Burden of Mortality Attributable to Diagnosed Diabetes: A Nationwide Analysis Based on Claims Data From 65 Million People in Germany

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EPIDEMIOLOGY/HEALTH SERVICES RESEARCH

OBJECTIVE

In Germany, as in many other countries, nationwide data on mortality attributable to diagnosed diabetes are not available. This study estimated the absolute number of excess deaths associated with diabetes (all types) and type 2 diabetes in Germany.

RESEARCH DESIGN AND METHODS

A prevalence approach that included nationwide routine data from 64.9 million people insured in the German statutory health insurance system in 2010 was used for the calculation. Because nationwide data on diabetes mortality are lacking in Germany, the mortality rate ratio from the Danish National Diabetes Register was used. The absolute number of excess deaths associated with diabetes was calculated as the number of deaths due to diabetes minus the number of deaths due to diabetes with a mortality that was as high as in the population without diabetes. Furthermore, the mortality population-attributable fraction was calculated.

RESULTS

A total of 174,627 excess deaths were due to diabetes in 2010, including 137,950 due to type 2 diabetes. Overall, 21% of all deaths in Germany were attributable to diabetes and 16% were attributable to type 2 diabetes. Most of the excess deaths (34% each) occurred in the 70- to 89-year-old age-group.

CONCLUSIONS

In this first nationwide calculation of excess deaths related to diabetes in Germany, the results suggest that the official German estimates that rely on information from death certificates are grossly underestimated. Countries without national cohorts or diabetes registries could easily use this method to estimate the number of excess deaths due to diabetes.

For the year 2013, the Diabetes Atlas Group estimated that 5.1 million deaths worldwide and 619,847 deaths in Europe were attributable to diabetes (1). Diabetes is among the 10 most common causes of death worldwide (2). Between 1990 and 2010, the number of deaths attributable to diabetes has doubled (2). People with diabetes have a reduced life expectancy of ∼5 to 6 years (3). The most common cause of death in people with diabetes is cardiovascular disease (3,4). Over the past few decades, a reduction of diabetes mortality has been observed in several countries

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(5–9). However, the excess risk of death is still higher than in the population without diabetes, particularly in younger age-groups (4,9,10). Unfortunately, in most countries worldwide, reliable data on diabetes mortality are lacking (1). In a few European countries, such as Denmark (5) and Sweden (4), mortality analyses are based on national diabetes registries that include all age-groups. However, Germany and many other European countries do not have such national registries. Until now, age-standardized hazard ratios for diabetes mortality between 1.4 and 2.6 have been published for Germany on the basis of regional studies and surveys with small respondent numbers (11–14). To the best of our knowledge, no nationwide estimates of the number of excess deaths due to diabetes have been published for Germany, and no information on older age-groups >79 years is currently available.

In 2012, changes in the regulation of data transparency enabled the use of nationwide routine health care data from the German statutory health insurance system, which insures ~90% of the German population (15). These changes have allowed for new possibilities for estimating the burden of diabetes in Germany. Hence, this study estimates the number of excess deaths due to diabetes (ICD-10 codes E10–E14) and type 2 diabetes (ICD-10 code E11) in Germany, which is the number of deaths that could have been prevented if the diabetes mortality rate was as high as that of the population without diabetes.

RESEARCH DESIGN AND METHODS

Data

Routine health care data are collected and checked for plausibility and completeness by the Federal Social Insurance Authority for morbidity-related risk stratification reimbursement among the statutory health insurance funds in Germany. All insurees are assigned a unique pseudonym to avoid double counting when they change their statutory health insurance fund during the year (16). Data completeness and plausibility are examined according to a plausibility concept by the Federal Social Insurance Authority (§273 and §268 of the Code of Social Law V, §3 Data Transparency Regulation) (15,16). Aggregated data are provided by the German Institute of Medical Documentation and Information (DIMDI) for health service analysis in accordance with strict data protection regulations. Thus, information about insurees are grouped into 5-year age-bands (16). For analyses, people continuously insured for ≥360 days by statutory health insurance in 2010 were included. People who died, moved abroad, or switched to or from private insurance during the year 2010 and those with implausible information were excluded from the analysis (*n* = 4.6 million) (17). Altogether, we estimated the prevalence of an ascertained diagnosis of diabetes (ICD-10 codes E10–E14) and type 2 diabetes (ICD-10 code E11) on the basis of 64.9 million people, representing 93% of the entire population insured by the German statutory health insurance system. Overall, 10.1% of the German statutory health insurance system population had diabetes and 7.3% had type 2 diabetes in 2010 (17).

