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# BMJ Open

## All-cause mortality in adults with and without diabetes – Analysis of statutory health insurance claims data in Germany 2013-2014

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Complete List of Authors:	Schmidt, Christian; Robert Koch Institute, Department of Epidemiology and Health Monitoring Reitzle, Lukas; Robert Koch Institute, Department of Epidemiology and Health Monitoring Heidemann, Christin; Robert Koch Institute, Department of Epidemiology and Health Monitoring Paprott, Rebecca; Robert Koch Institute, Department of Epidemiology and Health Monitoring Ziese, Thomas; Robert Koch Institute, Department of Epidemiology and Health Monitoring Scheidt-Nave, Christa; Robert Koch-Institut, Dept. of Epidemiology and Health Monitoring Baumert, Jens; Robert Koch Institute, Department of Epidemiology and Health Monitoring
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4 1 All-cause mortality in adults with and without diabetes – Analysis of statutory  
5 2 health insurance claims data in Germany 2013-2014

6  
7 3 Christian Schmidt, research associate, Lukas Reitzle, research associate, Christin Heidemann  
8 4 senior research associate, Rebecca Paprott, research associate, Thomas Ziese, head of unit  
9 5 health reporting, Christa Scheidt-Nave, head of unit physical health, Jens Baumert, senior  
10 6 research associate

11  
12 7 All authors: Department of Epidemiology and Health Monitoring, Robert Koch Institute, Berlin,  
13 8 Germany, General-Pape-Str. 62-66, 12101 Berlin

14  
15 9 **Corresponding author:**

16  
17 10 Christian Schmidt  
18 11 Tel. +4930187543269; E-Mail: [schmidtchri@rki.de](mailto:schmidtchri@rki.de)  
19 12 Department of Epidemiology and Health Monitoring  
20 13 Robert Koch Institute, Berlin, Germany  
21 14

22  
23 15 **Email-Addresses of Authors:**

24 16 Lukas Reitzle: [reitzlel@rki.de](mailto:reitzlel@rki.de)  
25 17 Christin Heidemann: [heidemannc@rki.de](mailto:heidemannc@rki.de)  
26 18 Rebecca Paprott: [paprottr@rki.de](mailto:paprottr@rki.de)  
27 19 Thomas Ziese: [zieset@rki.de](mailto:zieset@rki.de)  
28 20 Christa Scheidt-Nave: [scheidt-navec@rki.de](mailto:scheidt-navec@rki.de)  
29 21 Jens Baumert: [baumertj@rki.de](mailto:baumertj@rki.de)  
30 22

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3 25 **Abstract**

4  
5 26 Objectives

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7 27 Little is known about the age-specific excess mortality pattern of people with diagnosed  
8 28 diabetes in Germany. Thus, our goal was to determine the excess mortality in diagnosed  
9 29 diabetes overall and stratified by age and sex based on claims data.

10  
11 30 Design

12  
13 31 Routine data analysis using a claims dataset from all statutory health insured persons in  
14 32 Germany in 2013, which accounts for about 90% of the population.

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16 33 Participants

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18 34 We included persons who lived in Germany, were insured at least 360 days, were not self-  
19 35 paying any health services and were aged 30 years or older leading to a total number of 47.3  
20 36 million insured persons for analyses.

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22 37 Exposure

23  
24 38 Diabetes was determined by ICD-10 codes E10 to E14, which were documented in 2013 in at  
25 39 least two quarters on an outpatient setting or at least once on an inpatient setting.

26  
27 40 Outcome measures

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29 41 The vital status in the study population was drawn from the claims dataset for the year 2014.  
30 42 We derived the excess mortality estimated as an age-adjusted mortality rate ratio (MRR) by  
31 43 sex and for age groups using a Poisson model.

32  
33 44 Main Results

34  
35 45 We found age-adjusted MRRs (95% CI) for diabetes of 1.52 (1.51 to 1.52) for women and 1.56  
36 46 (1.56 to 1.56) for men. These figures declined with increasing age and were highest for age 30  
37 47 to 34 years with 6.76 (4.99 to 9.15) for women and 6.87 (5.46 to 8.64) for men and lowest for  
38 48 age 95 years and older with 1.13 (1.10 to 1.15) for women and 1.11 (1.05 to 1.17) for men.

39  
40 49 Conclusions

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42 50 For the first time, we derived deeply age-stratified figures on excess mortality in diabetes for  
43 51 Germany. Establishing a sustainable analysis of excess mortality is aimed at within the  
44 52 framework of diabetes surveillance.

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3 54 **Strengths and limitations of this study**  
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- 5 55 • The study is based on documented data of all statutorily insured patients  
6 accounting for about 90% of the German population.  
7 56  
8  
9 57 • Mortality rates derived from the study data showed very good agreement with  
10 data from official death statistics covering the entire German population.  
11 58  
12  
13 59 • For the first time, this analysis allowed to assess detailed age-related patterns  
14 in women and men in the German population.  
15 60  
16  
17 61 • Our results are robust with respect to variation of the case definition of  
18 diabetes.  
19 62  
20  
21 63 • The study data are limited to documented diagnoses, i.e. no information about  
22 undiagnosed morbidity is available.  
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## 66 **Introduction**

67 Diabetes mellitus is a chronic metabolic disease of high public health impact in  
68 Germany and worldwide.<sup>1</sup> According to the Global Burden of Disease Study 2017  
69 diabetes ranks among the top 10 leading causes of death globally.<sup>2</sup> Available treatment  
70 with insulin and glucose lowering drugs has greatly reduced the risk of acute  
71 complications and premature mortality. Nevertheless, persons with diabetes still have  
72 a higher age-adjusted risk of death compared to persons without diabetes mainly  
73 because of an increased risk of micro- and macrovascular complications.<sup>3</sup>

74 Monitoring diabetes-associated mortality over time is an important part of national  
75 diabetes surveillance activities, as the age-specific excess risk of death among persons  
76 with diabetes compared to those without diabetes serves as an indicator of quality of  
77 diabetes care. Some countries, such as Sweden, Denmark and Scotland have  
78 established national diabetes registers, and along with a legal basis for individual  
79 health data linkage, these data allow a reliable assessment of diabetes-associated  
80 mortality in comparison to the general population<sup>4 5</sup> or population-based controls.<sup>6</sup>  
81 Results from these countries consistently demonstrate a significantly higher risk of  
82 death in association with diabetes, but greatly vary with regard to the overall  
83 magnitude of excess risk as well as sex differences. A recent meta-analysis of diabetes-  
84 associated all-cause-mortality based on 86 prospective cohorts showed a higher  
85 pooled adjusted relative risk of death among women than men (1.93 vs. 1.74 ).<sup>7</sup> The  
86 studies from Sweden as well as a further study from Australia have been age  
87 disaggregated, indicating that excess mortality among persons with type 2 diabetes  
88 significantly decreases with increasing chronological age.<sup>6 8</sup>

89 In Germany, a national diabetes surveillance system is currently being established at  
90 the Robert Koch Institute as the national public health institute. One of the main goals  
91 is to cover the diabetes-associated mortality continuously ([www.diabsurv.rki.de](http://www.diabsurv.rki.de)). Over  
92 the past 20-years a number of epidemiological studies in Germany have provided  
93 estimates of mortality rate ratios (MRRs) comparing mortality rates among persons  
94 with and without diabetes. The results from these studies vary due to differences in  
95 study design and study populations, methodological issues, regional vs. national data,  
96 follow-up time, and insight from age- and sex-stratified analyses is limited due to the

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3 97 small number of observations.<sup>9</sup> In addition to these population-based estimates, a  
4  
5 98 recent study estimated diabetes-associated MRRs for the population 65-90 years of  
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7 99 age in Germany based on mathematical modeling using official death statistics, and  
8  
9 100 prevalence and incidence estimates derived from statutory health insurance (SHI)  
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11 101 claims data.<sup>10</sup>

12  
13 102 Information on mortality has recently been added to a SHI claims dataset with  
14  
15 103 complete records of all insured persons, which is accessible to health researchers in  
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17 104 Germany. The present study for the first time used outpatient and inpatient SHI claims  
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19 105 data drawn from this dataset to analyse observed mortality rates for adults in  
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21 106 Germany with and without diagnosed diabetes. Our main aim was to provide  
22  
23 107 estimates of MRRs associated with diabetes within strata of narrow age bands and sex.

## 24 108 **Methods**

### 25 109 **Source of data**

26  
27  
28 110 We used the SHI claims research dataset hosted by the German Institute for Medical  
29  
30 111 Documentation and Information (DIMDI).<sup>11</sup> According to the Data Transparency  
31  
32 112 Regulation Act (DaTraV) 2012 this dataset has been made accessible to authorized  
33  
34 113 health researchers. Originally, these data were collected within the scope of the  
35  
36 114 German morbidity-based risk-adjustment scheme.<sup>12</sup> The dataset includes medical data  
37  
38 115 from approximately 70 million people covered by SHI, which are about 90% of the  
39  
40 116 German population. The DaTraV data contain complete data on outpatient and  
41  
42 117 inpatient diagnoses as well as prescribed drugs and the vital status.<sup>11</sup> Therefore, the  
43  
44 118 data can be analyzed across all sectors of care and providers within the SHI system. For  
45  
46 119 reasons of data protection, there is no direct access to these stored individual data.  
47  
48 120 Analyses are limited to aggregate data, which can be requested from the DIMDI data  
49  
50 121 processing centre. A research question needs to be submitted together with an  
51  
52 122 analytical scheme or a syntax query for data analysis. The request has to be approved  
53  
54 123 by the data processing centre and the aggregated results are checked and transmitted  
55  
56 124 to the applicant.

57  
58 125 We developed an SQL script for the analysis of mortality rates among persons with and  
59  
60 126 without diabetes based on DaTraV datasets 2013 and 2014. As described in detail



1  
2  
3 127 below, the SQL script had to take into account several specifics of the data, including  
4  
5 128 assessment of vital status and the case definition for diabetes.<sup>13</sup>  
6

### 7 129 **Study population**

8  
9 130 Information from more than 70 million SHI persons was available for the year 2013  
10  
11 131 (Figure 1). In addition to the individual SHI identification number, the year of birth and  
12  
13 132 sex were checked for unique assignment to the insured person. Persons with an  
14  
15 133 insured period of less than 360 days, persons who cover at least partly their own  
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17 134 health expenditure and persons with main residence abroad were excluded from the  
18  
19 135 analysis, because this may have precluded documentation of diabetes within the year  
20  
21 136 2013.

