Demographic Components of Diabetes Prevalence

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Research in Context

Evidence before this study

We searched Google scholar for articles with terms “diabetes”, “prevalence”, “incidence” and “mortality”. Qualitatively it appears well known that mortality influences prevalence negatively and incidence positively and many papers have pointed this out; but only one study has made an attempt to quantify the effects [1], however not subdivided by age, and found that the major driver of changes in prevalence was the existing imbalance between incidence and mortality rates. A precise quantification of the effect of actually observed (changes in) diabetes incidence and mortality on prevalence is lacking.

Added value of this study

This study is the first to precisely quantify the relative contributions of changes in mortality and incidence as well as that of epidemiological imbalance to the changes in prevalence of diabetes, both in terms of prevalence and absolute number of diabetes patients in Denmark.

Moreover it describes a precise formal framework for this type of calculations that is readily applicable in other settings where incidence and mortality rates of diabetes are available.

Implications of all the available evidence

The major driver of diabetes prevalence in Denmark is the increasing incidence rates and the epidemiological imbalance already present in 1995 each contributing about a quarter of all prevalent cases in 2012; the decreasing mortality among diabetes patients only accounts for about 7.5% of the present number of diabetes patients.

Abstract

The prevalence of diabetes has been increasing dramatically the last decades. It is also known that incidence rates of diabetes has been increasing and that mortality — both among persons with and without diabetes — has been decreasing. But it is not known to which extent these two components have influenced the prevalence of diabetes.

This paper defines the relative contribution of incidence and mortality to changes in prevalence in proper demographic terms, and uses Danish register data for the period 1995–2011 to address the question statistically precise in a Danish context, using age- and period-specific prevalence, incidence and mortality rates, based on data from the Danish National Diabetes Register.

The average annual increase in diabetes incidence was some 4%, the average decrease in mortality among persons without diabetes about 2.5%, whereas the average annual decrease in mortality among diabetes patients was 4%. The fraction of prevalent cases of DM at the end of 2011 attributable to declining mortality was 7.5%, the fraction attributable to increasing incidence rates was 30% and the fraction attributable to the non-steady state imbalance between incidence and mortality rates in 1995 was 25%.

In conclusion, the major driver of the increasing prevalence of DM in Denmark over the period 1995–2011 is the increasing incidence rates, whereas the declining mortality rates play a smaller albeit not insignificant role.

Keywords: Demography, Diabetes, Incidence, Mortality, Prevalence, Trends.

Introduction

Diabetes (DM) is among the leading causes of death in Europe with diabetic macro- and microvascular complications resulting in increased disability and enormous health care costs [2]. As a consequence, systematic and timely diabetes surveillance is essential for planning and implementing health policy. Many countries have faced a rapid increase in diabetes prevalence [3]. Data from the US Center for Disease Control show a near quadrupling of diagnosed diabetes from 5.5 million persons in 1980 to 21.1 million in 2010 [4]. The most recent Scottish Diabetes Survey (2013) estimates that 5.1% of the population had a diagnosis of diabetes in Scotland at the start of 2013, compared to 4.1% in 2007 [5]. The large increase in prevalence is presumably caused by an increase in incidence due to underlying risk factors, primarily obesity and aging of the population. However, a significant decline in mortality has been reported, both in type 1 [6, 7, 8] and type 2 diabetes [9, 10, 11]. Also in the non-diabetic background populations there has been a decrease in mortality, but not to the same extent as among persons with diabetes. Based on regional registers, the notion of a rise in diabetes incidence in Denmark has been challenged in a paper by Støvring *et al.*. [12]. The core message by these authors is that there is no apparent change in diabetes incidence but an increase in prevalence and a decrease in mortality. By the classical relationship between prevalence, incidence and duration (=survival with diabetes):

$$\text{prevalence} = \text{incidence} \times \text{duration}$$

the authors suggest that the rise in prevalence is largely attributable to a decrease in mortality, that is increasing duration. The formula is however only a rough approximation to reality as it concerns a steady-state situation and does not take age into account. As such, it should be more regarded as a *qualitative* statement about the relation ship between the quantities.

A number of papers have pointed this qualitative relationship out too, for example [13, 14], The only study that has attempted a quantification is Evans *et al.* [1], however not quantifying effects by age, and using a very crude age adjustment with age-classes 20 years wide.

The motivation for the present work is 1) a wish to place the discussion of contributions from changing incidence and mortality rates on prevalence of diabetes at a firm theoretical foundation, 2) to quantify the relative sizes of these contributions to prevalence and thereby 3) to show how to use this machinery in a practical context.

Specifically, we use the age-specific prevalences of diabetes as of 1 January 1995 as starting point and apply age- and period-specific incidence and mortality rates to predict

the prevalences in the period 1 January 1995 through 1 January 2012. By using either the observed rates or rates assumed constant after 1995 we obtain predicted prevalences in 2012 under different scenarios. Differences between scenarios are then defined as the fraction of the prevalences attributable to different factors.

Methods

Prevalence, incidence and mortality

The following is to some extent a repetition of standard theory from demography / probability theory, and the extension to several age-classes and time-varying incidence and mortality rates is if not straight-forward, then well-known from any curriculum in demography and probability theory.