To estimate the absolute number of people with diabetes in each age-group, the respective prevalences were multiplied by the overall number of people in each age-band (18). Furthermore, the overall mortality of Germans was calculated by using the German period life table and age distribution of Germany from 2010 (18,19).

Nationwide data on mortality ratios for diabetes and no diabetes are not available for Germany. Although estimates of diabetes-specific mortality are available from cohort studies, these are too heterogeneous because they originate from various regions in Germany and use different age-groups as well as different age standardizations (11–13). Thus, the age- and sex-specific mortality rate ratios between people with diabetes and without diabetes were used from a Danish study wherein the Danish National Diabetes Register was linked to the individual mortality data from the Civil Registration System that includes all people residing in Denmark (5). Because the Danish National Diabetes Register is one of the most accurate diabetes registries in Europe, with a sensitivity of 86% and positive predictive value of 90% (5), we are convinced that the Danish estimates are highly valid and reliable. Denmark and Germany have a comparable standard of living and health care system. The diabetes prevalence in these countries is similar (Denmark 7.2%, Germany 7.4% [20]) and mortality of people with and without diabetes comparable, as shown in the European mortality database, an initiative from the World Health Organization. The crude death rate of non–insulin-dependent diabetes (ICD-10 code E11) per 100,000 deaths in 2010 was 9.8 in Denmark and 9.6 in Germany. The crude death rate of all causes per 100,000 deaths was 930 in Denmark (2012) and 1,072 in Germany (2014) (21). Furthermore, several examples can be found in the literature that show that relative risks are stable measures across many different populations (22). Nevertheless, residual differences in mortality between Denmark and Germany may still be present; hence, we conducted two sensitivity analyses that reflect the uncertainty of the estimations. In the first sensitivity analysis, we assumed that the mortality rate ratio in Germany can differ from the Danish population by ±15%, as we previously assumed in a similar study (17). In the second analysis, we considered the average annual decrease in mortality rate ratio, which was 1.4% (95% CI 0.9–1.8) in men and 0.7% (95% CI 0.2–1.2) in women (5).

Statistical Analysis

The number of excess deaths stratified by age $E(a)$ was calculated as $E(a) = D_1(a) - D_0(a)$, where $D_1(a)$ is the number of deaths within the population of people with diabetes who were age a in 2010 and $D_0(a)$ is the age-specific number of deaths of people with diabetes if mortality was the same as that in the population without diabetes. $D_1(a)$ and $D_0(a)$ were calculated as follows: $D_1(\mathrm{a}) = C(a) \times \{1 - \exp[-m_1(a)]\}$ and $D_0 = C(a) \times \{1 - \exp[-m_0(a)]\}$, where m_1 and m_0 are the mortality of people with and without diabetes, respectively, and $C(a)$ is the number people with diabetes. To estimate $C(a)$, the number of people in Germany, $N(a)$, was multiplied by the age-specific prevalence of diabetes, $p = p(a)$.

Mortality m_1 and m_0 for Germany were calculated by using the mortality rate ratio R from the Danish National Diabetes Register. For this, we decomposed the general mortality of people in Germany (m) into the mortality of people with and without diabetes: $m = p \times m_1 + (1 - p)m_0$, which can also be written as $m = m_0\,[p(R - 1) + 1]$. Hence, mortality m_0 and m_1 of people without and with diabetes can be determined as $m_0 = m/[p(R - 1) + 1]$ and $m_1 = R \times m_0$. In addition to excess deaths, the mortality population-attributable fraction (PAF) was estimated. $PAF(a)$ is defined as the proportion of deaths attributable to diabetes and was calculated as the number of excess deaths divided by the number of total deaths: $PAF(a) = E(a)/[N(a)\{1 - \exp[-m(a)]\}]$.

All analyses were stratified by sex. Statistical analyses were performed by using R version 3.2.1 software (The R Foundation for Statistical Computing, Vienna, Austria). The code for the primary analysis can be found in the Supplementary Data. Because of strict regulations on data protection, German routine statutory health insurance system (DIMDI) data are only available in anonymous and aggregated form (§5 Data Transparency Regulation, paragraph 4); therefore, ethics committee approval was not necessary. Moreover, all data used for the analysis have already been published (5,17).

