearly connected (current age = age at diagnosis + duration of diabetes) we cannot separate the effects of them without further assumptions (see e.g. [7]). For example, we may claim that mortality increases more by current age, if we are willing to assume that it increases correspondingly less by diabetes duration and age at diabetes diagnosis. Hence if we include all three variables in a model we cannot make a claim as to an isolated effect of any particular of the three.

Specifically, suppose we aim to describe the mortality rates (μ) as a function of current age, a; duration of diabetes, d and age at diagnosis, $e = a - d$ ("e" for age at diagnosis; $e$ntry into diabetes), then we have that $a - d - e = 0$. If we formally set up a model with only the effect of current age and age at diagnosis of diabetes:

$$\log\big(\mu(a,d)\big) = f(a) + h(e)$$

it is only superficially that this does not include duration: since $a-d-e=0$, we may write:

$$\begin{aligned}\log\big(\mu(a,d)\big) &= f(a) + h(e)\\ &= f(a) + h(e) + \gamma(a-e-d)\\ &= \big(f(a)+\gamma a\big) + \big(h(e)-\gamma e\big) - \gamma d\end{aligned}$$

Thus, even if duration is not formally included in the model we may claim that is has any *linear* effect we like, by simply asserting that the age and age at diagnosis effects are different by a similar linear amount. Thus there is no way to allocate a "correct" duration effect, let alone effects of current age and age at diagnosis. One might of course on purely external grounds (*i.e.* unrelated to the data at hand) assert that there is no duration effect, but this can never be founded in data.

Therefore, it makes more sense to set up a model with non-linear effects of all three variables. But we still have the problem from the linear dependence:

$$\begin{aligned}\log\big(\mu(a,d)\big) &= f(a) + g(d) + h(e)\\ &= f(a) + g(d) + h(e) + \gamma(a-d-e)\\ &= \big(f(a)+\gamma a\big) + \big(g(d)-\gamma d\big) + \big(h(e)-\gamma e\big)\\ &= \tilde{f}(a) + \tilde{g}(d) + \tilde{h}(e)\end{aligned}$$

Here it is seen that we can have two *different* sets of three effects that together produce the same mortality rates; moreover this would be the case for *any* value of γ we care to stick into the formula.

Even if we cannot separate the three effects in the model, we can still make perfectly valid predictions from the model, and certain contrasts will also be identifiable from the model. Notably it is possible to estimate the mortality rate-ratio at a given age (a) between persons diagnosed at different ages, e_1 and e_0, and hence with durations $a - e_1$ and $a - e_0$:

$$\begin{aligned}\log(\mathrm{RR}_{e_1 \text{vs } e_0}) =& f(a) + g(a-e_1) + h(e_1) -\\ & f(a) - g(a-e_0) - h(e_0)\\ =& g(a-e_1) - g(a-e_0) + h(e_1) - h(e_0)\end{aligned}$$

Using another set of effects $\tilde{f}$, $\tilde{g}$ and $\tilde{h}$ the sum of which is distinguished from these by a term $\gamma(a-d-e)$:

$$\begin{aligned}
\log(\mathrm{RR}_{e_1 \text{vs } e_0}) =& \tilde{g}(a-e_1) - \tilde{g}(a-e_0) + \tilde{h}(e_1) - \tilde{h}(e_0) \\
=& \big(g(a-e_1) - \gamma(a-e_1)\big) - \\
& \big(g(a-e_0) - \gamma(a-e_0)\big) + \\
& \big(h(e_1) - \gamma e_1\big) - \\
& \big(h(e_0) - \gamma e_0\big) \\
=& g(a-e_1) - g(a-e_0) + h(e_1) - h(e_0) + \gamma(-a+e_1+a-e_0-e_1+e_0) \\
=& g(a-e_1) - g(a-e_0) + h(e_1) - h(e_0)
\end{aligned}$$

This shows that these contrasts are invariant under *any* reparametrization, and hence *are* identifiable from any parametrization of the model.

Since the intercept and the linear effects of current age, age at diagnosis and duration of diabetes cannot be separated, we reported the estimated mortality as a function of current age, using separate curves for persons diagnosed at ages 30, 45 etc. (different between T1D and T2D); each curve stretching from the age at diagnosis and 20 years on (20 years being the range of duration for which we have reasonably reliable information). The mortality curves are thus showing the *joint* effect of current age, age at diagnosis and duration of disease (see *e.g.* [8].)

1.3.5 Mortality data range

Since only persons included after 1996-01-01 have a reliable date of diagnosis, mortality analyses using age at diagnosis and duration were restricted to persons included after this date. For comparability with other studies, age-specific mortality rates ignoring both age at diagnosis and duration were reported both for the restricted group of patients diagnosed after 1996-01-01 and for all patients (that is, also including the prevalent cases as of 1996-01-01).

Analyses were made separately for men and women and for T1D and T2D separately. We computed M/W mortality rate-ratios for each type of diabetes, and T1D/T2D mortality rate-ratios for men and women separately.

1.3.6 Standardized Mortality Ratio (SMR)

We used the data from persons without DM to calculate empirical mortality rates among persons without diabetes, classified by sex, age, date of follow-up and date of birth. Multiplying these with the corresponding person years among diabetes patients yielded the expected number of deaths during T1D and T2D follow-up.

The SMR was modeled exactly as the mortality by current age, duration of diabetes and age at diagnosis, but using the log of the expected number of deaths as offset deriving the SMR as the mortality rate-ratio between T1D, resp. T2D and no DM.

1.4 Sensitivity analyses

Due to the larger uncertainty of T1D/T2D classification prior to 2005 we made separate mortality analyses using only follow-up after 2005, shown in ESM figure 5 — compared

with ESM figure 4.