22 137 After these exclusions but mainly due to an insurance period of less than 360 days,  
23  
24 138 about 65.8 million persons were considered eligible for analysis. In addition, persons  
25  
26 139 aged younger than 30 years were excluded for data protection reasons due to the  
27  
28 140 small number of deaths among persons with diabetes in these age groups. The final  
29  
30 141 study population hence comprised a total of 47.3 million persons (Figure 1). Of these,  
31  
32 142 6.5 million persons with diabetes fulfilled the case definition for diabetes and 40.8  
33  
34 143 million persons were defined as having no diabetes. As the flow chart reveals, 0.29  
35  
36 144 million persons in the population with diabetes and 0.48 million persons in the  
37  
38 145 population without diabetes died in 2014 (Figure 1).  
39

40 146

### 41 147 **Patient and public involvement**

42 148 No patient involved.  
43  
44 149

45  
46 150 **Figure 1** Flow chart of selection of study population with excluding criteria and sample  
47  
48 151 sizes

### 49 50 51 152 **Definition of diabetes**

52  
53 153 We used the International Classification of Diseases (ICD-10) codes E10.- to E14.- to  
54  
55 154 define diabetes:

- 56  
57  
58 155 • E10.- Type 1 diabetes mellitus  
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- 156 • E11.- Type 2 diabetes mellitus
- 157 • E12.- Malnutrition related diabetes mellitus
- 158 • E13.- Other specified diabetes mellitus, for example diabetes related to
- 159 pancreatic insufficiency
- 160 • E14.- Unspecified diabetes mellitus.

161 In the outpatient setting, documentation of an additional ICD-tag “G” is required to  
162 indicate a confirmed diagnosis of diabetes. In the present analysis, this additional  
163 requirement was applied to all data originating in the outpatient setting, in order to  
164 increase the validity of the case definition for diabetes. Furthermore, an outpatient  
165 diagnosis of diabetes had to be documented in at least two quarters of the year for  
166 validation reasons. This definition is related to the m2Q criterion, which was originally  
167 used for reimbursement and is also recommended for epidemiological studies<sup>14</sup>. In  
168 the case of inpatient-documented diagnosis, one primary or secondary diagnosis of  
169 diabetes in the year 2013 was sufficient to identify a diabetes case.

170 In order to examine the impact of potential misclassification on the results, we  
171 conducted sensitivity analyses applying modified case definitions for diagnosed  
172 diabetes based on less stringent criteria: first, documentation of at least one confirmed  
173 outpatient diagnosis or one inpatient diagnosis in 2013 (“m1Q criterion”), and  
174 secondly, documentation of only one confirmed outpatient diagnosis in 2013 without  
175 any documented inpatient diagnosis.

### 177 **Assessment of mortality**

178 We calculated the mortality rates based on the vital status in 2014, since in the event  
179 of death no diagnoses for the year of death are available in the dataset.<sup>11</sup> The reason  
180 for this approach is that the SHI claims dataset was originally created only for  
181 morbidity-adjusted reimbursement of SHI companies and diagnoses in the year of  
182 death were not transmitted. Therefore, we used the difference of the year 2014 and  
183 the year of birth to calculate the age groups.

184 In order to examine whether assessment of vital status in the SHI claims dataset  
185 produced plausible results, we compared the observed overall mortality rates as total  
186 counts per 100,000 persons across age groups and stratified by sex with the  
187 corresponding mortality rates from the official cause of death statistics in Germany for

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3 188 the year 2014.<sup>15</sup> As illustrated in Figure 2 mortality rates per 100,000 persons based on  
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5 189 data from both sources showed high consistency in both sexes and in nearly all age  
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7 190 groups, with only minor deviations among middle-aged men and women 85 years of  
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9 191 age and older.

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11 192 **Figure 2** Age-specific mortality rates per 100,000 persons stratified by sex for the year  
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13 193 2014 as obtained from official cause of death statistics (Destatis) and claims data  
14  
15 194 (Datrav). The blue line indicates results from official statistics; the green line indicates  
16  
17 195 results from the DaTraV dataset.

### 18 196 **Statistical analysis**

19  
20 197 We estimated age- and sex-specific MRRs and 95% confidence intervals using Poisson  
21  
22 198 regression. We applied the GENMOD procedure implemented in the statistical  
23  
24 199 software SAS (Version 9.4 for Windows)<sup>16</sup>. Due to the aggregated count data of our  
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26 200 study population, we applied a count model for MRR estimations. We preferred a  
27  
28 201 Poisson model to a log-binomial model or negative binomial model, as the Poisson  
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30 202 distribution provides a good approximation to the underlying binomial distribution due  
31  
32 203 to increasing sample size and better convergence properties<sup>16</sup>. One central  
33  
34 204 assumption of the model is equality of mean and variance, which is often not fulfilled  
35  
36 205 for count data. In our analyses, we had to handle a large sample size, which tends to  
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38 206 result in a lower variance with respect to the mean value, what is called  
39  
40 207 underdispersion and could lead to biased, smaller standard errors. Therefore, we used  
41  
42 208 the residual deviance as scale parameter.

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44 209 We estimated MRRs separately for both sexes and over 5-year age groups for adults in  
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46 210 the age range 30 to 95 years and older. We also calculated age-adjusted MRRs  
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48 211 stratified by sex based on the 5-year age groups.

49  
50 212 In order to assess the impact of modified case definitions on the study results, we  
51  
52 213 conducted two sensitivity analyses calculating the age-adjusted MRRs for men and  
53  
54 214 women as described above.

1  
2  
3 215 **Results**

4  
5 216 **Description of the study population**

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7 217 Compared to men, women were overrepresented in the population without diabetes,  
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9 218 whereas proportions of men and women were similar in the population with diabetes  
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11 219 (Table 1). Accordingly, the diabetes prevalence among women (12.8%) was lower than  
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13 220 in men (14.9%). As expected, the population with diabetes had a higher mean age  
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15 221 compared to the population without diabetes. On average, women were older than  
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17 222 men among persons with and without diabetes. In terms of absolute numbers, more  
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19 223 women than men died in 2014 in the population with and without diabetes. However,  
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21 224 age-specific and age-standardized mortality rates per 1,000 persons were consistently  
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23 225 higher among men than women in both populations. In both sexes, mortality rates per  
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25 226 1,000 persons were markedly higher among individuals with than without diabetes  
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27 227 (Table 1).  
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229 **Table 1** Descriptive characteristics of the study population by diabetes status and sex  
 230 (DaTraV, age  $\geq$  30 years)

	No diabetes		Diabetes	
	Women	Men	Women	Men
Population size in M. (2013)	22,5	18,3	3,3	3,2
Proportion (%) 2013	55.1	44.9	50.8	49.2
Mean age in years 2013	55.9	53.6	71.5	67.9
Number of deaths 2014	254,408	220,305	148,491	140,024
Mortality rate per 1,000 persons*	12.00	12.74	19.96	21.91
Mortality rate per 1,000 persons across age groups*				
30 to 34 years	0.30	0.62	2.03	4.26
35 to 39 years	0.45	0.87	1.86	4.38
40 to 44 years	0.77	1.40	3.75	5.31
45 to 49 years	1.29	2.34	4.62	7.64
50 to 54 years	2.23	4.13	6.95	10.18
55 to 59 years	3.41	6.73	9.19	14.55
60 to 64 years	5.21	10.71	11.18	19.84
65 to 69 years	7.80	15.44	15.42	25.84
70 to 74 years	11.63	22.35	22.56	38.24
75 to 79 years	19.15	33.64	35.17	55.34
80 to 84 years	40.02	62.14	62.97	89.99
85 to 89 years	83.06	111.42	113.91	144.18
90 to 94 years	157.24	191.04	194.06	229.21
95 years and older	270.33	303.74	304.13	336.90

231 \*age-standardized to the German population 2013 using all displayed age groups

232

## 233 **Main Analysis**

234 **Figure 3** MRRs for persons with diabetes compared to persons without diabetes by sex  
235 and age groups. Overall estimates are adjusted using all displayed age groups.

236 MRR estimates in association with diagnosed diabetes as obtained from Poisson  
237 regression are depicted in Figure 3. For both sexes, the age-specific MRR estimates  
238 decreased with increasing chronological age from 6.76 among women and 6.87 among  
239 men in the youngest age group to 3.12 among women and 2.46 among men aged 50-  
240 54 years to 1.13 among women and 1.11 among men aged 95 years and older. Except  
241 for persons younger than 40 years of age, MRR estimates in association with diabetes  
242 were higher among women than men. In particular, among persons 50-79 years, the  
243 MRR was between 1.26 and 1.12 significantly times higher among women than men.

244 Overall adjusted MRR estimates were comparable for women and men (1.52 vs. 1.56).  
245 Constraining our analysis to persons below 90 years of age reversed the overall age-  
246 adjusted MRRs regarding sex with still comparable estimates of 1.66 for women and  
247 1.61 for men.

## 248 **Sensitivity analyses**

249 An excess risk of death in association with diabetes among men and women was  
250 confirmed in two sensitivity analyses applying less stringent case definitions for  
251 diabetes (Table 2).

252 Compared to the main analysis, where the case definition for diabetes required  
253 documentation of a confirmed diabetes diagnosis in at least two quarters of the year  
254 2013 for outpatient data or one inpatient diagnosis of diabetes in 2013, the first case  
255 definition in Table 2 additionally includes persons with only one confirmed outpatient  
256 diagnosis of diabetes in 2013. This means that about 0.5 million persons were added to  
257 the population with diabetes and at the same time removed from the population  
258 without diabetes compared to the numbers used for the main analysis as shown in  
259 Figure 1. Results of this sensitivity analysis were similar to those of the main analysis,  
260 with only slightly lower overall MRR estimates of 1.51 among women and 1.55 among  
261 men. In contrast, markedly attenuated overall MRR estimates were obtained in the  
262 second sensitivity analysis, where the case definition for diabetes was based on the

documentation of only one confirmed outpatient diagnosis. Still, the age-adjusted MRRs resulting from this case definition showed a significantly nearly 20% higher risk of death in men and women with diagnosed diabetes compared to those without diagnosed diabetes (Table 2).