RESULTS

In total, 174,627 excess deaths (137,950 from type 2 diabetes) could have been prevented in 2010 if mortality was the same in people with and without diabetes. Overall, 21% of all deaths in Germany were attributable to diabetes, and 16% were attributable to type 2 diabetes (Tables 1 and 2). Slightly more male than female excess deaths occurred in 2010 (Tables 1 and 2). Altogether, 92,924 male excess deaths related to diabetes (73,427 due to type 2 diabetes) and 81,703 female excess deaths related to diabetes (64,523 due to type 2 diabetes) were found. Most of the excess deaths occurred in the 70- to 79- and 80- to 89-year-old age-groups (~34% each) (Figs. 1 and 2 and Tables 1 and 2). Substantial sex differences were found in diabetes-related excess deaths. From the age of ~40 years, the number of male excess deaths due to diabetes started to grow, but the number of female excess deaths increased with a delay. Thus, the highest number of male excess deaths due to diabetes occurred at the age of ~75 years, whereas the peak of female excess deaths was ~10 years later. The same pattern was observed for the analysis of excess deaths due to type 2 diabetes.

The age-specific mortality rates of patients with diabetes and type 2 diabetes were similar (Supplementary Figs. 1–4). The diabetes mortality rates increased with age and were always higher than in the population without diabetes. The largest differences in mortality rates between people with and without diabetes were observed in the younger age-groups.

Sensitivity Analyses

The first sensitivity analysis assumed that the mortality rate ratio R in Germany differs from the Danish population. Thus, we calculated the excess deaths by modifying R by ±15%. With this assumption, the number of excess deaths would have been within the range of 137,459–212,108 (and between 107,294 and 169,588 for type 2 diabetes). Furthermore, we took the annual decrease of the mortality rate ratio into account, which was observed in the Danish study (−1.4% in men and −0.7% in women). Thus, the total number of excess deaths would have been 160,773 due to diabetes and 126,424 due to type 2 diabetes (Tables 1 and 2). More information on age-specific analyses is shown in Supplementary Tables 1–6.

Table 1—Age-specific male and female excess deaths due to diagnosed diabetes (ICD-10 codes E10–E14) in people >40 years of age in Germany (2010)

	Male $E(a)$	Female $E(a)$	Total $E(a)$	PAF(a)
Age-group (years)				
40–49	2,402 (2.6)	1,001 (1.2)	3,403 (1.9)	13.4
50–59	9,261 (10.0)	3,762 (4.6)	13,023 (7.5)	22.5
60–69	19,727 (21.2)	9,055 (11.1)	28,782 (16.5)	28.1
70–79	35,585 (38.3)	23,499 (28.8)	59,084 (33.8)	26.6
80–89	23,342 (25.1)	35,723 (43.7)	59,065 (33.8)	19.0
90–99	2,606 (2.8)	8,684 (10.6)	11,290 (6.5)	10.6
Total	92,924 (100.0)	81,703 (100.0)	174,627 (100.0)	20.6
Total (R + 15%)*	111,281	100,827	212,108	25.1
Total (R − 15%)*	74,647	62,812	137,459	16.2
Total (R − 1.4% in men, R − 0.7% in women)†	83,813	76,960	160,773	19.0

Data are n (%) unless otherwise indicated. *First sensitivity analysis: mortality rate ratio 15% above or below the Danish estimates (Danish National Diabetes Register) (5). †Second sensitivity analysis: mortality rate ratio from Denmark (Danish National Diabetes Register) diminished by 1.4% per year in men and 0.7% per year in women (5).

CONCLUSIONS

To the best of our knowledge, these nationwide estimates of the number of excess deaths due to diabetes are the first in the German population. To calculate these estimates, we included nationwide prevalence data from 64.9 million people insured by the German statutory health insurance system and mortality rate ratios from the Danish National Diabetes Register, which are comparable to the mortality ratios of the German population. The analysis revealed that 174,627 deaths (137,950 due to type 2 diabetes) could have been prevented if the mortality was the same in people with diabetes as in the population without diabetes. Approximately 21% of all deaths were attributable to diabetes in Germany (16% attributable to type 2 diabetes).