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Table ESM 1: *Persons, follow-up time and ages and dates of entry and follow-up from the Danish Diabetes Register. Includes also persons over 100 years of age and time during non-residency in Denmark. Medians and inter-quartile ranges (IQR, 25th and 75th percentiles).* <1996 *refer to the prevalent cases as of 1st January 1996;* 1996+ *refer to diabetes cases included in the register after this date.*

No. persons	Sex	T1D	T2D	DM
< 1996	M	12,378	30,338	42,716
	W	9,596	31,129	40,725
	M+W	21,974	61,467	83,441
1996+	M	11,646	192,418	204,064
	W	8,173	152,767	160,940
	M+W	19,819	345,185	365,004
Total	M+W	41,793	406,652	448,445

		T1D			T2D		
		Median	IQR		Median	IQR	
Date of inclusion[1,2]							
1996+	M	2005.7	2000.5	2010.9	2008.5	2003.1	2012.4
	W	2005.6	2000.4	2011.0	2008.3	2002.8	2012.3
Age at inclusion[1]							
1996+	M	30.7	15.7	47.6	62.1	53.0	70.6
	W	26.8	12.4	48.5	64.6	54.1	74.2
Person-years							
< 1996	M	21.0	9.5	21.0	8.9	3.6	18.2
	W	21.0	9.3	21.0	9.1	3.8	18.9
1996+	M	8.9	4.3	14.5	6.0	3.0	10.5
	W	9.3	4.4	14.9	6.1	3.1	10.9
Date of follow-up[2,3]							
< 1996	M	2006.5	2000.7	2006.5	2000.4	1997.8	2005.1
	W	2006.5	2000.6	2006.5	2000.6	1997.9	2005.5
1996+	M	2011.0	2008.0	2013.9	2012.5	2008.8	2014.6
	W	2011.0	2008.1	2014.0	2012.3	2008.7	2014.6
Age at follow-up[3]							
< 1996	M	53.5	41.3	65.3	70.9	62.5	78.2
	W	55.5	41.3	71.0	76.0	66.6	82.7
1996+	M	36.5	20.6	52.4	65.9	57.1	73.9
	W	32.4	17.4	53.8	68.4	58.2	77.7

[1] Persons included before 1996 do not have a reliable date of inclusion, hence neither date nor age at inclusion can be meaningfully computed.

[2] Dates are coded so that 1st January 2006 is 2006.000 and 31st December 2006 is 2006.997.

[3] Median and IQR for the median date/age of follow-up for each person.

Table ESM 2: *Number of prevalent diabetes patients in Denmark at 1 January each year 1996–2017 by diabetes type and sex. Includes also persons over 100 years of age.*

	T1D		T2D		%T1		All DM		
Date	M	W	M	W	M	W	M	W	M+W
1996	12,328	9,549	30,269	31,313	28.9	23.4	42,597	40,862	83,459
1997	12,677	9,776	33,790	34,110	27.3	22.3	46,467	43,886	90,353
1998	12,958	9,986	36,952	36,433	26.0	21.5	49,910	46,419	96,329
1999	13,222	10,113	40,711	39,166	24.5	20.5	53,933	49,279	103,212
2000	13,386	10,235	44,398	42,132	23.2	19.5	57,784	52,367	110,151
2001	13,560	10,295	47,960	44,905	22.0	18.7	61,520	55,200	116,720
2002	13,729	10,371	51,627	47,480	21.0	17.9	65,356	57,851	123,207
2003	13,845	10,452	56,329	51,822	19.7	16.8	70,174	62,274	132,448
2004	13,948	10,479	61,908	56,419	18.4	15.7	75,856	66,898	142,754
2005	14,012	10,567	67,642	61,118	17.2	14.7	81,654	71,685	153,339
2006	14,072	10,644	72,161	64,348	16.3	14.2	86,233	74,992	161,225
2007	14,209	10,715	76,556	66,962	15.7	13.8	90,765	77,677	168,442
2008	14,339	10,801	81,389	70,320	15.0	13.3	95,728	81,121	176,849
2009	14,485	10,901	87,374	74,596	14.2	12.8	101,859	85,497	187,356
2010	14,648	10,979	93,778	78,796	13.5	12.2	108,426	89,775	198,201
2011	14,745	11,078	101,220	83,763	12.7	11.7	115,965	94,841	210,806
2012	14,860	11,177	112,085	93,133	11.7	10.7	126,945	104,310	231,255
2013	14,988	11,289	119,930	99,369	11.1	10.2	134,918	110,658	245,576
2014	15,116	11,458	125,077	103,338	10.8	10.0	140,193	114,796	254,989
2015	15,304	11,614	129,587	106,584	10.6	9.8	144,891	118,198	263,089
2016	15,512	11,826	134,172	109,844	10.4	9.7	149,684	121,670	271,354
2017	15,684	11,930	139,209	113,307	10.1	9.5	154,893	125,237	280,130

Table ESM 3: *Crude prevalence (%) of diabetes in Denmark at 1 January 1996–2017 by diabetes type and sex. Includes also persons over 100 years of age.*

	T1D		T2D		All DM		
Date	M	W	M	W	M	W	M+W
1996	0.47	0.36	1.16	1.17	1.64	1.53	1.58
1997	0.48	0.37	1.29	1.27	1.78	1.64	1.71
1998	0.49	0.37	1.41	1.36	1.90	1.73	1.81
1999	0.50	0.38	1.54	1.45	2.05	1.83	1.94
2000	0.51	0.38	1.68	1.56	2.19	1.94	2.06
2001	0.51	0.38	1.81	1.66	2.32	2.04	2.17
2002	0.52	0.38	1.94	1.74	2.45	2.13	2.29
2003	0.52	0.38	2.11	1.90	2.62	2.28	2.45
2004	0.52	0.38	2.31	2.06	2.83	2.45	2.64
2005	0.52	0.39	2.52	2.23	3.04	2.61	2.82
2006	0.52	0.39	2.68	2.34	3.20	2.73	2.96
2007	0.52	0.39	2.83	2.43	3.35	2.82	3.08
2008	0.53	0.39	2.99	2.54	3.52	2.93	3.22
2009	0.53	0.39	3.19	2.68	3.72	3.07	3.39
2010	0.53	0.39	3.41	2.82	3.94	3.21	3.57
2011	0.53	0.39	3.66	2.98	4.19	3.38	3.78
2012	0.54	0.40	4.04	3.30	4.57	3.70	4.13
2013	0.54	0.40	4.30	3.51	4.84	3.91	4.37
2014	0.54	0.40	4.46	3.64	5.00	4.04	4.52
2015	0.54	0.41	4.59	3.73	5.13	4.13	4.63
2016	0.54	0.41	4.70	3.81	5.24	4.22	4.73
2017	0.54	0.41	4.83	3.90	5.38	4.31	4.84