Diabetes incidence and mortality in the population is fully described by a 3-state model, with three transition rates (Figure 1). If each of these rates is assumed to depend on sex, and continuously on age, calendar time and date of birth, it is possible to use the continuous age-distribution of prevalent diabetes patients at the start of the observation period (1 January 1995) in conjunction with the incidence and mortality rates for the period to predict the prevalence at the end of the period, 1 January 2012.

This is simply done by using a sex-, age- and period-specific transitions between the three states "No DM", "DM" and "Dead" (Figure 1). In each step, the population at a given time in a given (say 1-year) age-class with and without diabetes is updated for one year, so that we know how many at that time are in the three states the year after.

Specifically, we considered transitions over a small interval of length ℓ and using the notation $\mathrm{P}_{\text{No DM,DM}}(\ell)$ for $\mathrm{P}\{\text{DM at } (a+\ell, p+\ell) \mid \text{No DM at } (a,p)\}$, we used the following transition probabilities:

$$
\begin{aligned}
\mathrm{P}_{\text{No DM,No DM}}(\ell) &= \exp\bigl(-(\lambda+\mu_{\text{ND}})\ell\bigr) \\
\mathrm{P}_{\text{DM,DM}}(\ell) &= \exp\bigl(-\mu_{\text{DM}}\ell\bigr) \\
\mathrm{P}_{\text{No DM,DM}}(\ell) &= \frac{\lambda}{\lambda+\mu_{\text{ND}}}\Bigl(1-\exp\bigl(-(\lambda+\mu_{\text{ND}})\ell\bigr)\Bigr) \approx \lambda\ell \\
\mathrm{P}_{\text{No DM,Dead}}(\ell) &= \frac{\mu_{\text{ND}}}{\lambda+\mu_{\text{ND}}}\Bigl(1-\exp\bigl(-(\lambda+\mu_{\text{ND}})\ell\bigr)\Bigr) \approx \mu_{\text{ND}}\ell \\
\mathrm{P}_{\text{DM,Dead}}(\ell) &= 1-\exp\bigl(-\mu_{\text{DM}}\ell\bigr) \approx \mu_{\text{DM}}\ell
\end{aligned}
$$

The rates are assumed to depend on a and p, but this has been left out of the formulae for clarity of exposition. The reason to choose ℓ small is that the above approximations should be valid, notably that the probability of two transitions No DM→DM→Dead occurring in

one interval should be negligible. This will render the updating machinery reasonably accurate to predict the observed prevalences at the end of the study period.

Data

We modeled incidence and mortality rates using data from the Danish National Diabetes Register (NDR) [15, 16], the Human Mortality Database [17] and the data-bank of Statistics Denmark to provide

- the number of events of diabetes,
- number of deaths among persons with and without diabetes and
- follow-up time (risk time, person-years)

classified by sex, age, date of follow-up and date of birth (Lexis triangles). The midpoint of the Lexis triangles were coded for each entry for continuous modeling of effects [18].

We also used the NDR to enumerate the number of prevalent cases of diabetes in 1-year age-classes at each of the dates 1 January 1995 through 1 January 2012, and from Statistics Denmark we obtained population size at each of these dates, all subdivided by sex and 1-year age-class.

All analyses were done separately for men and women.

Statistical methods

We fitted separate log-link binomial models for men and women to the no. of prevalent cases at each of the dates 1 January 1995 through 1 January 2012, using natural splines (restricted cubic splines) to describe the age-dependence. These models thus provided estimates of diabetes prevalence as a continuous function of age.

We fitted age-period-cohort models [18] for diabetes incidence rates and mortality among persons with and without diabetes, separately for each sex. Effects of age, date of follow-up (period) and date of birth (cohort) were modeled continuously by natural splines (restricted cubic splines), and the models thus provide predicted incidence and mortality rates as continuous functions of age and date of follow-up.

Since we only use the age-period-cohort (APC) models for prediction of rates, the usual identification problem of the parametrization of effects in APC models is not relevant here. We estimated the average time trend from the APC models using the observed number of events as weights as described in Carstensen [18].

Demographic methods

We used the models fitted to predict the incidence and mortality rates at the midpoint of all months from 1 January 1995 through 1 January 2012 at the start of each of 1200 age-classes, *i.e.* we used $\ell = 1$ month (formally 365.25/12 days). For updating the prevalence in age class $(a, a + \ell)$ at time p to the prevalence in age-class $(a + \ell, a + 2\ell)$ at time $p + \ell$, we used rates predicted at age $a + \ell$ at time $p + \frac{\ell}{2}$. As a check on the appropriateness of the calculations, the predicted prevalences at the end of the study period is compared with the actual observed.

The same exercise was then repeated in scenarios where we fixed the (age-specific) incidence and/or mortality rates to be as in 1995. The difference between predicted prevalences under these scenarios and the actually observed will then represent the contributions to the prevalence in 2012 from increasing incidence and decreasing mortality respectively.

Specifically, the contribution from changing incidence rates were computed in two different ways:

1. Difference between results with 1995-fixed resp. observed incidence rates using the mortality rates as observed over the period.