Similar to the current analysis, the global burden of mortality attributable to diabetes was estimated from the International Diabetes Federation (IDF) (1,23). In 2010, an estimated number of 634,054 (619,847 in 2013) excess deaths were due to diabetes in Europe in the 20- to 79-year-old age-group, comprising 11% (10.2% in 2013) of all causes of death. The differences between our estimates of attributable deaths (21% for diabetes) and those of the IDF may be explained by the different data sources used for the calculations. The IDF used age- and sex-specific relative risks of death for people with diabetes compared with those without diabetes from the Diabetes Epidemiology: Collaborative Analysis of Diagnostic Criteria in Europe (DECODE) study, which were derived from 30,000 subjects from 20 European studies (1,23). The analysis from the Danish National Diabetes Register included records from ~360,000 people with diabetes; these records were linked to the mortality data

Table 2—Age-specific male and female excess deaths due to diagnosed type 2 diabetes (ICD-10 code E11) in people >40 years of age in Germany (2010)

	Male *E*(*a*)	Female *E*(*a*)	Total *E*(*a*)	PAF(*a*)
Age-group (years)				
40–49	1,635 (2.2)	658 (1.0)	2,293 (1.7)	9.1
50–59	7,156 (9.7)	2,838 (4.4)	9,994 (7.2)	17.2
60–69	15,807 (21.5)	7,141 (11.1)	22,948 (16.6)	22.4
70–79	28,423 (38.7)	18,713 (29.0)	47,136 (34.2)	21.2
80–89	18,388 (25.0)	28,338 (43.9)	46,726 (33.9)	15.0
90–99	2,019 (2.7)	6,834 (10.6)	8,853 (6.4)	8.3
Total	73,427 (100.0)	64,523 (100.0)	137,950 (100.0)	16.3
Total (*R* + 15%)*	89,033	80,555	169,588	20.0
Total (*R* − 15%)*	58,263	49,031	107,294	12.7
Total (*R* − 1.4% in men and *R* − 0.7% in women)†	65,822	60,602	126,424	14.9

Data are *n* (%) unless otherwise indicated. *First sensitivity analysis: mortality rate ratio 15% above or below the Danish estimates (Danish National Diabetes Register) (5). †Second sensitivity analysis: mortality rate ratio from Denmark (Danish National Diabetes Register) diminished by 1.4% per year in men and 0.7% per year in women (5).

from the Civil Registration System, which includes all people in Denmark (5). The mortality rate ratios found in the DECODE study (23) and an analysis of the Danish National Diabetes Register (5) decreased with increasing age. Within the various age-groups, the estimates were slightly lower in the DECODE study than in the Danish National Diabetes Register analysis. However, the IDF reported an increasing number of excess deaths with increasing age. The highest number of excess deaths was observed in the oldest age-group of 70–79 years (1,23), which is in accordance with the current findings because we identified most of the excess deaths in the 70- to 79- and 80- to 89-year-old age-groups (~34% each for all types of diabetes and type 2 diabetes). The high number of deaths in these age-groups can partly be explained by the general life expectancy in Germany. Furthermore, there was a synergy effect of age and diabetes duration with longer durations in older age-groups, which also was found in a U.S. study in 72,000 people with type 2 diabetes (24). Accordingly, the number of severe complications, such as end-stage renal disease, eye disease, lower-extremity amputation, stroke, and heart failure, and mortality also increased considerably in the older age-groups (24). In summary, the estimated PAF reflects not only the cause-and-effect relationship between diabetes and death but also the relationship between all diabetes-related diseases and death. Most people with diabetes die as a result of micro- and macrovascular complications. In addition, people with diabetes may have an elevated risk for other life-threatening diseases, such as cancer (25). Thus, the attributable risk provides information on the absolute excess mortality risk in people with diabetes compared with those without diabetes.

The analysis also revealed that mortality in people with diabetes is much higher than that of the population without diabetes, irrespective of age. In addition, the largest differences in mortality were present in the younger age-groups. These results are in accordance with previous studies worldwide (3,4,7,9) and regional studies in Germany (11–13).

According to official numbers from the Federal Statistical Office, 858,768 people died in Germany in 2010, with 23,131 deaths due to diabetes, representing 2.7% of the all-cause mortality (26). Hence, in Germany, diabetes is not ranked among the top 10 most common causes of death, although this has been an established fact worldwide for several years (2). We found that 21% of all deaths were attributable to diabetes and 16% were attributable to type 2 diabetes; hence, we suggest that the number of excess deaths attributable to diabetes is strongly underestimated if we rely on reported causes of death from death certificates, as official statistics do. Estimating diabetes-related mortality is challenging because most people die as a result of diabetes complications and comorbidities, such as cardiovascular disease and renal failure, which often are reported as the underlying cause of death (1,23). For this reason, another approach is to focus not only on the underlying cause of death but also on the multiple causes of death to assess any mention of a disease on the death certificate (27). In a study from Italy, the method of assessing multiple causes of death revealed that in 12.3% of all studied death certificates, diabetes was mentioned, whereas only 2.9% reported diabetes as the underlying cause of death (27), corresponding to a four times higher proportion of death related