Table ESM 4: *Number of incident diabetes cases during each year 1996–2016 by diabetes type and sex. Excludes persons over 100 years of age and persons not resident at date of diagnosis.*

	T1D		T2D		All DM		
Period	M	W	M	W	M	W	M+W
1996	678	516	6,115	5,290	6,793	5,806	12,599
1997	684	489	5,839	4,918	6,523	5,407	11,930
1998	657	454	6,529	5,295	7,186	5,749	12,935
1999	592	413	6,739	5,707	7,331	6,120	13,451
2000	596	392	6,593	5,604	7,189	5,996	13,185
2001	586	415	6,795	5,449	7,381	5,864	13,245
2002	602	386	8,022	7,334	8,624	7,720	16,344
2003	545	386	9,146	7,673	9,691	8,059	17,750
2004	509	388	9,259	7,751	9,768	8,139	17,907
2005	517	379	8,174	6,510	8,691	6,889	15,580
2006	554	382	8,172	5,940	8,726	6,322	15,048
2007	564	384	8,738	6,792	9,302	7,176	16,478
2008	546	367	9,846	7,554	10,392	7,921	18,313
2009	568	357	10,762	7,720	11,330	8,077	19,407
2010	529	367	11,867	8,704	12,396	9,071	21,467
2011	496	358	15,593	13,150	16,089	13,508	29,597
2012	486	315	12,782	10,017	13,268	10,332	23,600
2013	471	351	10,215	7,971	10,686	8,322	19,008
2014	465	341	9,883	7,358	10,348	7,699	18,047
2015	476	375	9,987	7,638	10,463	8,013	18,476
2016	460	316	10,666	7,855	11,126	8,171	19,297
Sum	11,581	8,131	191,722	152,230	203,303	160,361	363,664

Table ESM 5: *Number of deaths among diabetes patients during each year 1996–2016 by diabetes type and sex. Only diabetes patients diagnosed since 1996-01-01.*

	T1D		T2D		All DM			non-DM
Period	M	W	M	W	M	W	M+W	M+W
1996	14	12	255	222	269	234	503	53,839
1997	28	16	577	455	605	471	1,076	53,020
1998	50	30	860	715	910	745	1,655	51,549
1999	85	34	1,217	908	1,302	942	2,244	51,971
2000	101	58	1,435	1,180	1,536	1,238	2,774	50,206
2001	97	83	1,737	1,356	1,834	1,439	3,273	50,734
2002	142	70	1,929	1,616	2,071	1,686	3,757	50,474
2003	141	100	2,279	1,828	2,420	1,928	4,348	49,280
2004	157	102	2,349	1,968	2,506	2,070	4,576	47,276
2005	196	111	2,600	2,194	2,796	2,305	5,101	46,366
2006	189	129	2,736	2,335	2,925	2,464	5,389	46,122
2007	186	108	2,990	2,529	3,176	2,637	5,813	46,507
2008	206	128	3,083	2,536	3,289	2,664	5,953	45,115
2009	194	129	3,507	2,797	3,701	2,926	6,627	45,008
2010	199	125	3,664	2,970	3,863	3,095	6,958	44,088
2011	166	107	3,831	2,999	3,997	3,106	7,103	42,294
2012	151	105	4,159	3,138	4,310	3,243	7,553	41,579
2013	147	84	4,336	3,341	4,483	3,425	7,908	41,183
2014	114	95	4,613	3,544	4,727	3,639	8,366	39,944
2015	123	81	4,796	3,779	4,919	3,860	8,779	40,947
2016	133	76	4,988	3,874	5,121	3,950	9,071	40,643

Table ESM 6: *Number of deaths among diabetes patients during each year 1996–2016 by diabetes type and sex. Includes both diabetes patients diagnosed from 1996-01-01 as well as prevalent cases of diabetes at this date.*

	T1D		T2D		All DM			non-DM
Period	M	W	M	W	M	W	M+W	M+W
1996	363	334	2,798	2,621	3,161	2,955	6,116	53,839
1997	442	311	2,819	2,734	3,261	3,045	6,306	53,020
1998	420	340	2,928	2,709	3,348	3,049	6,397	51,549
1999	453	331	3,193	2,864	3,646	3,195	6,841	51,971
2000	453	361	3,168	2,965	3,621	3,326	6,947	50,206
2001	433	357	3,276	2,988	3,709	3,345	7,054	50,734
2002	513	323	3,453	3,117	3,966	3,440	7,406	50,474
2003	473	381	3,667	3,226	4,140	3,607	7,747	49,280
2004	466	319	3,655	3,169	4,121	3,488	7,609	47,276
2005	487	329	3,724	3,362	4,211	3,691	7,902	46,366
2006	450	337	3,832	3,381	4,282	3,718	8,000	46,122
2007	425	278	3,911	3,544	4,336	3,822	8,158	46,507
2008	382	261	3,984	3,407	4,366	3,668	8,034	45,115
2009	357	256	4,464	3,639	4,821	3,895	8,716	45,008
2010	348	235	4,452	3,773	4,800	4,008	8,808	44,088
2011	311	200	4,614	3,714	4,925	3,914	8,839	42,294
2012	258	170	4,926	3,804	5,184	3,974	9,158	41,579
2013	240	143	5,054	3,994	5,294	4,137	9,431	41,183
2014	180	135	5,327	4,104	5,507	4,239	9,746	39,944
2015	185	118	5,431	4,345	5,616	4,463	10,079	40,947
2016	174	124	5,598	4,363	5,772	4,487	10,259	40,643