**Table 2** Sensitivity analyses applying modified diabetes case definitions: number of persons by diabetes status and age-adjusted MRRs stratified by sex (DaTraV, age  $\geq$  30 years).

	Women		Men	
	N (no diabetes / diabetes)	MRRs (95% CI)	N (no diabetes / diabetes)	MRRs (95% CI)
Sensitivity analysis 1*	22.3 M/ 3.6 M	1.51 (1.51 to 1.51)	18.1 M/ 3.4 M	1.55 (1.55 to 1.55)
Sensitivity analysis 2#	22.3 M/ 0.25 M	1.19 (1.18 to 1.20)	18.1 M/ 0.21 M	1.20 (1.19 to 1.21)

\* Documentation of at least one outpatient (confirmed) or inpatient diagnosis of diabetes in 2013

# Documentation of only one outpatient (confirmed) diagnosis of diabetes in 2013. Deviations from figures in figure 1 are due to rounding.

## Discussion

### Main findings

To the best of our knowledge, we present for the first time deeply age-stratified MRR estimates in association with diagnosed diabetes among men and women 30 years of age and older in Germany based on SHI claims data covering about 90% of the population. Overall, men and women with diabetes had an about 50% higher age-adjusted risk of death compared to adults without diabetes. Across strata of increasing age, the diabetes-associated MRRs considerably decreased with slightly higher estimates among women than men in the population aged 40-80 years. Results persisted in sensitivity analyses applying modified case definitions for diabetes, with the exception of markedly reduced albeit still significantly higher diabetes-associated risk of death based on the least stringent case definition for diabetes requiring only one outpatient diagnosis for diabetes throughout the year 2013.

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3 286 Our findings regarding age-related decreases in diabetes-associated MRRs partly agree  
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5 287 with results from two previous nationwide studies in Germany.<sup>10 17</sup> A population-based  
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7 288 cohort study based on 12-year-mortality follow-up of adults participating in the  
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9 289 German National Health Interview and Examination Survey 1998 (GNHIES98) reported  
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11 290 decreasing age-specific diabetes-associated MRRs in both sexes as well as overall age-  
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13 291 adjusted MRR estimates of similar magnitude as in the present study.<sup>17</sup> In this previous  
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15 292 analysis no sex differences in MRRs from all causes in association with diagnosed type  
16  
17 293 2 diabetes were observed, although significant detection of a sex differential may  
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19 294 have been precluded by a limited number of deaths among adults with diabetes.  
20  
21 295 Tönnies et al. calculated type-2-diabetes-associated MRR applying an illness-death  
22  
23 296 model, with estimates on diabetes prevalence and incidence derived from SHI claims  
24  
25 297 data and mortality rates of the general population from official death statistics. These  
26  
27 298 authors reported age-related decreases in MRRs, but considerably higher overall age-  
28  
29 299 adjusted MRR estimates, with higher estimates among women than men (3.0 vs.  
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31 300 2.3).<sup>10</sup> For comparison with this previous study which focused on the population 65-90  
32  
33 301 years of age in Germany we limited our analyses to the population aged 65-90 years  
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35 302 and found no differences in MRRs between women and men (1.47 versus 1.48).  
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37 303 Consistent with our results, nationwide studies in several other countries based on  
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39 304 diabetes registers or diabetes surveillance systems have reported a higher diabetes-  
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41 305 associated risk of all-cause mortality compared to general population or population  
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43 306 based controls.<sup>4-6 8 18</sup>  
44  
45 307 The Swedish national diabetes register and the Australian diabetes surveillance  
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47 308 showed that the excess risk of death in association with diagnosed type 2 diabetes  
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49 309 declined with increasing chronological age.<sup>6 8</sup> Although the present study could not  
50  
51 310 differentiate by type of diabetes, these results are in line with our findings, since type 2  
52  
53 311 diabetes accounts for the vast majority of diabetes cases among older adults. The age-  
54  
55 312 related decline in diabetes-associated excess risk of all-cause mortality might be due to  
56  
57 313 the different onsets of diabetes on the life span and the associated disease durations.  
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59 314 It may reflect increases in competing risk of death in older age groups as well as  
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315 survival disadvantage in association with increased diabetes duration. In addition, the



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3 316 number of severe comorbidities in people with and without diabetes converges with  
4  
5 317 increasing age.

6  
7 318 With regard to sex differences in diabetes-associated relative risk or excess risk of all-  
8  
9 319 cause mortality, previous studies from other countries showed conflicting findings.<sup>4 5 8</sup>  
10  
11 320 Our age-specific estimates of diabetes-associated MRRs showed higher risk estimates  
12  
13 321 among women than among men for persons aged 50-79. This higher risk among  
14  
15 322 women declined with increasing age and diminished in the oldest age groups. This  
16  
17 323 consistent pattern is comparable to a study from Australia for 2004-2010 which  
18  
19 324 showed higher standardized mortality ratios (SMRs) in women than in men especially  
20  
21 325 for persons aged 50-79 years and very similar SMRs for women and men aged 80 years  
22  
23 326 or older (1.03 and 0.98).<sup>8</sup> A recently conducted systematic review and meta-analysis  
24  
25 327 including 49 studies with 86 prospective cohorts showed a combined MRR of 1.93 for  
26  
27 328 women and 1.74 for men with a pooled women-to-men RRR of 1.13.<sup>7</sup> However  
28  
29 329 estimates across studies ranged from 1.24 to 3.67 in women and from 1.32 to 3.13 in  
30  
31 330 men, pooled women-to-men RRR varied from 0.64 to 1.74.<sup>7</sup> Overall, differences in  
32  
33 331 study results regarding a sex differential in excess risk of diabetes-associated all-cause  
34  
35 332 mortality might, at least in part, be explained by differences in the age range,  
36  
37 333 underestimation of older people, time of follow-up and applied methods for risk  
38  
39 334 estimation.

40  
41 335 Prospective population-based studies are needed to obtain a deeper insight into the  
42  
43 336 role of sex difference in diabetes-associated mortality risks by taking relevant risk  
44  
45 337 factors such as lifestyle behavior and co-morbidities into account.

### 46 338 **Practical implications**

47 339 Our findings confirm that diagnosed diabetes in Germany is still associated with a  
48  
49 340 significantly elevated, several times higher risk of death among men and women, in  
50  
51 341 particular in younger and middle age. This emphasizes the need for effective primary  
52  
53 342 and secondary prevention. Further improvements in the early detection of diabetes,  
54  
55 343 particularly in younger ages, alongside with evidence based treatments, could  
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57 344 contribute to a reduction in excess mortality.

58 345 Our results open the perspective to close an important gap in diabetes surveillance in  
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60 346 Germany, as the SHI claims dataset appears to be suitable for close monitoring of

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3 347 diabetes-associated excess risk of death, which is a key indicator in the national  
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5 348 diabetes surveillance system. In addition, the dataset will permit calculation of closely  
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7 349 related indicators, including the absolute number of deaths in association with  
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9 350 diabetes, and composite indicators of disease burden, including healthy life years and  
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11 351 the number of years lost in association with diabetes. Thus, including SHI claims data  
12  
13 352 dataset will harness the potential for improved health information systems as a basis  
14  
15 353 for the surveillance of diabetes and other noncommunicable diseases (NCD).

### 16 354 **Strengths and limitations**

17  
18 355 The main strength of our analysis is the completeness of the dataset, since about 90%  
19  
20 356 of the German population is covered by SHI. Mortality rates derived from the SHI  
21  
22 357 claims dataset showed good agreement with data from official death statistics, which  
23  
24 358 underlines the potential for generalization of our results. Our findings from sensitivity  
25  
26 359 analyses support the validity of the data. We consistently showed an excess risk of all-  
27  
28 360 cause mortality in association with diagnosed diabetes based on varying case  
29  
30 361 definitions for diabetes.

31 362 Taken together, our results demonstrate that the DaTraV dataset could essentially  
32  
33 363 contribute to close current gaps in diabetes surveillance with an overall good  
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35 364 documentation quality of diabetes and the advantage to consider inpatient as well as  
36  
37 365 outpatient data for case definition.

38 366 A great disadvantage of routine datasets based solely on documented diagnoses is that  
39  
40 367 no information about undiagnosed morbidity can be drawn. National surveys with an  
41  
42 368 additional HbA1c measurement in blood samples of participants show a relevant  
43  
44 369 proportion of undiagnosed diabetes. Although this proportion has decreased over  
45  
46 370 time, it is still relatively high<sup>19</sup> and at the same time is related to a slightly higher  
47  
48 371 excess mortality than diagnosed diabetes.<sup>17 20</sup> For this reason the current routine data  
49  
50 372 analysis is likely to underestimate the excess mortality in diabetes.