2. Difference between results with 1995-fixed resp. observed incidence rates using the mortality rates fixed at the 1995 level.

— and vice versa for the contribution from the changing mortality rates.

The contributions from changing incidence resp. mortality were taken as the average of the two approaches for each.

Finally, we took the difference between the observed prevalences in 1995 and those predicted for 2012 by fixing *both* incidence and mortality rates to the 1995 level throughout, as the component of prevalence attributable to the demographic imbalance in 1995. This is thus the change in prevalence occurring from the fact that incidence and mortality rates in 1995 were *not* in a steady-state equilibrium with equal number of incident cases of DM and deaths among DM patients.

A full account of all calculations is available as:
http://bendixcarstensen.com/DMreg/Prevalence/Xprev.pdf

Results

In the study period there were a bit more than 90 mil. person-years and over 370,000 new cases of diabetes and some 960,000 deaths, of which almost 160,000 among diabetes

patients (Tables 1 , 2). Even though the last of the periods is only 5 years long, there are more diagnoses and deaths in this, partly due to the increasing diabetes incidence, but primarily due to the aging population in general.

Trends in incidence and mortality rates

From the fitted age-period-cohort model we extracted the average annual trend in rates; as seen from table 3 there was a clear increase in incidence of diabetes of 4% per year, while mortality was *de*creasing; 2.5% per year for persons without diabetes, but 4% per year for persons with diabetes.

Components of prevalence

The prevalences at 1 January 2012, as predicted from the age-specific prevalences in 1995 and the fitted incidence and mortality rates from the age-period-cohort models for the rates, showed a very good agreement with the observed prevalences in 2012, as is seen from figure 2. Thus the prediction method is sufficiently accurate to yield credible results for the scenarios considered.

The components of the prevalences as derived from the models are shown in figure 3, where it is seen that the fraction of the diabetes prevalence attributable to decreasing mortality is quite substantial in older ages. However it is equally clear that the dominant components in the changing diabetes prevalence are the increasing incidence and the fact that the prevailing incidence and mortality rates in 1995 were not in equilibrium with the prevalences.

We multiplied the components of prevalence as derived with the number of persons in the Danish population in different ages to produce the *number* of diabetes patients in the population attributable to each of the causes. This is shown in figure 4.

It is seen that the mortality decrease has a comparatively small impact on the number of cases, because the effect is largest in the older ages where the number of prevalent diabetes cases is limited anyway.

The fraction of diabetes cases attributable to declining mortality is about 7.5%, whereas the fraction attributable to increasing incidence of diabetes is almost 30%, and 25% attributable to the imbalance between incidence, mortality and prevalence already present in 1995. The number of cases present in the Danish population using the age-specific prevalences from 1 January 1995 with the age-distribution as of 1 January 2012 represent the remaining 37%. These figures are only slightly different between men and women, as seen in figure 4.

The development of the components as a fraction of all prevalent diabetes cases in

different ages is shown in figure 5, and not surprisingly, the mortality decrease has the largest impact on the prevalences in older ages. We found that the fraction attributable to mortality decline was less than 5% in age 60, a bit larger in age 70 and almost 15% at age 80 for men, and slightly less in women (Figure 5).

Discussion

We have shown that over the last decades in Denmark, the decline in mortality has had some impact on the increasing prevalence of diabetes, whereas the major drivers of the prevalence increase have been the increase in diabetes incidence as well as the imbalance between incidence and mortality already present in 1995.

The absolute number of cases attributable to the different components is of course heavily dependent on the particular age-distribution in the Danish population. The patterns of birth has been very similar throughout Europe in the 1940es and 50es, with a baby-boom in the late 1940es, thus rendering a large part of today's population in the age-range where diabetes incidence is increasing. But even so these absolute numbers are less generalizable than the age-specific components of prevalence.

The finding of a decline in diabetes-related mortality is encouraging, although the resulting increase in diabetes prevalence obviously challenges the health care system. A larger number of older people will survive with diabetes complications with increased costs of diabetes treatment, as well as costs related to screening for and treatment of complications. Contrary, the observed increase in diabetes incidence calls for intensified preventive strategies in persons without diabetes. Thus, the increasing diabetes prevalence has different public health consequences according to the contributing prevalence components, a finding that underscores the value of such a detailed examination.

Comparison with other studies

Few studies have addressed the relative contributions of mortality versus incidence to diabetes prevalence. A recent study from Israel observed a deceleration in the upward trend in diabetes prevalence despite declining mortality [19].

Støvring *et al.* [12] merely analyzed relative annual changes in incidence, prevalence and mortality, and no formal quantification of the relative impact of mortality and incidence changes were made, so it is not possible to make a precise comparison. But the authors concluded that "Although our data do not allow a firm conclusion as to why prevalence is rising, we believe that the decrease in mortality should be taken into account. Otherwise, incorrect conclusions could be drawn about the relation between the western lifestyle and

the rising number of diabetics." This is indeed confirmed by this study as we estimate that as much as 7.5% of the current diabetes cases can be ascribed to the last 17 years' decreasing mortality, less for ages under 70, somewhat more for older ages.