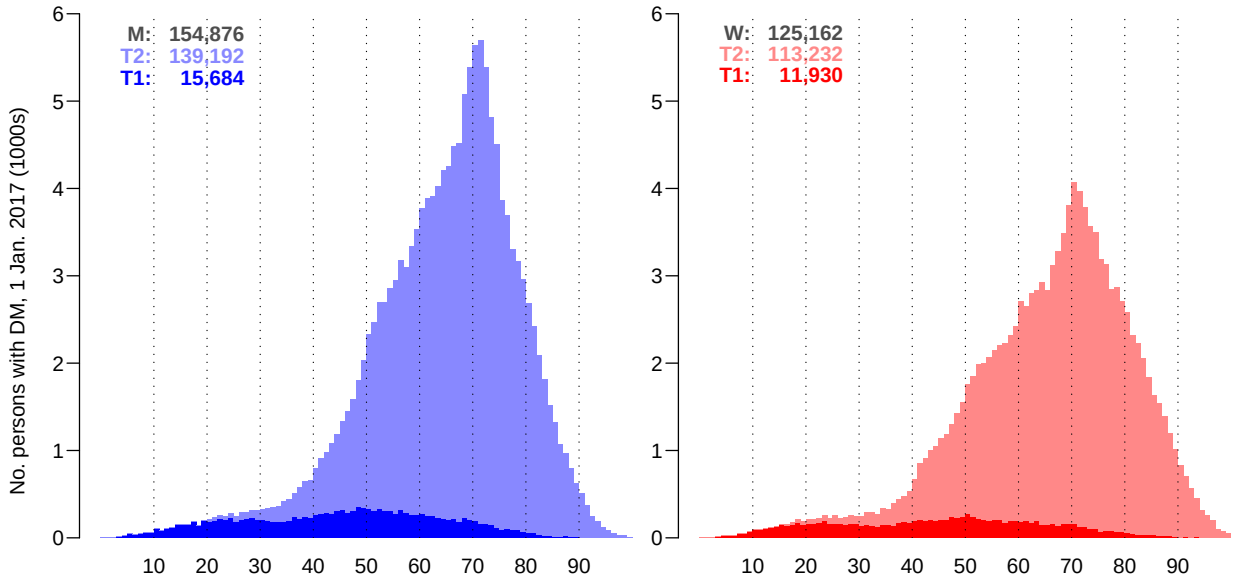

Figure ESM 1: *Number of T1D (dark color) and T2D (bright color) patients in Denmark as of 1 January 2017, the blue bars are men, red bars are women. The numbers in the corner of the plots indicate the number of prevalent cases, the black numbers are the total number of prevalent cases.*