51 373 There are a number of limitations which arise from the specific construction of the  
52  
53 374 DaTraV dataset, which originally served economic but not research purposes. We had  
54  
55 375 to determine cases of diabetes in the data in 2013 only, in order to identify persons  
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57 376 who died in 2014 among persons with and without diabetes. This implies that those  
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59 377 who died with newly documented diabetes in 2014 are not detectable in the data as  
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3 378 diabetes cases and hence will be counted as persons without diabetes. We cannot  
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5 379 exclude that this also contributed to an underestimation of diabetes-associated excess  
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7 380 mortality. Since diabetes is a chronic disease, and long-term complications account for  
8  
9 381 the majority of diabetes-associated deaths, we assume that this had only little impact  
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11 382 on our results. The planned revision of the Data Transparency Regulations in Germany  
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13 383 could help to overcome current shortcomings.  
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15 384 Furthermore, the currently missing stratification of the dataset according to  
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17 385 geographic region and social status or social deprivation should be possible in the  
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19 386 future, hence we will be able to analyze and compare mortality trends within Germany  
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21 387 as well as at a national level with other countries.  
22  
23 388 The present study included adults 30 years of age and older, and type 2 diabetes is  
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25 389 likely to account for most cases of documented diabetes. Nevertheless, it will be  
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27 390 important to overcome current limitations to differentiate between major types of  
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29 391 diabetes in claims data. The main problem is the frequent coding of an unspecific  
30  
31 392 diabetes (ICD-10: E14.-) or even diagnoses that are mutually exclusive (E10.- and E11.-)  
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33 393 in the data.<sup>21</sup> A recent analysis of the here used dataset has demonstrated that  
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35 394 including information on medication may improve assignment of unspecific diabetes  
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37 395 codes to type 2 diabetes.<sup>22</sup> Among children and adolescents type 1 diabetes is the  
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39 396 predominant type of diabetes. As insulin treatment is required here, documented  
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41 397 insulin use is an essential part of the case definition for type 1 diabetes, and also helps  
42  
43 398 to clarify diabetes definition.<sup>23</sup>

## 42 399 **Conclusions**

44 400 Diabetes-related risk of death is a key indicator for monitoring diabetes epidemiology  
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46 401 and quality of diabetes care. Establishing sustainable time trends for this indicator as  
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48 402 part of the national diabetes surveillance system in Germany is of great need, but was  
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50 403 so far precluded by the lack of a valid and timely accessible dataset. Results of the  
51  
52 404 present study demonstrate that analysis of SHI claims data may provide a solution in  
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54 405 closing this information gap. Further research is needed to analyze and to improve the  
55  
56 406 quality of the data, in particular with regard to case definitions. In this case, the SHI  
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58 407 claims data could also serve to calculate and monitor the absolute number of diabetes-  
59  
60 408 associated deaths as well as composite indicators of disease burden, such as diabetes-

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3 409 associated healthy life years and years of life lost. Stratification of SHI claims data  
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5 410 according to geographic region and social status or social deprivation will be possible  
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7 411 in the future, hence we will be able to analyze and compare diabetes-associated  
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9 412 mortality trends within Germany but also with international developments.<sup>3</sup> This will  
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11 413 strengthen surveillance activities for the prevention and control of diabetes and other  
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13 414 major NCD at a national level and also enhance international collaboration in diabetes  
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15 415 and NCD surveillance and burden of disease estimates.  
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For peer review only

417 **Footnotes**

418

419 **Contributors:** CS, JB and CH designed the study. CS, LR and JB performed the analysis. CS, CSN  
420 and JB wrote the initial version of the manuscript. LR, RP and TZ revised the manuscript. All  
421 authors read and approved the final manuscript. All authors had full access to all of the data  
422 (including statistical reports and tables) in the study and can take responsibility for the  
423 integrity of the data and the accuracy of the data analysis. CS is the lead author and guarantor.

424

425 **Transparency declaration:** The lead author affirms that this manuscript is an honest, accurate,  
426 and transparent account of the study being reported; that no important aspects of the study  
427 have been omitted; and that any discrepancies from the study as planned (and, if relevant,  
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429

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435

436 **Competing interests:** All authors have completed the Unified Competing Interest form at  
437 [www.icmje.org/coi\\_disclosure.pdf](http://www.icmje.org/coi_disclosure.pdf) (available on request from the corresponding author) and  
438 declare: no support from any organisation for the submitted work, no financial relationships  
439 with any organisations that might have an interest in the submitted work in the previous three  
440 years no other relationships or activities that could appear to have influenced the submitted  
441 work.

442 **Ethics approval:** This study was not approved by a research ethics committee, because our  
443 study did not meet the criteria for human subjects research.

444 **Data sharing:** The SQL code for requesting aggregated data and statistical codes available from  
445 the corresponding author at [schmidtchri@rki.de](mailto:schmidtchri@rki.de).

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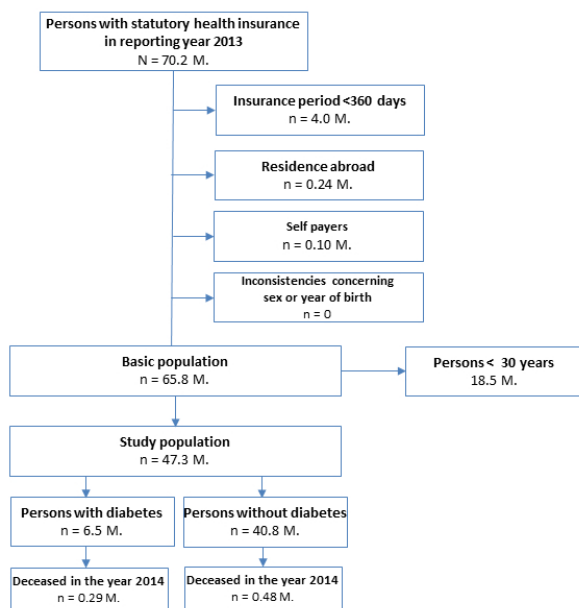


Figure 1 Flow chart of selection of study population with excluding criteria and sample sizes.

Figure 1 Flow chart of selection of study population with excluding criteria and sample sizes

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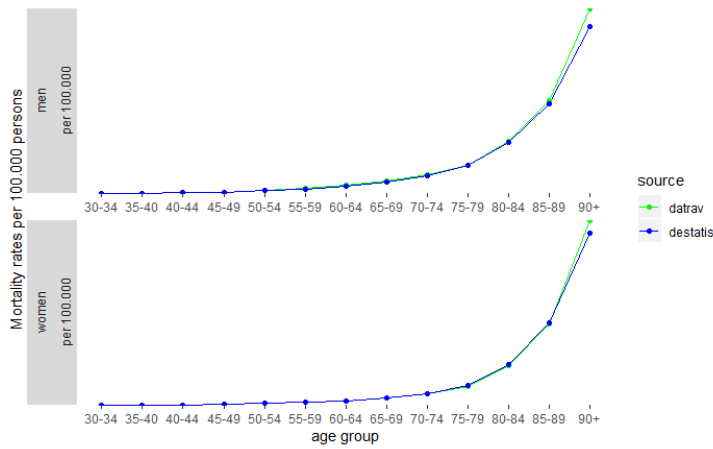
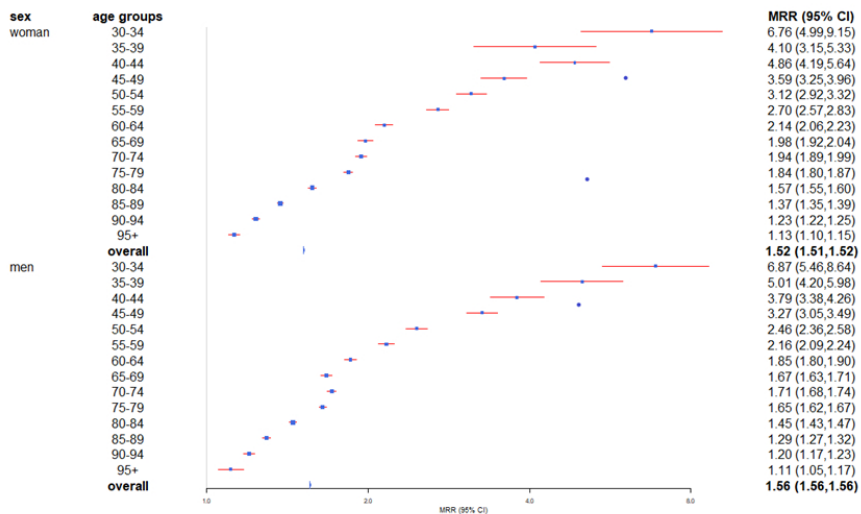


Figure 2 Age-specific mortality rates per 100,000 persons stratified by sex for the year 2014 as obtained from official cause of death statistics (Destatis) and claims data (Datrav). The blue line indicates results from official statistics; the green line indicates results from the DaTraV dataset.

Figure 2 Age-specific mortality rates per 100,000 persons stratified by sex for the year 2014 as obtained from official cause of death statistics (Destatis) and claims data (Datrav). The blue line indicates results from official statistics; the green line indicates results from the DaTraV dataset.

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**Figure 3** MRRs for persons with diabetes compared to persons without diabetes by sex and age groups. Overall estimates are adjusted using all displayed age groups.

Figure 3 MRRs for persons with diabetes compared to persons without diabetes by sex and age groups. Overall estimates are adjusted using all displayed age groups.

254x190mm (96 x 96 DPI)

STROBE Statement—Checklist of items that should be included in reports of *cohort studies*

	Item No	Recommendation	Page No
<b>Title and abstract</b>	1	(a) Indicate the study's design with a commonly used term in the title or the abstract	2
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found	2
<b>Introduction</b>			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4,5
Objectives	3	State specific objectives, including any prespecified hypotheses	5
<b>Methods</b>			
Study design	4	Present key elements of study design early in the paper	2,5-6
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	2,5-6
Participants	6	(a) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	6, 7
		(b) For matched studies, give matching criteria and number of exposed and unexposed	NA
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	6,7
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	5,6
Bias	9	Describe any efforts to address potential sources of bias	8
Study size	10	Explain how the study size was arrived at	6
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	8
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding	8
		(b) Describe any methods used to examine subgroups and interactions	8
		(c) Explain how missing data were addressed	NA
		(d) If applicable, explain how loss to follow-up was addressed	NA
		(e) Describe any sensitivity analyses	8,11
<b>Results</b>			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	6
		(b) Give reasons for non-participation at each stage	NA
		(c) Consider use of a flow diagram	6
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	8-10
		(b) Indicate number of participants with missing data for each variable of interest	NA
		(c) Summarise follow-up time (eg, average and total amount)	NA
Outcome data	15*	Report numbers of outcome events or summary measures over time	10

1	Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	10,11
2			(b) Report category boundaries when continuous variables were categorized	NA
3			(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	NA
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9	Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	11,12
10				
11	<b>Discussion</b>			
12				
13	Key results	18	Summarise key results with reference to study objectives	12-14
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15	Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	15,16
16				
17	Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	12-14
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20	Generalisability	21	Discuss the generalisability (external validity) of the study results	15,16
21				
22	<b>Other information</b>			
23	Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	18
24				
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\*Give information separately for exposed and unexposed groups.

**Note:** An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at <http://www.plosmedicine.org/>, Annals of Internal Medicine at <http://www.annals.org/>, and Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is available at <http://www.strobe-statement.org>.