Evans *et al.* [1] used Tayside (Scotland) data to attempt a quantification of the relative contributions of incidence and mortality. They showed that 60% of the increase in diabetes prevalence over the period 1993–2004 was attributable to the initial imbalance between incidence and mortality; 25% to the increasing incidence and only 11% to decreasing mortality, which in very broad terms can be said to be qualitatively similar to our results. However the paper use very broad age-classes (divided only at 45, 65 and 85) leaving ample space for residual confounding by changing age-structure of the population of diabetes patients, so understandably the paper presents no age-specific effects, and thus their conclusions for the overall prevalence may be strongly dependent on the particular age-distribution of the Scottish population and changes in it. Moreover it is not clear from the paper to what extent the authors took the mortality change in the non-diabetic population (as those available for new diagnoses) under different scenarios into account. Finally the comparison made was only with the scenario with incidence and mortality fixed at the initial level and not with the actually observed rates, so the results are not entirely comparable with ours although the populations in Scotland and Denmark in many respects are quite similar.

Strengths and limitations

We developed a model for partitioning prevalence changes in three parts, which was based on application of well-known demographic concepts and classical epidemiological modeling of occurrence rates. While this machinery in principle is straight-forward to use in any context, it does rely on the availability of detailed register data of diabetes incidence and mortality.

Moreover, it is important that the predictive capability of the models be checked against the observed development in diabetes prevalence. This was done using the observed prevalences in 1995 and estimated incidence and mortality rates to project prevalences through the period, and showed excellent agreement between observed and predicted prevalences throughout. Therefore we conclude that the modeling of rates have been sufficiently accurate to give credible results.

The register-based approach in our study has clear limitations. Firstly, the study cannot distinguish between type 1 and type 2 diabetes. Secondly, it is not possible to determine whether the observed increase in diabetes incidence reflects a true change in incidence or whether it is caused by intensified diagnostic activity, resulting in more low-risk people

with diabetes being included in the national diabetes register. Finally, a recent study has suggested that some misclassification exists with occurrence of false-positive cases in the register [20], primarily due to the blood glucose criteria used (see [16], 3rd & 4th criterion, p. 2188). Conversely, there may be people diagnosed with diabetes who are not detected in the register, but the extent of this problem is unknown. All three mentioned limitations may give rise to imprecision of incidence and mortality estimates, but it is not possible to disentangle how these potential biases may influence the direction of the findings in the current study.

It is however possible to repeat all analyses using a definition of inclusion in the NDR without the blood-glucose criteria. The number of diabetes patients at 1 January 2012 will then shrink from 313,633 to 248,393, but more interestingly, the annual increase in incidence will be 3.6% (and not 4%) and the annual decrease in mortality for DM patients will be 3.7% (and not 4%), so lesser changes in both.

Despite this, the fraction of cases attributable to declining mortality will change from 7.6%(M) and 7.5%(W) to 7.9%(M) and 8.4%(W), and the fractions attributable to incidence changes from 29.3%(M) and 30.6%(W) to 24.8%(M) and 22.9%(W). Thus it seems that a diabetes definition with smaller sensitivity and larger specificity of diabetes diagnosis will attribute a larger fraction of prevalence to changes in mortality and less to the changes in diabetes incidence. It is likely that the modified definition of DM include persons with more severe disease, and thus that it is for the more severe cases of DM that changes in mortality have had the largest impact on prevalence. This is however not possible to analyze in further detail, because more detailed information on severity of DM is not available for all patients.

A full account of both sets of calculations with further details is available as:
http://bendixcarstensen.com/DMreg/Prevalence/Xprev.pdf

Conclusion

This demographic study of diabetes prevalence in Denmark shows that the increasing prevalence of type 2 diabetes is substantially influenced both by the decline in mortality affecting primarily the oldest part of the population, as well as the increase in incidence with effects across the age-spectrum. The major drivers of the prevalence increase have been the increase in diabetes incidence as well as the imbalance between incidence and mortality already present in 1995.

The prevalence components have differential consequences for the health care system, and deserve a more detailed examination, in particular when prediction of future prevalences is undertaken.

Key messages

- The major driver of changes in prevalence of diabetes in Denmark is the increase in incidence rates of diabetes, and the existing imbalance between incidence and mortality.
- The decrease in mortality rates over the period 1995–2011 contributes less than 10% of the prevalent cases at 1 January 2012, however still represents a success in treatment of diabetes.
- A formal way of partitioning contributions to prevalence change based on knowledge of changes in incidence and mortality rates is presented.

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Disclosures

Both authors are employees of Steno Diabetes Center, a clinic and research institution owned by NovoNordisk; both authors own shares in NovoNordisk. MEJ is PI on trial sponsored by AstraZeneca.