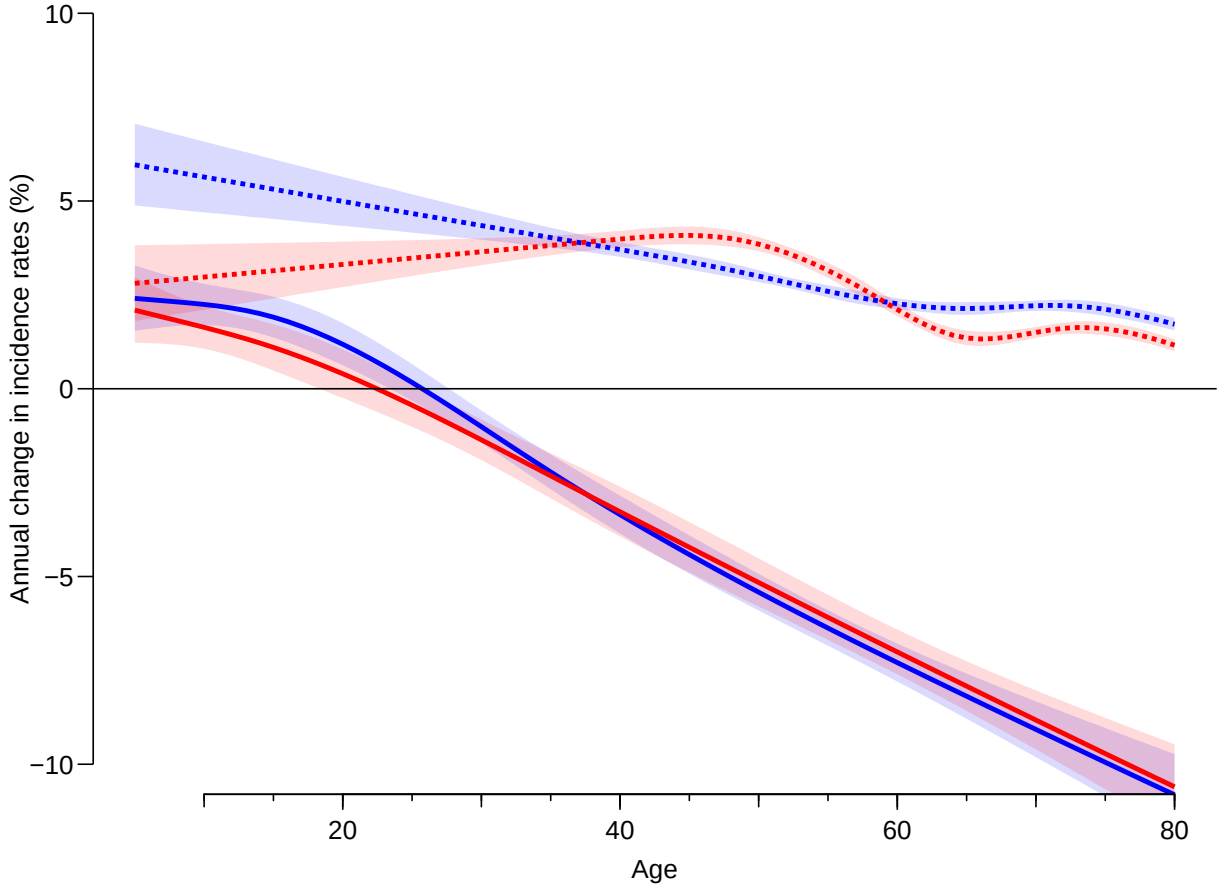

Figure ESM 2: *Age-specific average annual change in incidence rates of T1D and T2D in Denmark 1996–2016; a.k.a. "local drifts". Estimates are from models with a smooth effect of age and an interaction between a smooth age term and a linear calendar time term (varying coefficients model). Full lines are T1D, broken lines T2D, blue curves are men, red curves women. The shaded areas indicate 95% confidence intervals.*
It is seen that a summary of overall annual increase in T2D of 3.5% is quite reasonable, but that the change in incidence rates of T1D is positive under age 20 and negative over age 30.

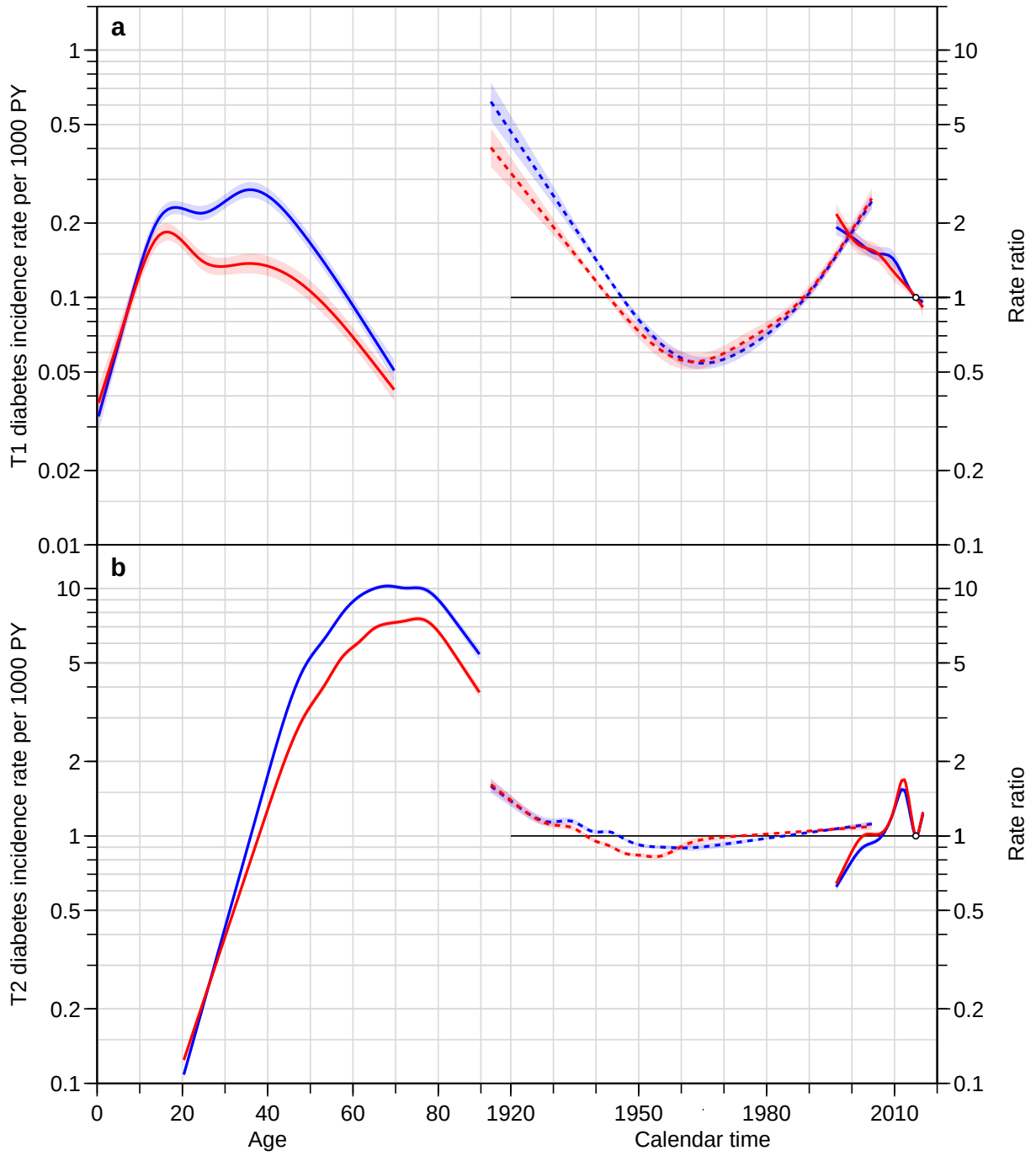

Figure ESM 3: *Estimates of effects from Age-Period-Cohort models for diabetes incidence rates in Denmark, using smooth effects of age, period and cohort (restricted cubic splines): Age-specific incidence rates (leftmost curves) as of 1 January 2015, period effects relative to this (rightmost curves, full lines) and cohort residual curves (middle set of curves — broken lines). Upper panel: T1D, lower panel: T2D. Blue curves are men, red curves women; shaded areas represent 95% confidence intervals.*
Note that all vertical axes have the same relative *extent, namely a factor 150 from bottom to top. Likewise, one year of age, date of birth and date of FU has the same physical extent on the horizontal axes.*