# BMJ Open

## Excess mortality in adults with documented diabetes in Germany – Routine data analysis of all insurance claims in Germany 2013-2014

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1 **Excess mortality in adults with documented diabetes in Germany – Routine data**  
2 **analysis of all insurance claims in Germany 2013-2014**

3 Christian Schmidt, research associate, Lukas Reitzle, research associate, Christin Heidemann  
4 senior research associate, Rebecca Paprott, research associate, Thomas Ziese, head of unit  
5 health reporting, Christa Scheidt-Nave, head of unit physical health, Jens Baumert, senior  
6 research associate

7 All authors: Department of Epidemiology and Health Monitoring, Robert Koch Institute, Berlin,  
8 Germany

9 **Corresponding author:**

10 Christian Schmidt  
11 Tel. +4930187543269; E-Mail: [schmidtchri@rki.de](mailto:schmidtchri@rki.de)  
12 Robert Koch Institut, Berlin, Germany  
13 ISNI: 0000000109403744

14  
15 **Email-Addresses of Authors:**

16 Lukas Reitzle: [reitzlel@rki.de](mailto:reitzlel@rki.de)  
17 Christin Heidemann: [heidemannc@rki.de](mailto:heidemannc@rki.de)  
18 Rebecca Paprott: [paprottr@rki.de](mailto:paprottr@rki.de)  
19 Thomas Ziese: [zieset@rki.de](mailto:zieset@rki.de)  
20 Christa Scheidt-Nave: [scheidt-navec@rki.de](mailto:scheidt-navec@rki.de)  
21 Jens Baumert: [baumertj@rki.de](mailto:baumertj@rki.de)

22  
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3 **25 Abstract**

4  
5 26 Objectives

6  
7 27 Little is known about the age-specific excess mortality pattern of people with diagnosed  
8 28 diabetes in Germany. Thus, our goal was to determine the excess mortality in diagnosed  
9 29 diabetes overall and stratified by age and sex based on claims data.

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11 30 Design

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13 31 Routine data analysis using a claims dataset from all statutory health insured persons in  
14 32 Germany in 2013, which accounts for about 90% of the population.

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16 33 Participants

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18 34 We included persons who lived in Germany, were insured at least 360 days, were not self-  
19 35 paying any health services and were aged 30 years or older leading to a total number of 47.3  
20 36 million insured persons for analyses.

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22 37 Exposure

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24 38 Diabetes was determined by ICD-10 codes E10 to E14, which were documented in 2013 in at  
25 39 least two quarters on an outpatient setting or at least once on an inpatient setting.

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27 40 Outcome measures

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29 41 The vital status in the study population was drawn from the claims dataset for the year 2014.  
30 42 We derived the excess mortality estimated as an age-adjusted mortality rate ratio (MRR) by  
31 43 sex and for age groups using a Poisson model.

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33 44 Main Results

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35 45 We found age-adjusted MRRs (95% CI) for diabetes of 1.52 (1.51 to 1.52) for women and 1.56  
36 46 (1.56 to 1.56) for men. These figures declined with increasing age and were highest for age 30  
37 47 to 34 years with 6.76 (4.99 to 9.15) for women and 6.87 (5.46 to 8.64) for men and lowest for  
38 48 age 95 years and older with 1.13 (1.10 to 1.15) for women and 1.11 (1.05 to 1.17) for men.

39  
40 49 Conclusions

41  
42 50 We derived deeply age-stratified figures on excess mortality in diabetes for Germany.  
43 51 Establishing a sustainable analysis of excess mortality is aimed at within the framework of  
44 52 diabetes surveillance.



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3 54 **Strengths and limitations of this study**  
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- 5 55 • This is the first study in Germany, which analyses excess mortality of diabetes  
6 on the basis of routine data covering almost the entire German population.  
7 56  
8  
9 57 • The completeness of the study data in terms of deaths and documented  
10 diagnosis allows calculating nearly unbiased and deep stratified  
11 58  
12 59 diabetes-related mortality.  
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14 60 • We have not distinguished the type of diabetes because routine data contain  
15 implausible double diagnoses of type 1 and type 2 diabetes in the same person.  
16 61  
17 62 • The study data are limited to documented diagnoses, i.e. no information about  
18 undiagnosed morbidity is available.  
19 63  
20 64 • In principle, the study data allows a continuous assessment of changes in  
21 mortality, which is suitable for public health surveillance.  
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## 67 **Introduction**

68 Diabetes mellitus is a chronic metabolic disease of high public health impact in  
69 Germany and worldwide.<sup>1</sup> According to the Global Burden of Disease Study 2017  
70 diabetes ranks among the top 10 leading causes of death globally.<sup>2</sup> Available treatment  
71 with insulin and glucose lowering drugs has greatly reduced the risk of acute  
72 complications and premature mortality. Nevertheless, persons with diabetes still have  
73 a higher age-adjusted risk of death compared to persons without diabetes mainly  
74 because of an increased risk of micro- and macrovascular complications.<sup>3</sup>

75 Monitoring diabetes-related mortality over time is an important part of national  
76 diabetes surveillance activities, as the age-specific excess risk of death among persons  
77 with diabetes compared to those without diabetes serves as an indicator of quality of  
78 diabetes care. Some countries, such as Sweden, Denmark and Scotland have  
79 established national diabetes registers, and along with a legal basis for individual  
80 health data linkage, these data allow a reliable assessment of diabetes-related  
81 mortality in comparison to the general population<sup>4,5</sup> or population-based controls.<sup>6</sup>  
82 Results from these countries consistently demonstrate a significantly higher risk of  
83 death in association with diabetes, but greatly vary with regard to the overall  
84 magnitude of excess risk as well as sex differences. A recent meta-analysis of diabetes-  
85 related all-cause mortality based on 86 prospective cohorts showed a higher pooled  
86 adjusted relative risk of death among women than men (1.93 vs. 1.74 ).<sup>7</sup> The studies  
87 from Sweden as well as a further study from Australia have been age disaggregated,  
88 indicating that excess mortality among persons with type 2 diabetes significantly  
89 decreases with increasing chronological age.<sup>6,8</sup>

90 In Germany, a national diabetes surveillance system is currently being established at  
91 the Robert Koch Institute as the national public health institute. One of the main goals  
92 is to cover the diabetes-related mortality continuously ([www.diabsurv.rki.de](http://www.diabsurv.rki.de)). Over the  
93 past 20-years a number of epidemiological studies in Germany have provided  
94 estimates of mortality rate ratios (MRRs) comparing mortality rates among persons  
95 with and without diabetes. The results from these studies vary due to differences in  
96 study design and study populations, methodological issues, regional vs. national data,  
97 follow-up time, and insight from age- and sex-stratified analyses is limited due to the

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3 98 small number of observations.<sup>9</sup> In addition to these population-based estimates, a  
4  
5 99 recent study estimated diabetes-related MRRs for the population 65-90 years of age in  
6  
7 100 Germany based on mathematical modeling using official death statistics, and  
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9 101 prevalence and incidence estimates derived from statutory health insurance (SHI)  
10  
11 102 claims data.<sup>10</sup> Due to partly conflicting findings stated above, further research is  
12  
13 103 needed to increase knowledge on diabetes-related excess mortality, especially with  
14  
15 104 respect to differences in magnitude by age, sex, region and time trend.

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17 105 Information on mortality has recently been added to a SHI claims dataset with  
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19 106 complete records of all insured persons in Germany. As almost 90% of the population  
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21 107 is covered by statutory health insurance, this data source has enormous potential for  
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23 108 public health research, including detailed analyses of mortality patterns. The present  
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25 109 study for the first time used outpatient and inpatient SHI claims data drawn from this  
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27 110 dataset to analyse observed mortality rates for adults in Germany with and without  
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29 111 diagnosed diabetes. Up to now, diabetes-related MRRs from the age of 30 years in 5-  
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31 112 years age bands have not been available for the German population. Against this  
32  
33 113 background our main aim was to provide for the first time estimates of MRRs related  
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35 114 to diabetes within strata of narrow age bands and sex for Germany and thus adds  
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37 115 important knowledge in diabetes-related excess mortality. Deeply stratified mortality  
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39 116 rates based on valid data are important for the surveillance of diabetes in Germany, as  
40  
41 117 they allow a comparison over time and with other countries.

## 41 **Methods**

### 42 **Source of data**

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45 120 We used the SHI claims research dataset hosted by the German Institute for Medical  
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47 121 Documentation and Information (DIMDI).<sup>11</sup> According to the Data Transparency  
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49 122 Regulation Act (DaTraV) 2012 this dataset has been made accessible to authorized  
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51 123 health researchers. Originally, these data were collected within the scope of the  
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53 124 German morbidity-based risk-adjustment scheme.<sup>12</sup> The dataset includes medical data  
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55 125 from approximately 70 million people covered by SHI, which are about 90% of the  
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57 126 German population. The DaTraV data contain complete data on outpatient and  
58  
59 127 inpatient diagnoses as well as prescribed drugs and the vital status.<sup>11</sup> Therefore, the  
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128 data can be analyzed across all sectors of care and providers within the SHI system. For

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3 129 reasons of data protection, there is no direct access to these stored individual data.  
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5 130 Analyses are limited to aggregate data, which can be requested from the DIMDI data  
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7 131 processing centre. A research question needs to be submitted together with an  
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9 132 analytical scheme or a syntax query for data analysis. The request has to be approved  
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11 133 by the data processing centre and the aggregated results are checked and transmitted  
12  
13 134 to the applicant.

14 135 We developed an SQL script for the analysis of mortality rates among persons with and  
15  
16 136 without diabetes based on DaTraV datasets 2013 and 2014. As described in detail  
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18 137 below, the SQL script had to take into account several specifics of the data, including  
19  
20 138 assessment of vital status and the case definition for diabetes.<sup>13</sup>

### 21 22 139 **Study population**

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24 140 Information from more than 70 million SHI persons was available for the year 2013  
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26 141 (Figure 1). In addition to the individual SHI identification number, the year of birth and  
27  
28 142 sex were checked for unique assignment to the insured person. Persons with an  
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30 143 insured period of less than 360 days, persons who cover at least partly their own  
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32 144 health expenditure and persons with main residence abroad were excluded from the  
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34 145 analysis, because this may have precluded documentation of diabetes within the year  
35  
36 146 2013.