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Table 1: *Events and person-years (in 1000s) in the Danish population in the 17 year study period 1995–2011.*

		No diabetes			Diabetes	
		DM diag	Deaths	P-years	Deaths	P-years
Men	1995-2000	41,775	129,184	12,740.5	19,403	301.0
	2001-2006	67,423	138,354	15,425.5	28,592	542.0
	2007-2011	85,117	124,886	15,565.0	35,261	801.3
	Total	194,315	392,424	43,731.1	83,256	1,644.3
Women	1995-2000	38,617	133,223	13,068.4	18,002	294.4
	2001-2006	62,505	147,536	15,793.7	25,970	522.3
	2007-2011	75,792	132,416	15,900.7	31,161	758.9
	Total	176,914	413,175	44,762.9	75,133	1,575.6
M+W	Total	371,229	805,599	88,494.0	158,389	3,219.9

Table 2: *Events and person-years (in 1000s) in the Danish population in the 17 year study period 1995–2011.*

		No diabetes			Diabetes	
		DM diag	Deaths	P-years	Deaths	P-years
Men	1995	7,743	27,434	2,531.0	3,747	51.7
	1996	8,008	26,616	2,542.8	3,697	55.7
	1997	7,916	25,633	2,550.3	3,826	59.9
	1998	8,808	25,022	2,556.1	3,895	64.4
	1999	9,300	24,479	2,560.4	4,238	69.3
	2000	9,608	23,913	2,564.6	4,272	74.5
	2001	10,206	23,915	2,569.0	4,408	80.1
	2002	11,170	23,458	2,572.0	4,790	86.2
	2003	12,364	22,460	2,573.0	4,940	93.1
	2004	12,462	23,055	2,573.0	5,015	100.5
	2005	11,613	21,553	2,573.9	5,167	107.5
	2006	12,090	21,803	2,577.0	5,335	114.1
	2007	12,709	21,415	2,583.6	5,532	120.9
	2008	13,994	21,135	2,593.3	5,628	128.8
	2009	14,290	20,653	2,600.5	6,189	136.9
	2010	14,962	20,425	2,604.3	6,195	145.4
	2011	17,072	19,455	2,606.3	6,382	155.1
	Total	194,315	392,424	43,731.1	83,256	1,644.3
Women	1995	7,131	27,919	2,599.1	3,630	51.0
	1996	7,377	26,892	2,609.4	3,450	54.6
	1997	7,522	26,580	2,615.5	3,540	58.6
	1998	8,034	25,617	2,620.4	3,562	62.7
	1999	8,553	26,215	2,624.1	3,820	67.4
	2000	8,872	25,408	2,627.7	3,970	72.1
	2001	9,469	25,471	2,631.6	4,113	77.3
	2002	10,778	25,611	2,633.7	4,282	83.2
	2003	11,348	23,435	2,633.7	4,487	89.8
	2004	11,465	24,606	2,633.2	4,406	96.8
	2005	10,573	23,005	2,633.8	4,712	103.2
	2006	10,911	22,935	2,636.0	4,892	109.1
	2007	11,768	23,079	2,640.5	5,012	115.3
	2008	12,654	22,233	2,647.7	5,019	122.5
	2009	12,349	22,147	2,654.5	5,266	129.8
	2010	12,808	21,444	2,659.7	5,572	136.9
	2011	15,302	20,578	2,662.4	5,400	145.3
	Total	176,914	413,175	44,762.9	75,133	1,575.6
M+W	Total	371,229	805,599	88,494.0	158,389	3,219.9

Table 3: *Average annual change (%) in incidence and mortality rates in Denmark over the period 1995–2011.*

		% change (95%c.i.)
No diabetes:		
DM incidence	Men	3.9 (3.8; 4.0)
	Women	4.0 (3.9; 4.1)
Mortality	Men	−2.7 (−2.8;−2.6)
	Women	−2.3 (−2.4;−2.2)
Diabetes:		
Mortality	Men	−4.0 (−4.2;−3.9)
	Women	−3.8 (−4.0;−3.7)

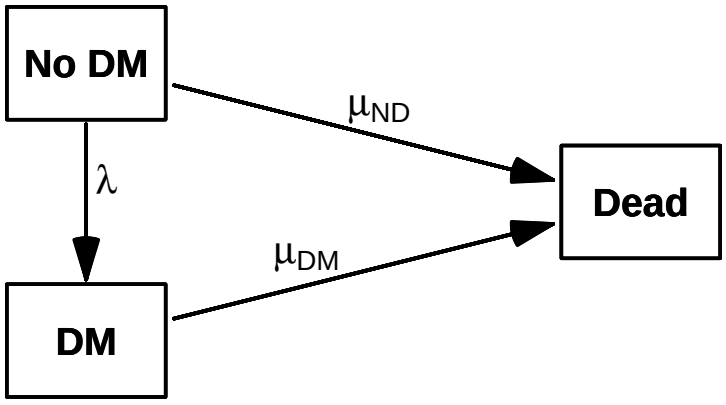

Figure 1: *States and transition rates used: λ: Incidence rate, μ_{ND}: mortality rate in persons without diabetes, μ_{DM}: mortality rate in persons with diabetes. Prevalence of diabetes is the fraction in state DM relative to all in states No DM and DM.*
Each rate is modeled separately for men and women, using an age-period-cohort model with continuous effects. The prevalence of diabetes is the fraction of persons in "DM" relative to all persons in "DM" and "No DM".