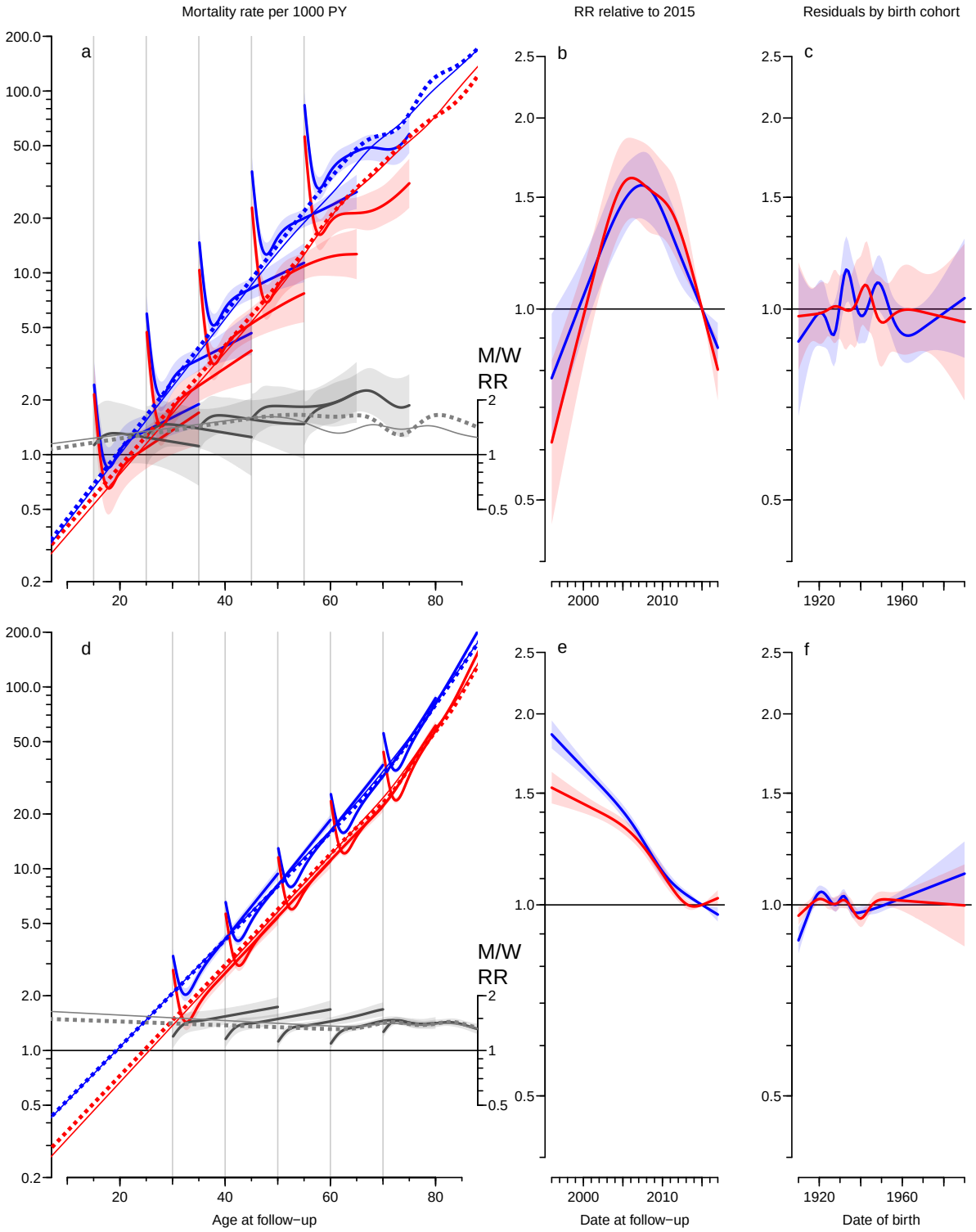

Figure ESM4: *Mortality (a,d), and RR relative to 2015-01-01 (b,e) and birth cohort residuals (c,f). Upper panels (a,b,c) are T1D and lower panels (d,e,f) are T2D. Leftmost plot shows the mortality rates at 2015-01-01 for persons diagnosed in ages 15, 25, . . . , followed for 0–20 years of diabetes duration. These curves are the same as those in figure 3 of the main paper. Broken lines in leftmost plot are mortality rates modeled ignoring age at diagnosis and duration of diabetes. Thin full lines are overall mortality also including prevalent cases as of 1996-01-01.*

Red curves are for women, blue for men, black are M/W RR; shaded areas indicate 95% confidence intervals.

