

The burden of diabetes-related mortality in France in 2002: an analysis using both underlying and multiple causes of death

Isabelle Romon · Eric Jouglu · Beverley Balkau ·
Anne Fagot-Campagna

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Abstract *Aim* To describe the burden of diabetes-related mortality in France. *Methods* Underlying and multiple causes (all causes listed) of death were extracted from the 2002 French national mortality registry. Death rates were standardized on the age structure of the European population. *Results* Diabetes was reported as the underlying cause of death in 11,177 certificates (2.1%), and as multiple causes in 29,357 certificates (5.3%), giving a ratio (multiple/underlying causes) of 2.6. When diabetes was a multiple cause, the mean age at death was 75 years in men, 81 years in women. The age-standardized mortality rates were 41.0/100,000 in men, 24.6/100,000 in women. The excess mortality observed in men (men/women ratio = 1.7) decreased with age. Geographic differences were observed: higher rates in the North-East, lower rates in the West of the country. In certificates mentioning diabetes, the most frequent cause of death was diseases of the circulatory system (76%). Coronary heart diseases, foot ulcers and renal diseases were more likely to be mentioned in certificates referring to diabetes than in those that did not. *Discussion* The use of multiple rather than underlying causes of death more than doubled diabetes-related mortality rates. While probably still under-estimated, the

burden of diabetes-related mortality corresponds to a high proportion of the total mortality, especially in men. Geographic differences partially reflect disparities in diabetes prevalence. Causes more frequently associated with diabetes include coronary heart disease and complications related to neuropathy and nephropathy.

Keywords Diabetes · Mortality · Multiple-causes · Diabetes complications · Epidemiology · France

Abbreviations

ICD-10 10th International Classification of Disease
CI Confidence interval
RR Relative risk
WHO World Health Organization

Introduction

In France, the prevalence of diabetes was estimated to be 3.8% in 2005, based on medical reimbursement claims for insulin and oral hypoglycaemic treatment from the major national medical insurance system. It was estimated to have increased by 5.7% per year between 2000 and 2005 [1], a phenomenon which is probably due to both population ageing and increases in overweight and obesity. Over the same period, the quality of care delivered to people with diabetes has improved [2] as has the overall life expectancy of the French population [3]. The impact of these changes on diabetes-related mortality is not known in France, but it has been suggested that although the overall mortality is declining in American and European populations, it is decreasing more slowly in people with diabetes [4, 5].

I. Romon (✉) · A. Fagot-Campagna
French Institute for Public Health Surveillance, Institut de Veille
Sanitaire (InVS), 12 rue du Val d'Osne, 94415 Saint-Maurice
Cedex, France
e-mail: i.romon@invs.sante.fr

E. Jouglu
French Institute of Health and Medical Research, Inserm-Cépidc,
Le Vesinet, France

B. Balkau
French Institute of Health and Medical Research, Inserm U780,
Villejuif, France

It is difficult to compare specific death rates in different countries, due to differences in certification practices [6–8]. However, the international model of death certificate recommended by the World Health Organization (WHO), the recent procedures introduced to improve the homogeneity of certification, and the increasing use of automated coding systems [9], facilitate more valid comparisons.

In the annual mortality statistics published for Europe [10], and those for the USA [11], the underlying cause of death is used as the reference for international comparisons. However, it is also of interest to compare rates based on both the underlying and the associated causes of death as in previous publications for chronic diseases, such as diabetes [12], chronic obstructive pulmonary diseases [13], nephrotic syndrome and essential hypertension [14].

The objectives of this analysis are to describe the burden of diabetes-related mortality in France, to identify the causes of death most frequently associated with diabetes, and to compare death rates in France to those in other countries, using both the underlying and multiple causes of death.

Research, design and methods

We used data from the French national mortality registry (Inserm-CépiDc), and extracted all death certificates of people living in metropolitan France (excluding overseas departments), who died in 2000–2002 (most recent years available). These certificates detail socio-demographic data (including sex, age at death and district of residence) and medical data reported by the certifying medical doctor according to the WHO recommendations. In 2000, France started coding causes of death using the 10th revision of the International Classification of Disease (ICD) [15], which doubled the number of items used to code the medical causes of death compared to the 9th revision [16]. Secondly, an automated coding system [17], similar to the one used in the USA, was introduced in France. This procedure selects the underlying cause and retrieves the corresponding code, complying closely with international standards. All these changes have resulted in increased reporting of diabetes [18].