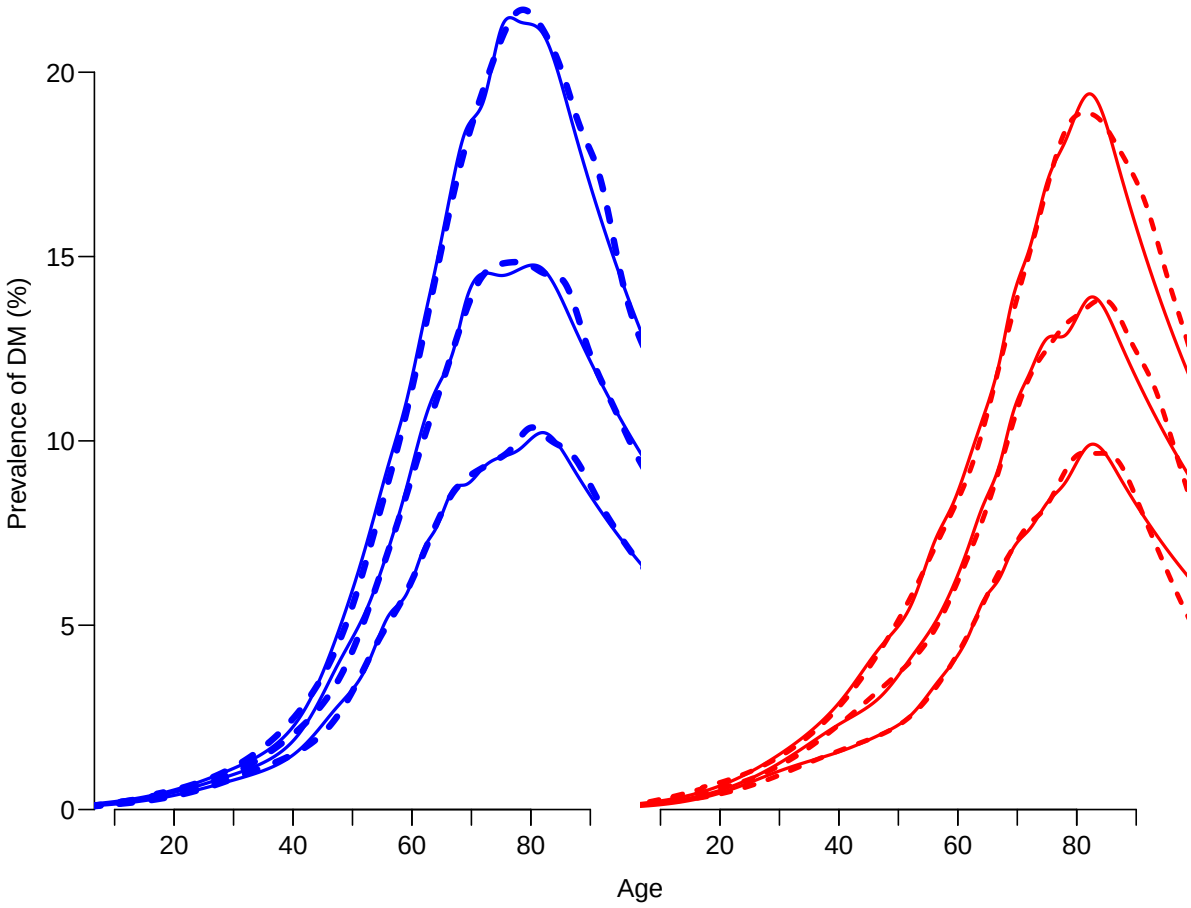

Figure 2: *Observed (full lines) and predicted (broken lines) prevalence of DM in Denmark (from low to high) 2000, 2006 and 2012. The observed prevalences are smoothed using natural splines. The predicted prevalences are based on the prevalences as of 1995 and estimated rates from age-period-cohort models for the incidence and mortality rates for the transitions in figure 1. Men in blue, women in red.*