37 147 After these exclusions but mainly due to an insurance period of less than 360 days,  
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39 148 about 65.8 million persons were considered eligible for analysis. In addition, persons  
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41 149 aged younger than 30 years were excluded for data protection reasons due to the  
42  
43 150 small number of deaths among persons with diabetes in these age groups. The final  
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45 151 study population hence comprised a total of 47.3 million persons (Figure 1). Of these,  
46  
47 152 6.5 million persons with diabetes fulfilled the case definition for diabetes and 40.8  
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49 153 million persons were defined as having no diabetes. As the flow chart reveals, 0.29  
50  
51 154 million persons in the population with diabetes and 0.48 million persons in the  
52  
53 155 population without diabetes died in 2014 (Figure 1).

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### 55 157 **Patient and public involvement**

56 158 No patient involved.

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## 160 **Definition of diabetes**

161 We used the International Classification of Diseases (ICD-10) codes E10.- to E14.- to  
162 define diabetes:

- 163 • E10.- Type 1 diabetes mellitus
- 164 • E11.- Type 2 diabetes mellitus
- 165 • E12.- Malnutrition related diabetes mellitus
- 166 • E13.- Other specified diabetes mellitus, for example diabetes related to  
167 pancreatic insufficiency
- 168 • E14.- Unspecified diabetes mellitus.

169 In the outpatient setting, documentation of an additional ICD-tag “G” is required to  
170 indicate a confirmed diagnosis of diabetes. In the present analysis, this additional  
171 requirement was applied to all data originating in the outpatient setting, in order to  
172 increase the validity of the case definition for diabetes. Furthermore, an outpatient  
173 diagnosis of diabetes had to be documented in at least two quarters of the year for  
174 validation reasons. This definition is related to the m2Q criterion, which was originally  
175 used for reimbursement and is also recommended for epidemiological studies<sup>14</sup>. In  
176 the case of inpatient-documented diagnosis, one primary or secondary diagnosis of  
177 diabetes in the year 2013 was sufficient to identify a diabetes case.

178 In order to examine the impact of potential misclassification on the results, we  
179 conducted sensitivity analyses applying modified case definitions for diagnosed  
180 diabetes based on less stringent criteria: first, documentation of at least one confirmed  
181 outpatient diagnosis or one inpatient diagnosis in 2013 (“m1Q criterion”), and  
182 secondly, documentation of only one confirmed outpatient diagnosis in 2013 without  
183 any documented inpatient diagnosis.

184

## 185 **Assessment of mortality**

186 We calculated the mortality rates based on the vital status in 2014, since in the event  
187 of death no diagnoses for the year of death are available in the dataset.<sup>11</sup> The reason  
188 for this approach is that the SHI claims dataset was originally created only for  
189 morbidity-adjusted reimbursement of SHI companies and diagnoses in the year of  
190 death were not transmitted. Therefore, we used the difference of the year 2014 and  
191 the year of birth to calculate the age groups.

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3 192 In order to examine whether assessment of vital status in the SHI claims dataset  
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5 193 produced plausible results, we compared the observed overall mortality rates as total  
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7 194 counts per 100,000 persons across age groups and stratified by sex with the  
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9 195 corresponding mortality rates from the official cause of death statistics in Germany for  
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11 196 the year 2014.<sup>15</sup> As illustrated in Figure 2 mortality rates per 100,000 persons based on  
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13 197 data from both sources showed high consistency in both sexes and in nearly all age  
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15 198 groups, with only minor deviations among middle-aged men and women 85 years of  
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17 199 age and older.

## 18 200 **Statistical analysis**

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20 201 We estimated age- and sex-specific MRRs and 95% confidence intervals using Poisson  
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22 202 regression. We applied the GENMOD procedure implemented in the statistical  
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24 203 software SAS (Version 9.4 for Windows)<sup>16</sup>. Due to the aggregated count data of our  
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26 204 study population, we applied a count model for MRR estimations. We preferred a  
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28 205 Poisson model to a log-binomial model or negative binomial model, as the Poisson  
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30 206 distribution provides a good approximation to the underlying binomial distribution due  
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32 207 to increasing sample size and better convergence properties<sup>16</sup>. One central  
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34 208 assumption of the model is equality of mean and variance, which is often not fulfilled  
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36 209 for count data. In our analyses, we had to handle a large sample size, which tends to  
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38 210 result in a lower variance with respect to the mean value, what is called  
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40 211 underdispersion and could lead to biased, smaller standard errors. Therefore, we used  
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42 212 the residual deviance as scale parameter.

43 213 We estimated MRRs separately for both sexes and over 5-year age groups for adults in  
44  
45 214 the age range 30 to 95 years and older. We also calculated age-adjusted MRRs  
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47 215 stratified by sex based on the 5-year age groups.

48 216 In order to assess the impact of modified case definitions on the study results, we  
49  
50 217 conducted two sensitivity analyses calculating the age-adjusted MRRs for men and  
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52 218 women as described above.

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3 219 **Results**

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5 220 **Description of the study population**

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7 221 Compared to men, women were overrepresented in the population without diabetes,  
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9 222 whereas proportions of men and women were similar in the population with diabetes  
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11 223 (Table 1). Accordingly, the diabetes prevalence among women (12.8%) was lower than  
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13 224 in men (14.9%). As expected, the population with diabetes had a higher mean age  
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15 225 compared to the population without diabetes. On average, women were older than  
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17 226 men among persons with and without diabetes. In terms of absolute numbers, more  
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19 227 women than men died in 2014 in the population with and without diabetes. However,  
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21 228 age-specific and age-standardized mortality rates per 1,000 persons were consistently  
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23 229 higher among men than women in both populations. In both sexes, mortality rates per  
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25 230 1,000 persons were markedly higher among individuals with than without diabetes  
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27 231 (Table 1).  
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233 **Table 1** Descriptive characteristics of the study population by diabetes status and sex  
 234 (DaTraV, age  $\geq$  30 years)

	No diabetes		Diabetes	
	Women	Men	Women	Men
Population size in M. (2013)	22,5	18,3	3,3	3,2
Proportion (%) 2013	55.1	44.9	50.8	49.2
Mean age in years 2013	55.9	53.6	71.5	67.9
Number of deaths 2014	254,408	220,305	148,491	140,024
Mortality rate per 1,000 persons*	12.00	12.74	19.96	21.91
Mortality rate per 1,000 persons across age groups*				
30 to 34 years	0.30	0.62	2.03	4.26
35 to 39 years	0.45	0.87	1.86	4.38
40 to 44 years	0.77	1.40	3.75	5.31
45 to 49 years	1.29	2.34	4.62	7.64
50 to 54 years	2.23	4.13	6.95	10.18
55 to 59 years	3.41	6.73	9.19	14.55
60 to 64 years	5.21	10.71	11.18	19.84
65 to 69 years	7.80	15.44	15.42	25.84
70 to 74 years	11.63	22.35	22.56	38.24
75 to 79 years	19.15	33.64	35.17	55.34
80 to 84 years	40.02	62.14	62.97	89.99
85 to 89 years	83.06	111.42	113.91	144.18
90 to 94 years	157.24	191.04	194.06	229.21
95 years and older	270.33	303.74	304.13	336.90

235 \*age-standardized to the German population 2013 using all displayed age groups

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## 237 **Main Analysis**

238 MRR estimates in association with diagnosed diabetes as obtained from Poisson  
239 regression are depicted in Figure 3. For both sexes, the age-specific MRR estimates  
240 decreased with increasing chronological age from 6.76 among women and 6.87 among  
241 men in the youngest age group to 3.12 among women and 2.46 among men aged 50-  
242 54 years to 1.13 among women and 1.11 among men aged 95 years and older. Except  
243 for persons younger than 40 years of age, MRR estimates in association with diabetes  
244 were higher among women than men. In particular, among persons 50-79 years, the  
245 MRR was between 1.26 and 1.12 significantly times higher among women than men.

246 Overall adjusted MRR estimates were comparable for women and men (1.52 vs. 1.56).  
247 Constraining our analysis to persons below 90 years of age reversed the overall age-  
248 adjusted MRRs regarding sex with still comparable estimates of 1.66 for women and  
249 1.61 for men.

## 250 **Sensitivity analyses**

251 An excess risk of death in association with diabetes among men and women was  
252 confirmed in two sensitivity analyses applying less stringent case definitions for  
253 diabetes (Table 2).

254 Compared to the main analysis, where the case definition for diabetes required  
255 documentation of a confirmed diabetes diagnosis in at least two quarters of the year  
256 2013 for outpatient data or one inpatient diagnosis of diabetes in 2013, the first case  
257 definition in Table 2 additionally includes persons with only one confirmed outpatient  
258 diagnosis of diabetes in 2013. This means that about 0.5 million persons were added to  
259 the population with diabetes and at the same time removed from the population  
260 without diabetes compared to the numbers used for the main analysis as shown in  
261 Figure 1. Results of this sensitivity analysis were similar to those of the main analysis,  
262 with only slightly lower overall MRR estimates of 1.51 among women and 1.55 among  
263 men. In contrast, markedly attenuated overall MRR estimates were obtained in the  
264 second sensitivity analysis, where the case definition for diabetes was based on the  
265 documentation of only one confirmed outpatient diagnosis. Still, the age-adjusted  
266 MRRs resulting from this case definition showed a significantly nearly 20% higher risk

of death in men and women with diagnosed diabetes compared to those without diagnosed diabetes (Table 2).

**Table 2** Sensitivity analyses applying modified diabetes case definitions: number of persons by diabetes status and age-adjusted MRRs stratified by sex (DaTraV, age  $\geq$  30 years).

	Women		Men	
	N in million (no diabetes / diabetes)	Mortality rate ratios (95% CI)	N in million (no diabetes / diabetes)	Mortality rate ratios (95% CI)
Sensitivity analysis 1*	22.3 / 3.6	1.51 (1.51 to 1.51)	18.1 / 3.4	1.55 (1.55 to 1.55)
Sensitivity analysis 2#	22.3 / 0.25	1.19 (1.18 to 1.20)	18.1 / 0.21	1.20 (1.19 to 1.21)

\* Documentation of at least one outpatient (confirmed) or inpatient diagnosis of diabetes in 2013

# Documentation of only one outpatient (confirmed) diagnosis of diabetes in 2013. Deviations from figures in figure 1 are due to rounding.