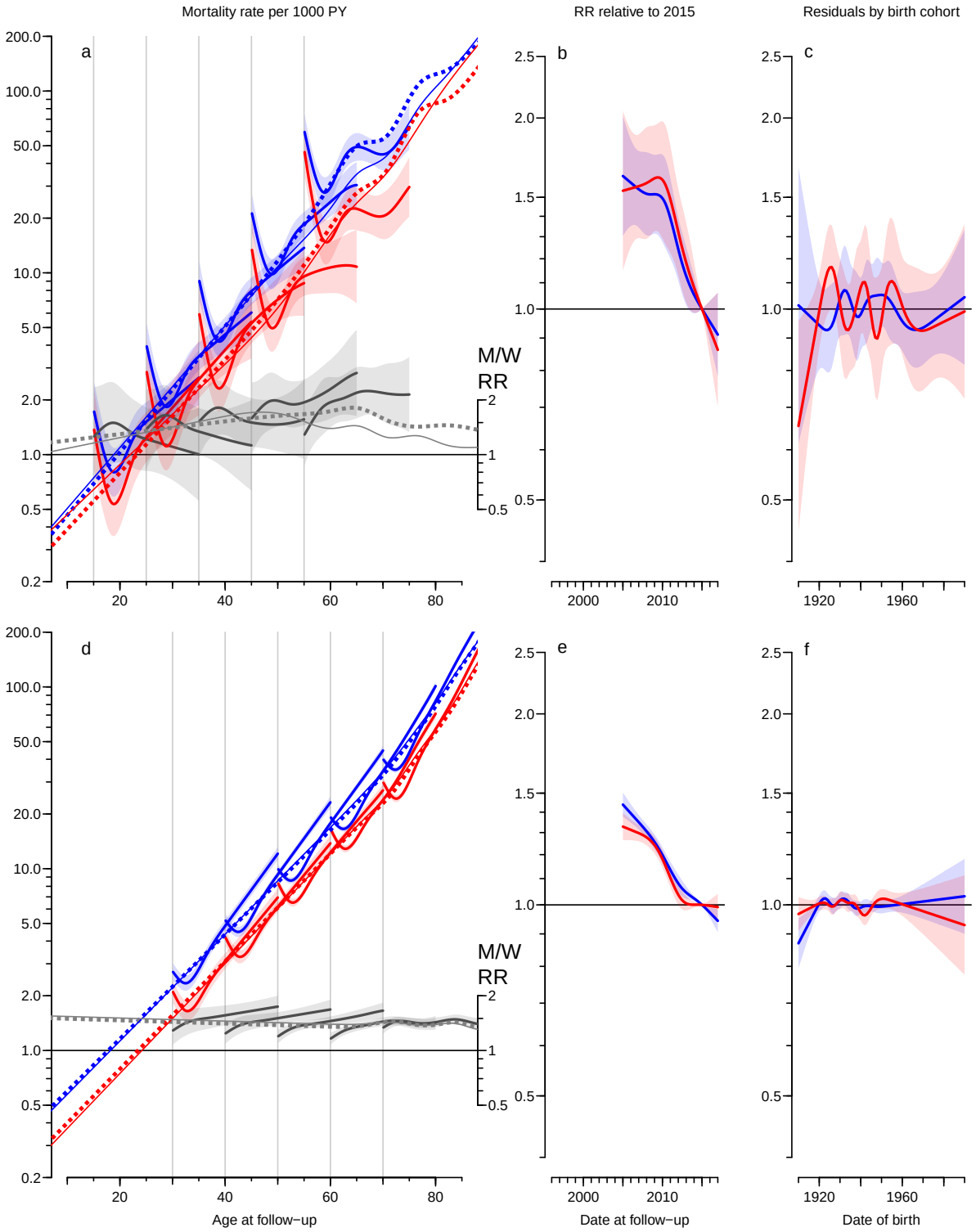

Figure ESM5: *Mortality (a,d), and RR relative to 2015-01-01 (b,e) and birth cohort residuals (c,f), based on follow up after 2005 only. Upper panels (a,b,c) are T1D and lower panels (d,e,f) are T2D. Leftmost plot shows the mortality rates at 2015-01-01 for persons diagnosed in ages 15, 25, . . . , followed for 0–20 years of diabetes duration. Broken lines in leftmost plot are mortality rates modeled ignoring age at diagnosis and duration of diabetes. Thin full lines are overall mortality also including prevalent cases as of 1996-01-01.*
Red curves are for women, blue for men, black are M/W RR; shaded areas indicate 95% confidence intervals.