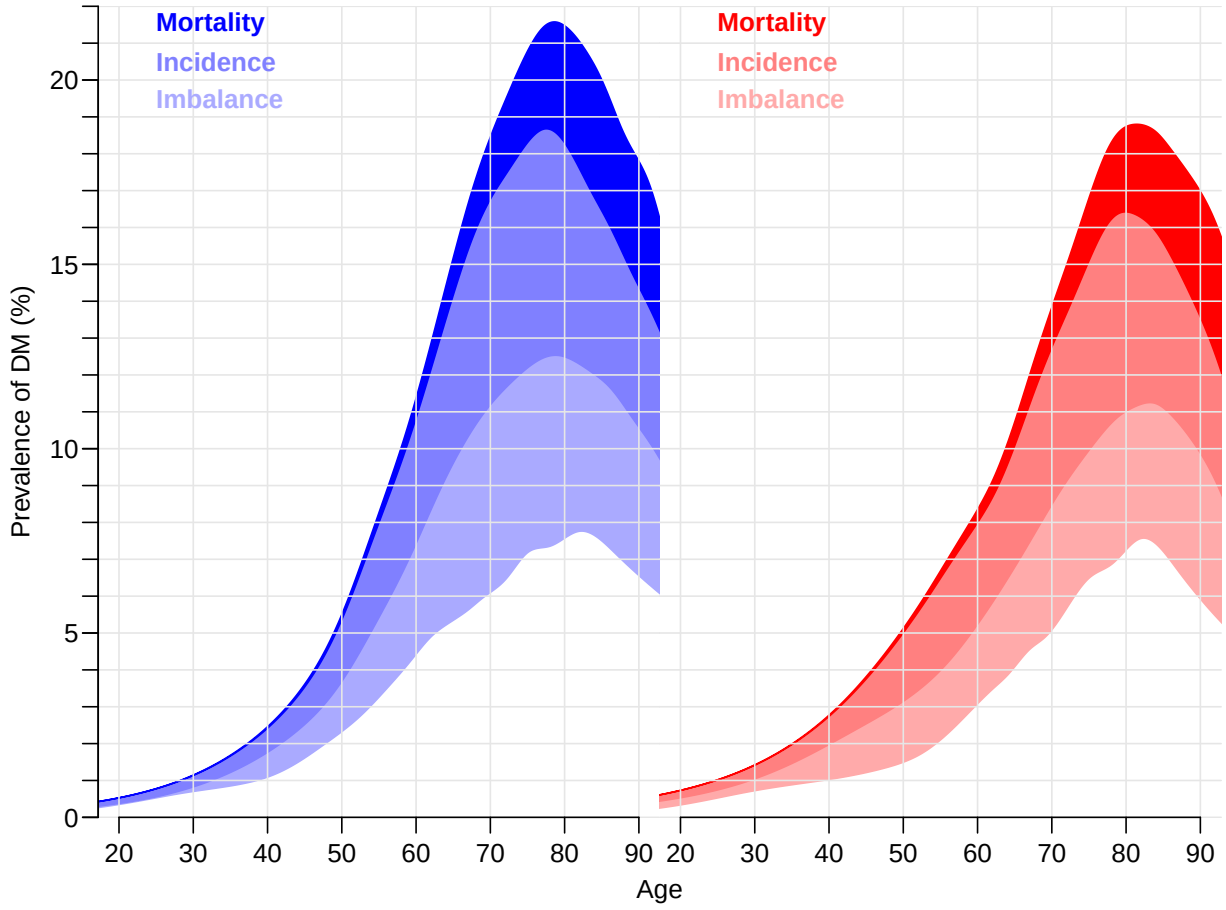

Figure 3: *Components of the changes in diabetes prevalence 1995–2012, based on prevalence in 1995 and models for incidence and mortality in the period. Men in blue, women in red.*