Diabetes, like any other disease, is classified as being the underlying cause of death only if it has been reported by the certifier as having initiated the morbid process leading to the death. Diabetes is considered to be one of the multiple causes of death if it is mentioned in the certificate, either as the underlying cause or as another cause (contributing to the death, but not directly related to the disease causing it). The ICD-10 codes corresponding to diabetes are: E10–E14 (diabetes mellitus), G590 (diabetic motor neurone disease), G632 (diabetic polyneuropathy), H280

(diabetic cataract), H360 (diabetic retinopathy), I792 (diabetic peripheral angiopathy), N083 (glomerular disorders in diabetes), M142 (diabetic arthropathy), O24 (pre-existing diabetes mellitus in pregnancy), P702 (neonatal diabetes mellitus).

We analysed the 2002 mortality data. However, when comparing rates for different geographic areas, we averaged the data for the 3 years from 2000 to 2002 to provide more precise estimates of death rates in each area. As deaths related to diabetes are rare before age 18 years, death certificates for this age-group were also reviewed for the 3 years.

To establish the advantages of adopting a multiple-cause approach, we calculated the ratio of the number of deaths in which diabetes was listed as a multiple cause to those in which diabetes was indicated as being the underlying cause [19].

Crude death rates were calculated for the population living in France estimated by the French National Institute for Statistics and Economic Studies (Insee) as the denominator [20]. To compute age-standardized mortality rates using the “direct method”, we calculated age-specific death rates within 5-year age groups, and applied them to the age structure of the 1976 European standard population (International Agency for Research on Cancer [21]).

As expectation of life was 76 years in men and 83 years in women in France in 2001 [3] and as diabetes is a chronic disease that mainly occurs in the elderly, “premature” diabetes-related mortality was defined as death occurring before age 75 years. We calculated the number of years of potential life lost in relation with diabetes, their contribution to the total number of years of life lost, and the average number of years of life lost per person.

We computed crude and age-adjusted relative risks to find out whether other specific causes of deaths were reported more or less often when diabetes was mentioned in the death certificate than when diabetes was not mentioned (regardless of whether this was as an underlying or associated cause). Results were presented only if the relation between diabetes and specific cause was significant. Variations by age and sex group were also analysed.

Results

The burden of diabetes on the overall mortality (Table 1)

In 2002, 533,107 deaths occurred in the French population. Diabetes was mentioned as an underlying cause for 11,177 deaths (2.1%), and as a multiple cause for 29,357 (5.5%). The contribution of diabetes to total mortality was higher for women than men: 2.4% vs. 1.8% of all deaths with

Table 1 Numbers of deaths, crude rates and age-standardized rates of mortality in which diabetes is reported as the underlying cause or among the multiple causes of death, by sex and age

	Diabetes as the underlying cause			Diabetes as one of multiple causes			Ratio (B/A)
	Number of deaths (A)	Crude rate (/100,000)	Adjusted rate ^a (/100,000)	Number of deaths (B)	Crude rate (/100,000)	Adjusted rate ^a (/100,000)	
Men							
<45 years	84	0.5	0.4	162	0.9	0.8	1.9
45–54 years	236	5.7	5.7	671	16.2	16.1	2.8
55–64 years	480	16.7	16.8	1,543	53.7	54.2	3.2
65–74 years	1,300	56.3	55.1	4,033	174.6	170.8	3.1
75–84 years	1,878	141.3	139.5	5,427	408.2	402.7	2.9
≥85 years	1,006	324.7	324.7	2,528	816.0	816.0	2.5
<75 years	2,100	7.7	7.1	6,409	23.4	21.6	3.1
≥75 years	2,884	175.9	185.8	7,955	485.3	506.0	2.8
Overall	4,984	17.2	14.2	14,364	49.5	41.0	2.9
Women							
<45 years	38	0.2	0.2	82	0.5	0.4	2.2
45–54 years	96	2.3	2.3	265	6.2	6.2	2.8
55–64 years	240	8.1	8.1	674	22.7	22.7	2.8
65–74 years	1,000	35.5	34.0	2,612	92.7	88.8	2.6
75–84 years	2,280	108.6	104.5	5,671	270.2	260.8	2.5
≥85 years	2,539	307.3	307.3	5,689	688.5	688.5	2.2
<75 years	2,100	7.7	7.1	6,409	23.4	21.6	3.1
≥75 years	2,884	175.9	185.8	7,955	485.3	506.0	2.8
Overall	6,193	20.2	9.9	14,993	48.9	24.6	2.4
Both sexes	11,177	18.7	11.8	29,357	49.2	31.7	2.6