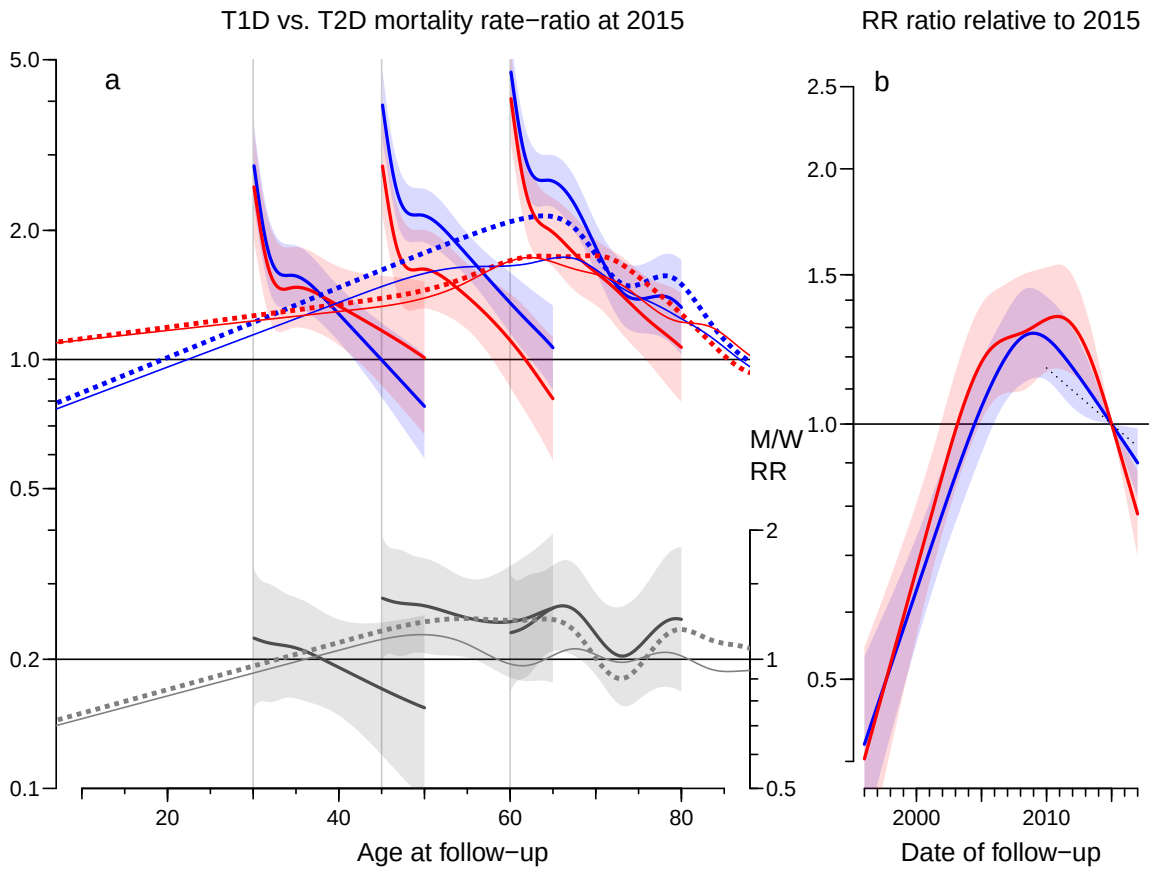

Figure ESM 6: *T1D versus T2D mortality RR at 2015-01-01. Leftmost plot shows the mortality RR at 2015-01-01 for persons diagnosed in ages 30, 45 and 60 years. Broken lines in leftmost plot are mortality RRs modeled ignoring age at diagnosis and duration of diabetes. Thin full lines are overall mortality RR also including prevalent cases as of 1996-01-01.*
Red curves are for women, blue for men, black are M/W RR ratio; shaded areas indicate 95% confidence intervals.

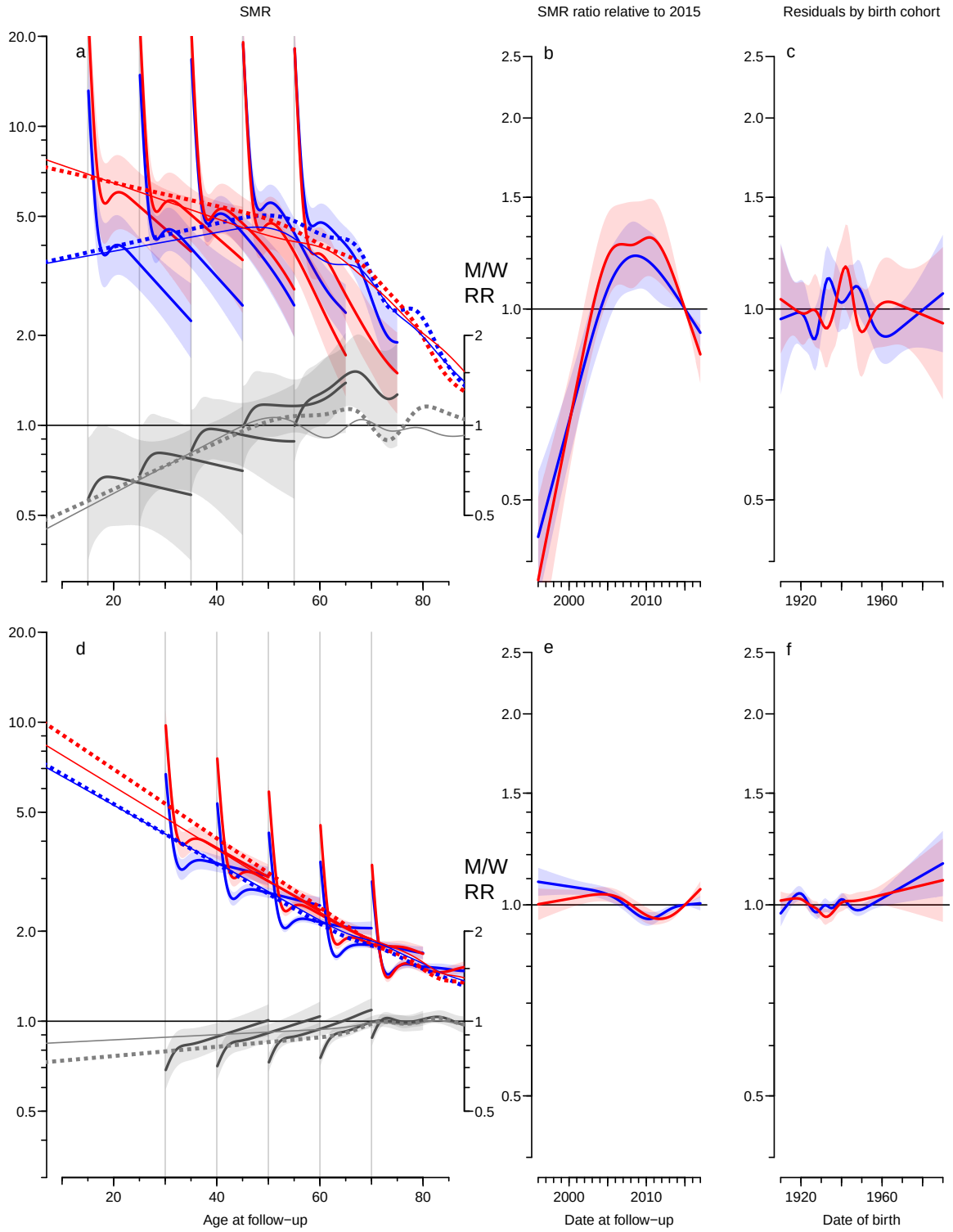

Figure ESM 7: *SMR (a,c) SMR-ratios relative to 2015-01-01 (b,d) and birth cohort residuals (c,f). The leftmost plots (a,c) shows the mortality rates at 2015-01-01 for persons diagnosed in ages 15, 30, 45, 60 and 75 followed for 0–20 years of diabetes duration. Broken lines in leftmost plot are SMR modeled ignoring age at diagnosis and duration of diabetes. Thin full lines represent SMR also including prevalent cases as of 1996-01-01.*
Red curves are for women, blue for men, black are SMR ratios between M and W; shaded areas indicate 95% confidence intervals.