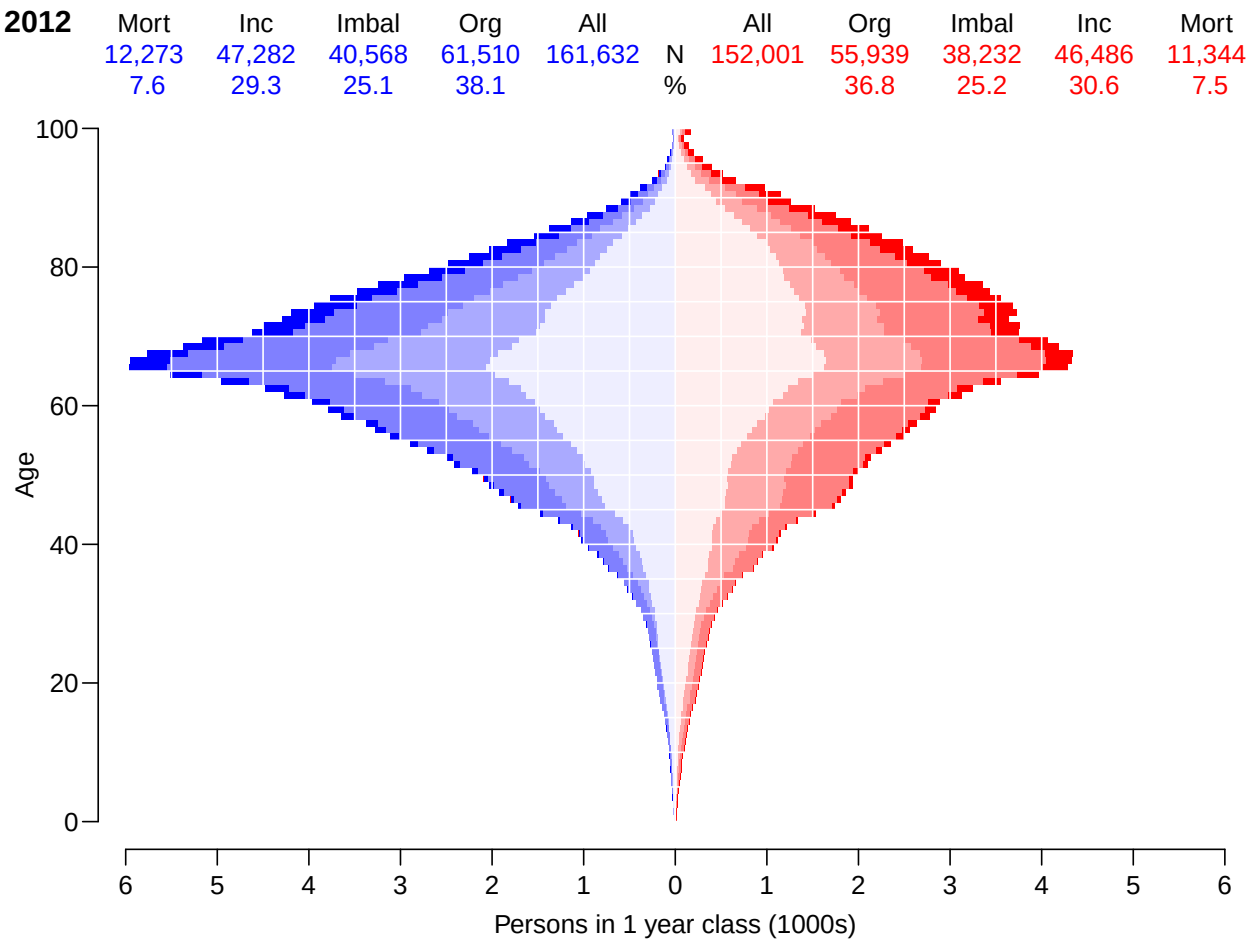

Figure 4: *Age-distribution of persons with diabetes according to components of the changes in diabetes prevalence 1995–2012. Men in blue, women in red.*

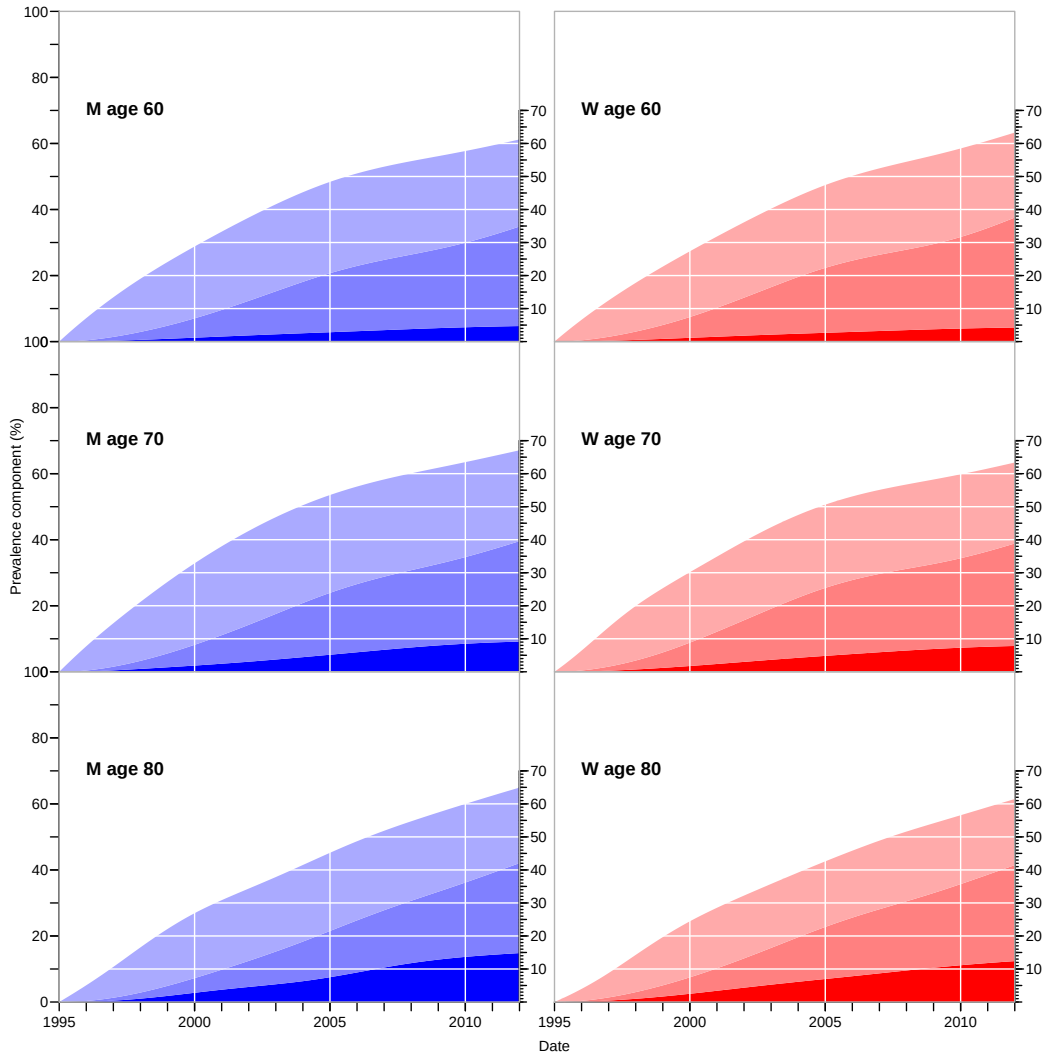

Figure 5: *Fraction of the prevalent cases at different times attributable to a) declining mortality (bottom, full color), b) increasing incidence (middle, pale color) and c) prevalence/mortality imbalance 1995 (top, weak color). The white area above the curves corresponds to the fraction of the cases that would have been alive if incidence and mortality rates had remained as in 1995. Men in blue, women in red.*