Metropolitan France, 2002

^a Age-standardized mortality rates using the direct method and the age structure of the 1976 European standard population (not detailed after 85 years)

diabetes as underlying cause, and 5.7% vs. 5.3% with diabetes as one of the multiple causes. Overall, the number of deaths with diabetes was increased by a factor of 2.6 when multiple rather than underlying causes were considered (2.4 in women and 2.9 in men). This ratio was particularly high (at least three) for men aged 45–74.

Mean age at death was 78 years (for both underlying and multiple causes), and was lower in men than in women (underlying: 75 vs. 80 years; multiple: 75 vs. 81 years).

The crude death rate for diabetes as an underlying cause was 18.7/100,000 and was lower in men than in women. The age-standardized rate was 11.8/100,000 and, in contrast to the crude rate, was higher in men than in women, reflecting differences in the age structures for men and women.

When diabetes was listed as a multiple cause, the crude death rate rose to 49.2/100,000; and was slightly higher in men than in women. The age-standardized rate reached 31.7/100,000; it was much higher in men than in women and, overall, increased steadily with age. This increase was greater for women: the overall men/women standardized

rate ratio was 1.7 and declined with age, from 2.4 before age 55 years, to 1.2 over age 85 years (multiple causes).

“Premature” diabetes-related mortality

In 2002, 198,855 deaths occurred before age 75 years. Diabetes was mentioned as the underlying cause of 3,474 of them (2%), and as a multiple cause of 10,042 (5%) (Table 1), with age-standardized death rates of 5.4/100,000 and 15.6/100,000, respectively. The average number of years lost before age 75 years due to diabetes as a multiple cause was estimated to be 3.3 years per person (men: 4.3 years, women: 2.2 years), which accounted for 3% of the total number of years lost.

Between 2000 and 2002, we identified 25 diabetes-related deaths that occurred before 18 years of age. Diabetic ketoacidosis was reported in 4 certificates, and a less specific complication of diabetes in six. In addition to diabetes, cystic fibrosis was reported in five other certificates, a neoplasm in three, prematurity or neonatal anoxia in two, heart disease in two, a pulmonary embolism in

one, an accidental injury in one and Friedreich disease in one.

Geographic variations in diabetes-related mortality (Fig. 1)

In 2000–2002, the highest standardized death rates for diabetes mentioned as a multiple cause were reported in north-eastern France (Alsace, Nord-Pas-de-Calais, Lorraine, Champagne-Ardenne, Picardie). Rates were lower (almost halved) in western areas (Bretagne, Basse-Normandie, Pays-de-la-Loire, Poitou-Charente, Ile-de-France, Corse and Provence-Alpes-Côte-d'Azur).

Causes of death associated with diabetes (Table 2)

In 2002, the causes of death most often mentioned as associated with diabetes were diseases of the circulatory system (in three cases out of four), diseases of the respiratory system (19%), neoplasms (17%), and diseases of the genito-urinary system (14%).

The age-adjusted risk of a certification of ischaemic heart diseases, infections of the skin, ulcers, infectious arthropathies, osteomyelitis and renal failure was at least two for cases when diabetes was mentioned. A higher risk was also found for septicaemia, mental and behavioural disorders due to alcohol, heart and cerebrovascular diseases and inflammatory polyarthropathies. A lower risk was found for neoplasms, tuberculosis and external causes of mortality. No significant association was found for diseases of the respiratory system.

The strength of the association between diabetes and diseases of the circulatory system decreased with age (<65 years: $RR_{\text{crude}} = 2.55$ [2.49–2.62]; ≥ 85 years: $RR_{\text{crude}} = 1.30$ [1.28–1.32]), as well as the associations

with infections of the skin, ulcers, infectious arthropathies, inflammatory polyarthropathies, osteomyelitis and renal failure. The association between diabetes and mental and behavioural disorders due to alcohol was only significant in men ($RR_{\text{age-adjusted}} = 1.47$ [1.36–1.59]), and it too decreased with age. An association between diabetes and pneumonia was found before age 65 years ($RR_{\text{crude}} = 1.45$ [1.24–1.69]).