## Discussion

### Main findings

To the best of our knowledge, we present for the first time deeply age-stratified MRR estimates in association with diagnosed diabetes among men and women 30 years of age and older in Germany based on SHI claims data covering about 90% of the population. Overall, men and women with diabetes had an about 50% higher age-adjusted risk of death compared to adults without diabetes. Across strata of increasing age, the diabetes-related MRRs considerably decreased with slightly higher estimates among women than men in the population aged 40-80 years. Results persisted in sensitivity analyses applying modified case definitions for diabetes, with the exception of markedly reduced albeit still significantly higher diabetes-related risk of death based on the least stringent case definition for diabetes requiring only one outpatient diagnosis for diabetes throughout the year 2013.

Our findings regarding age-related decreases in diabetes-related MRRs partly agree with results from two previous nationwide studies in Germany.<sup>10 17</sup> A population-based cohort study based on 12-year-mortality follow-up of adults participating in the

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3 291 German National Health Interview and Examination Survey 1998 (GNHIES98) reported  
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5 292 decreasing age-specific diabetes-related MRRs in both sexes as well as overall age-  
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7 293 adjusted MRR estimates of similar magnitude as in the present study.<sup>17</sup> In this previous  
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9 294 analysis no sex differences in MRRs from all causes in association with diagnosed type  
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11 295 2 diabetes were observed, although significantly detection of a sex differential may  
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13 296 have been precluded by a limited number of deaths among adults with diabetes.  
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15 297 Tönnies et al. calculated type-2-diabetes-related MRR applying an illness-death model,  
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17 298 with estimates on diabetes prevalence and incidence derived from SHI claims data and  
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19 299 mortality rates of the general population from official death statistics. These authors  
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21 300 reported age-related decreases in MRRs, but considerably higher overall age-adjusted  
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23 301 MRR estimates, with higher estimates among women than men (3.0 vs. 2.3).<sup>10</sup> For  
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25 302 comparison with this previous study which focused on the population 65-90 years of  
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27 303 age in Germany we limited our analyses to the population aged 65-90 years and found  
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29 304 no differences in MRRs between women and men (1.47 versus 1.48. The study by  
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31 305 Jacobs et al.<sup>18</sup> calculated, on the basis of the DaTraV dataset as well, the excessive  
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33 306 deaths for women and men over 40 years of age in Germany. As no such data were  
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35 307 available for Germany at that time, Jacobs et al. took the mortality rates from the  
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37 308 Danish National Diabetes Register. The study found absolute excess deaths related to  
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39 309 diabetes of 81,703 for women and 92,924 for men. In contrast, using the same  
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41 310 methods but the estimated MRRs for Germany in our study, we found considerably  
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43 311 fewer absolute excess deaths of 49,136 for women and 53,872 for men.

42 Consistent with our results, nationwide studies in several other countries based on  
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44 313 diabetes registers or diabetes surveillance systems have reported a higher  
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46 314 diabetes-related risk of all-cause mortality compared to general population or  
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48 315 population- based controls but differ in magnitude.<sup>4-6 8 19</sup>

49  
50 316 The Swedish national diabetes register and the Australian diabetes surveillance  
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52 317 showed that the excess risk of death in association with diagnosed type 2 diabetes  
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54 318 declined with increasing chronological age.<sup>6 8</sup> Although the present study could not  
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56 319 differentiate by type of diabetes, these results are in line with our findings, since type 2  
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58 320 diabetes accounts for the vast majority of diabetes cases among older adults. The age-  
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60 321 related decline in diabetes-related excess risk of all-cause mortality might be due to

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3 322 the different onsets of diabetes on the life span and the associated disease durations.  
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5 323 It may reflect increases in competing risk of death in older age groups as well as  
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7 324 survival disadvantage in association with increased diabetes duration. In addition, the  
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9 325 number of severe comorbidities in people with and without diabetes converges with  
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11 326 increasing age.

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13 327 With regard to sex differences in diabetes-related relative risk or excess risk of all-  
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15 328 cause mortality, previous studies from other countries showed conflicting findings.<sup>4 5 8</sup>  
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17 329 Our age-specific estimates of diabetes-related MRRs showed higher risk estimates  
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19 330 among women than among men for persons aged 50-79. This higher risk among  
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21 331 women declined with increasing age and diminished in the oldest age groups. This  
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23 332 consistent pattern is comparable to a study from Australia for 2004-2010 which  
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25 333 showed higher standardized mortality ratios (SMRs) in women than in men especially  
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27 334 for persons aged 50-79 years and very similar SMRs for women and men aged 80 years  
28  
29 335 or older (1.03 and 0.98).<sup>8</sup> A recently conducted systematic review and meta-analysis  
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31 336 including 49 studies with 86 prospective cohorts showed a combined MRR of 1.93 for  
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33 337 women and 1.74 for men with a pooled women-to-men RRR of 1.13.<sup>7</sup> However  
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35 338 estimates across studies ranged from 1.24 to 3.67 in women and from 1.32 to 3.13 in  
36  
37 339 men, pooled women-to-men RRR varied from 0.64 to 1.74.<sup>7</sup> Overall, differences in  
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39 340 study results regarding a sex differential in excess risk of diabetes-related all-cause  
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41 341 mortality might, at least in part, be explained by differences in the age range,  
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43 342 underestimation of older people, time of follow-up and applied methods for risk  
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45 343 estimation.

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47 344 Prospective population-based studies are needed to obtain a deeper insight into the  
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49 345 role of sex difference in diabetes-related mortality risks by taking relevant risk factors  
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51 346 such as lifestyle behavior, adherence to prescribed therapy and co-morbidities into  
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53 347 account.

### 54 348 **Practical implications**

55 349 Our findings confirm that diagnosed diabetes in Germany is still associated with a  
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57 350 significantly elevated, several times higher risk of death among men and women, in  
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59 351 particular in younger and middle age. This emphasizes the need for effective primary  
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352 and secondary prevention. Further improvements in the early detection of diabetes,

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3 353 particularly in younger ages, alongside with evidence-based treatments, could  
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5 354 contribute to a reduction in excess mortality.  
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7 355 Our results open the perspective to close an important gap in diabetes surveillance in  
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9 356 Germany, as the SHI claims dataset appears to be suitable for close monitoring of  
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11 357 diabetes-related excess risk of death, which is a key indicator in the national diabetes  
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13 358 surveillance system. In addition, the dataset will permit calculation of closely related  
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15 359 indicators, including the absolute number of deaths in association with diabetes, and  
16  
17 360 composite indicators of disease burden, including healthy life years and the number of  
18  
19 361 years lost in association with diabetes.<sup>20</sup> Thus, including SHI claims data dataset will  
20  
21 362 harness the potential for improved health information systems as a basis for the  
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23 363 surveillance of diabetes and other noncommunicable diseases (NCD).

### 24 364 **Strengths and limitations**

25 365 The main strength of our analysis is the completeness of the dataset, since about 90%  
26  
27 366 of the German population is covered by SHI. Mortality rates derived from the SHI  
28  
29 367 claims dataset showed good agreement with data from official death statistics, which  
30  
31 368 underlines the potential for generalization of our results. Our findings from sensitivity  
32  
33 369 analyses support the validity of the data. We consistently showed an excess risk of all-  
34  
35 370 cause mortality in association with diagnosed diabetes based on varying case  
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37 371 definitions for diabetes.

38 372 Taken together, our results demonstrate that the DaTraV dataset could essentially  
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40 373 contribute to close current gaps in diabetes surveillance with an overall good  
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42 374 documentation quality of diabetes and the advantage to consider inpatient as well as  
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44 375 outpatient data for case definition.

45 376 A great disadvantage of routine datasets based solely on documented diagnoses is that  
46  
47 377 no information about undiagnosed morbidity can be drawn. National surveys with an  
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49 378 additional HbA1c measurement in blood samples of participants show a relevant  
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51 379 proportion of undiagnosed diabetes. Although this proportion has decreased over  
52  
53 380 time, it is still relatively high<sup>21</sup> and at the same time is related to a slightly higher  
54  
55 381 excess mortality than diagnosed diabetes.<sup>17 22</sup> For this reason the current routine data  
56  
57 382 analysis is likely to underestimate the excess mortality in diabetes. In general, another  
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3 383 limitation of routine data is that this data cannot identify the ethnicity of individuals.  
4  
5 384 An ethnic risk profile is being discussed for diabetes in particular.<sup>23</sup>  
6  
7 385 There are a number of limitations which arise from the specific construction of the  
8  
9 386 DaTraV dataset, which originally served economic but not research purposes. We had  
10  
11 387 to determine cases of diabetes in the data in 2013 only, in order to identify persons  
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13 388 who died in 2014 among persons with and without diabetes. This implies that those  
14  
15 389 who died with newly documented diabetes in 2014 are not detectable in the data as  
16  
17 390 diabetes cases and hence will be counted as persons without diabetes. We cannot  
18  
19 391 exclude that this also contributed to an underestimation of diabetes-related excess  
20  
21 392 mortality. Since diabetes is a chronic disease, and long-term complications account for  
22  
23 393 the majority of diabetes-related deaths, we assume that this had only little impact on  
24  
25 394 our results. The planned revision of the Data Transparency Regulations in Germany  
26  
27 395 could help to overcome current shortcomings.  
28  
29 396 Furthermore, the currently missing stratification of the dataset according to  
30  
31 397 geographic region and social status or social deprivation should be possible in the  
32  
33 398 future, hence we will be able to analyze and compare mortality trends within Germany  
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35 399 as well as at a national level with other countries.  
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37 400  
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39 401 The present study included adults 30 years of age and older, and type 2 diabetes is  
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41 402 likely to account for most cases of documented diabetes. Nevertheless, it will be  
42  
43 403 important to overcome current limitations to differentiate between major types of  
44  
45 404 diabetes in claims data. The main problem is the frequent coding of an unspecific  
46  
47 405 diabetes (ICD-10: E14.-) or even diagnoses that are mutually exclusive (E10.- and E11.-)  
48  
49 406 in the data.<sup>24</sup> A recent analysis of the here used dataset has demonstrated that  
50  
51 407 including information on medication may improve assignment of unspecific diabetes  
52  
53 408 codes to type 2 diabetes.<sup>25</sup> Among children and adolescents type 1 diabetes is the  
54  
55 409 predominant type of diabetes. As insulin treatment is required here, documented  
56  
57 410 insulin use is an essential part of the case definition for type 1 diabetes, and also helps  
58  
59 411 to clarify diabetes definition.<sup>26</sup>  
60