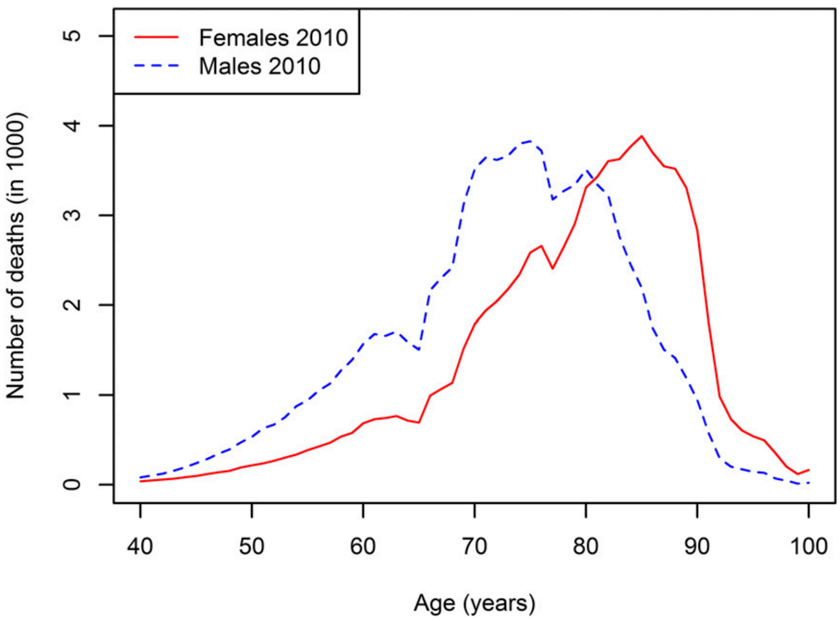

Figure 1—Age-specific number of excess deaths due to diagnosed diabetes (ICD-10 codes E10–E14) in Germany (2010).

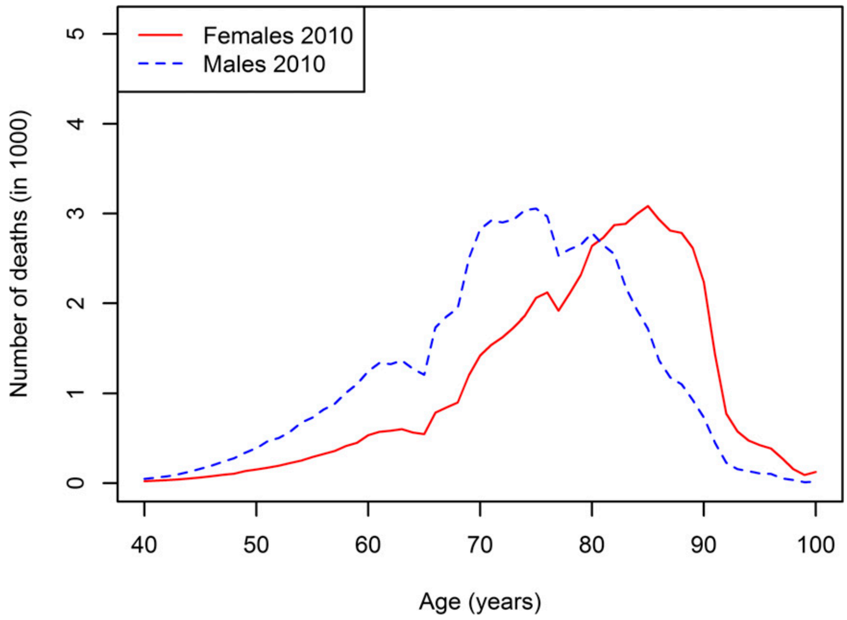

Figure 2—Age-specific number of excess deaths due to diagnosed type 2 diabetes (ICD-10 code E11) in Germany (2010).

to diabetes. Another nationwide analysis from Canada found that diabetes was more than twice as likely to be a contributing factor to death than the underlying cause of death from the years 2004–2008 (28). A recently published study from the U.S. that was based on two representative surveys from 1997 to 2010 found that 11.5% of all deaths were attributable to diabetes, which reflects a three to four times higher proportion of diabetes-related deaths (29). Overall, these results, together with the current calculations, demonstrate that deaths due to diabetes contribute to a much higher burden than previously assumed.

The number of deaths attributable to diabetes continues to rise. In the Global Burden of Disease Study 2015 (GBD 2015), a 32% increase in the total number of deaths due to diabetes was estimated between 2005 and 2015 (30), which among the 30 leading causes of death worldwide, is the second largest increase after Alzheimer disease and other dementias during that period. Hence, diabetes was the seventh most common cause of death after lower tracheal, bronchus, and lung cancer and before road injuries in 2015 (30). However, the increase in the total number of deaths due to diabetes was mainly attributed to demographic changes (30). Age-standardized death rates have decreased over the past few decades (5–9) possibly because of more-stringent treatment regimens with lipid-lowering and antihypertensive medications (4) and earlier detection of disease (9). More data are necessary to address to what extent these trends are applicable to Germany (i.e., improved treatment, medication, and disease management programs).

The strength of the current study is the method we used to estimate the number of excess deaths attributable to diabetes and type 2 diabetes at the national level. This method has been used for many years for various causes of death, such as cancer (31). Countries without nationwide cohorts or diabetes registries could easily use this approach to estimate the number of excess deaths due to diabetes for public health decisions. For this purpose, the use of the best available estimate of country-specific prevalence is necessary, as well as to identify a country with reliable mortality data available and that has a similar standard of living and health care system. For the calculation, we used nationwide German routine health care data, in which ~90% of the population is included, containing ICD-10 codes E10–E14 for diabetes and E11 for type 2 diabetes to estimate the respective diabetes prevalence and the mortality rate ratio from the Danish National Diabetes Register. Denmark and Germany are comparable according to their health care systems, standards of living, and mortality rates. Moreover, the Danish National Diabetes Register covers nearly 90% of all people with diabetes in Denmark; thus the Danish mortality rate ratios were ideally suited for our approach.

This analysis was not based on the underlying cause of death listed on death certificates because individual decisions on the cause of death often do not represent the primary cause of death, but rather a secondary disease of diabetes, which leads to an underestimation of deaths attributable to diabetes. Furthermore, this method enabled us to estimate excess deaths for the elderly population by using the prevalence of diabetes from all insurees in the German statutory health insurance system.

Several limitations should be mentioned. Because of the origin of the data used to estimate the diabetes prevalence (routine health claims data provided by DIMDI), the type of diagnosis may be fraught with inaccuracies. For this reason, we used a conservative approach for the prevalence estimation of all diabetes types and type 2 diabetes (only people with a confirmed diagnosis of diabetes). Prevalence estimates of type 2 diabetes are solely based on ICD-10 diabetes code E11 (17), which may explain the lower-than-expected proportion of all diabetes identified as type 2 (i.e., 70% vs. the expected proportion of 90–95%) because other ICD-10 codes, such as E12–E14 (malnutrition-related diabetes mellitus, other specified diabetes mellitus, and unspecified diabetes mellitus); double diagnoses; and implausible combinations of these ICD-10 codes were excluded from the data set. Moreover, a slightly over- or underestimation of diabetes prevalence could be present, as previously mentioned by Tamayo et al. (17), because the data set only included people with statutory health insurance for ≥360 days per year, indicating that we were unable to consider the health conditions of those who died, moved abroad, or changed to or from a private health insurance. Furthermore, we could not estimate the prevalence of people with undiagnosed diabetes because health claims data do not contain information on standardized glucose measurements or glycated hemoglobin values. Overall, we consider the current data set to be of high quality. First, incorrect codings seldom occur because the manipulation of ICD-10 codes is against the law.

However, false codings of diabetes type may occur in cases of an untypical diabetes course. Second, the data are primarily used for morbidity-related risk stratification reimbursement between insurance funds; thus, data handling is determined by strict regulations prescribed by German law (§273 and §268 of the Code of Social Law V, §3 Data Transparency Regulation). Finally, other studies have revealed similar prevalence estimates, which are in line with the current results (32,33).

Another limitation is that we used the Danish mortality rate ratios to calculate German mortality of people with and without diabetes because of the lack of appropriate data. Although we assume that the Danish estimates are highly reliable and the general and diabetes-specific mortality are comparable between Germany and Denmark, residual differences may be present. As a consequence, we conducted two different sensitivity analyses to account for uncertainties.

In conclusion, we have estimated for the first time in our knowledge the absolute number of excess deaths for people with diabetes and type 2 diabetes in Germany. The study found that 174,627 excess deaths were attributable to diabetes (deaths due to type 2 diabetes: 137,950) in 2010, which is considerably higher than the official German estimates that relied on information from death certificates. The method can be applied to other countries without national diabetes registries to determine the national burden of mortality attributable to diabetes.

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