## 412 **Conclusions**

413 Diabetes-related risk of death is a key indicator for monitoring diabetes epidemiology  
414 and quality of diabetes care. Establishing sustainable time trends for this indicator as  
415 part of the national diabetes surveillance system in Germany is of great need, but was  
416 so far precluded by the lack of a valid and timely accessible dataset. Results of the  
417 present study demonstrate that analysis of SHI claims data may provide a solution in  
418 closing this information gap. Further research is needed to analyze and to improve the  
419 quality of the data, in particular with regard to case definitions. In this case, the SHI  
420 claims data could also serve to calculate and monitor the absolute number of diabetes-  
421 related deaths as well as composite indicators of disease burden, such as diabetes-  
422 related healthy life years and years of life lost. Stratification of SHI claims data  
423 according to geographic region and social status or social deprivation will be possible  
424 in the future, hence we will be able to analyze and compare diabetes-related mortality  
425 trends within Germany but also with international developments.<sup>3</sup> This will strengthen  
426 surveillance activities for the prevention and control of diabetes and other major NCD  
427 at a national level and also enhance international collaboration in diabetes and NCD  
428 surveillance and burden of disease estimates.



430 **Footnotes**

431

432 **Contributors:** CS, JB and CH designed the study. CS, LR and JB performed the analysis. CS, CSN  
433 and JB wrote the initial version of the manuscript. LR, RP and TZ revised the manuscript. All  
434 authors read and approved the final manuscript. All authors had full access to all of the data  
435 (including statistical reports and tables) in the study and can take responsibility for the  
436 integrity of the data and the accuracy of the data analysis. CS is the lead author and guarantor.

437

438 **Transparency declaration:** The lead author affirms that this manuscript is an honest, accurate,  
439 and transparent account of the study being reported; that no important aspects of the study  
440 have been omitted; and that any discrepancies from the study as planned (and, if relevant,  
441 registered) have been explained.

442

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445 to promote and further develop the use of external sources of data to secure (establish and  
446 expand) national level diabetes surveillance is funded by the Federal Ministry of Health  
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448

449 **Competing interests:** All authors have completed the Unified Competing Interest form at  
450 [www.icmje.org/coi\\_disclosure.pdf](http://www.icmje.org/coi_disclosure.pdf) (available on request from the corresponding author) and  
451 declare: no support from any organisation for the submitted work, no financial relationships  
452 with any organisations that might have an interest in the submitted work in the previous three  
453 years no other relationships or activities that could appear to have influenced the submitted  
454 work.

455 **Ethics approval:** This study was not approved by a research ethics committee, because our  
456 study did not meet the criteria for human subjects research.

457 **Data sharing:** The SQL code for requesting aggregated data and statistical codes available from  
458 the corresponding author at [schmidtchri@rki.de](mailto:schmidtchri@rki.de).



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3 460 **Figure 1** Flow chart of selection of study population with excluding criteria and sample  
4 461 sizes.

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7 463 **Figure 2** Age-specific mortality rates per 100,000 persons stratified by sex for the year  
8 464 2014 as obtained from official cause of death statistics (Destatis) and claims data  
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10 466 results from the DaTraV dataset.

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15 468 **Figure 3** MRRs for persons with diabetes compared to persons without diabetes by sex  
16 469 and age groups. Overall estimates are adjusted using all displayed age groups.

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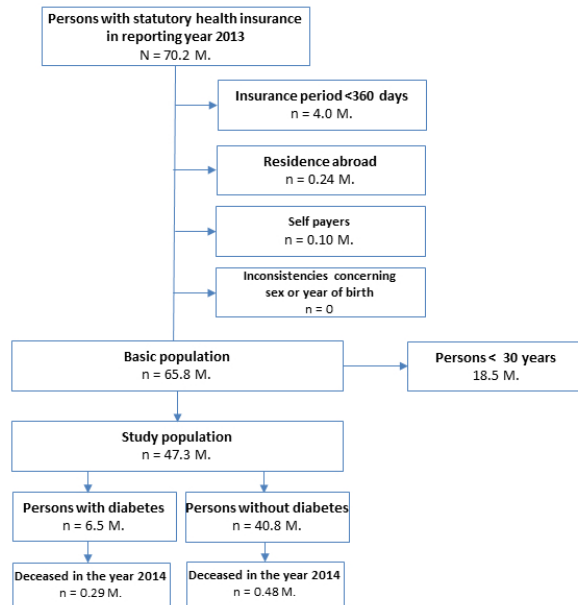


Figure 1 Flow chart of selection of study population with excluding criteria and sample sizes.

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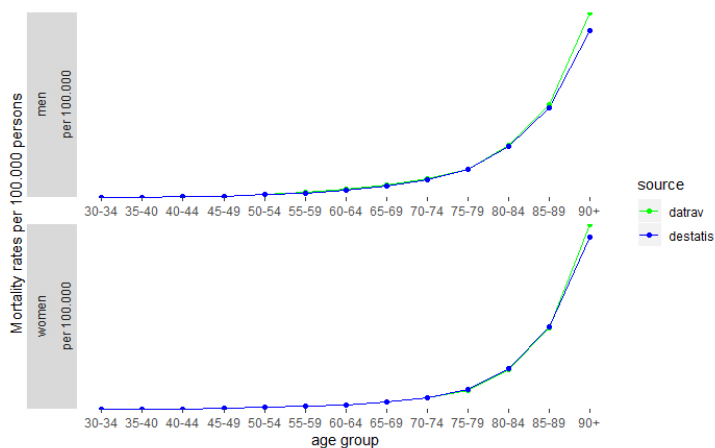
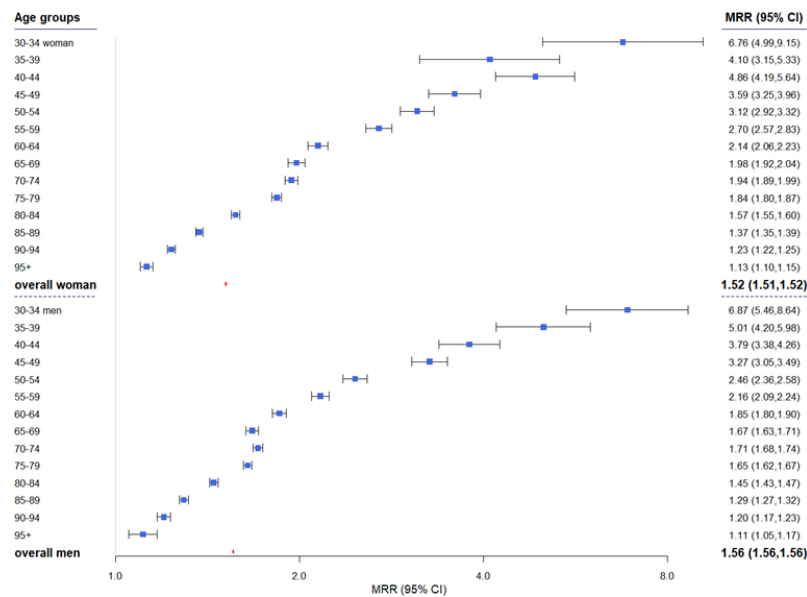


Figure 2 Age-specific mortality rates per 100,000 persons stratified by sex for the year 2014 as obtained from official cause of death statistics (Destatis) and claims data (Datrav). The blue line indicates results from official statistics; the green line indicates results from the DaTraV dataset.

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**Figure 3** MRRs for persons with diabetes compared to persons without diabetes by sex and age groups. Overall estimates are adjusted using all displayed age groups.

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STROBE Statement—Checklist of items that should be included in reports of *cohort studies*

	Item No	Recommendation	Page No
<b>Title and abstract</b>	1	(a) Indicate the study's design with a commonly used term in the title or the abstract	2
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found	2
<b>Introduction</b>			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4,5
Objectives	3	State specific objectives, including any prespecified hypotheses	5
<b>Methods</b>			
Study design	4	Present key elements of study design early in the paper	2,5-6
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	2,5-6
Participants	6	(a) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	6, 7
		(b) For matched studies, give matching criteria and number of exposed and unexposed	NA
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	6,7
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	5,6
Bias	9	Describe any efforts to address potential sources of bias	8
Study size	10	Explain how the study size was arrived at	6
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	8
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding	8
		(b) Describe any methods used to examine subgroups and interactions	8
		(c) Explain how missing data were addressed	NA
		(d) If applicable, explain how loss to follow-up was addressed	NA
		(e) Describe any sensitivity analyses	8,11
<b>Results</b>			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	6
		(b) Give reasons for non-participation at each stage	NA
		(c) Consider use of a flow diagram	6
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	8-10
		(b) Indicate number of participants with missing data for each variable of interest	NA
		(c) Summarise follow-up time (eg, average and total amount)	NA
Outcome data	15*	Report numbers of outcome events or summary measures over time	10

1	Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	10,11
2			(b) Report category boundaries when continuous variables were categorized	NA
3			(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	NA
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9	Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	11,12
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11	<b>Discussion</b>			
12				
13	Key results	18	Summarise key results with reference to study objectives	12-14
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15	Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	15,16
16				
17	Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	12-14
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20	Generalisability	21	Discuss the generalisability (external validity) of the study results	15,16
21				
22	<b>Other information</b>			
23	Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	18
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\*Give information separately for exposed and unexposed groups.

**Note:** An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at <http://www.plosmedicine.org/>, Annals of Internal Medicine at <http://www.annals.org/>, and Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is available at <http://www.strobe-statement.org>.