Discussion

In France, using multiple causes of death instead of only the underlying cause increased the number of diabetes-related deaths recorded by a factor of 2.6. This ratio varied with sex, age and time. It was higher than previously reported: 1.8 in 1970, 2.6 in 1987 [12] and 2.7 in 1999 [22]. In 2002, the ratio in the UK was estimated to be 4.2 (4.4 in men; 4.0 in women), versus 4.5 in Sweden (same in men and women), 2.5 in Quebec (2.5 in men; 2.6 in women) and 3.1 in the US (3.2 in men; 3.0 in women) (personal communication). In a study based on all deaths certificates issued during 1990–1998 in Minnesota, USA, diabetes was reported as the underlying cause rather than a multiple cause more frequently for women, the young, native Americans, single or widowed people and for some specific circumstances of death [23]. The multiple cause approach can provide a better assessment of diabetes-related mortality.

However, the multiple causes approach probably leads to an underestimation of the true burden of diabetes. In a previous French study based on a random sample of 959 people who died in 1992 without diabetes being mentioned on their death certificates, almost 10% actually did have diabetes [24]. A UK analysis also demonstrated a low rate

Fig. 1 Age-standardized mortality rates (/100,000) related to diabetes as the underlying cause or listed among the multiple causes of deaths in French regions in 2000–2002

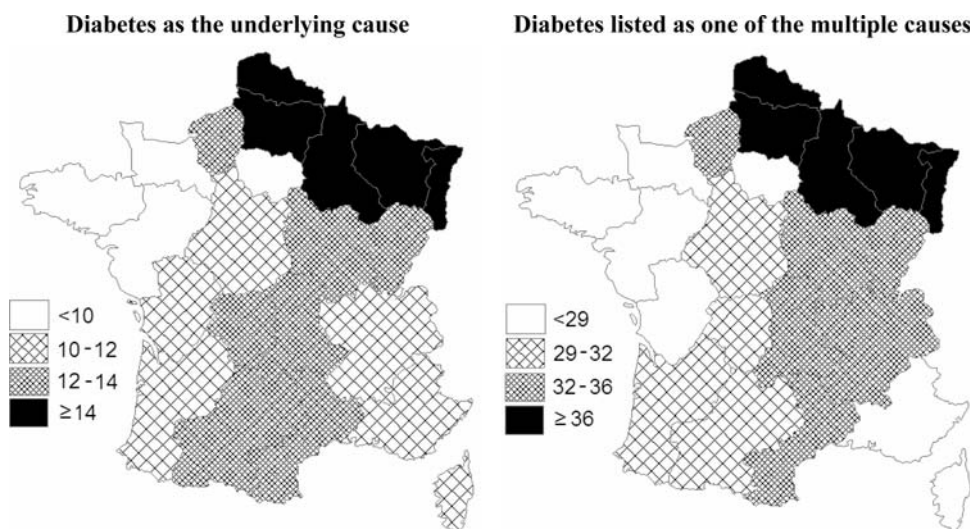


Table 2 Frequencies of specific causes of death mentioned in death certificates with and without a mention of diabetes, and measurements of the association between these causes and diabetes

Cause of death (ICD-10 code) (%)	Death certificates		RRa ^a (95%CI)
	With diabetes listed (N = 29,357)	Without diabetes listed (N = 503,750)	
Certain infectious and parasitic diseases (A00-B99)	10.0	7.0	1.4 (1.3–1.4)
Septicemia (A40–A41)	6.5	4.4	1.4 (1.3–1.5)
Tuberculosis (A15–19, B90)	0.3	0.4	0.7 (0.6–0.9)
Neoplasms (C00-D48)	17.4	32.3	0.5 (0.5–0.5)
Mental and behavioural disorders (F00-F99)	10.9	10.0	1.2 (1.1–1.2)
Due to the use of alcohol (F10)	2.6	2.3	1.4 (1.3–1.5)
Diseases of the circulatory system (I00-I99)	75.7	46.4	1.6 (1.6–1.6)
Ischaemic heart diseases (I20-I25)	25.8	11.0	2.2 (2.2–2.3)
Other heart diseases (I30-I33, I39-I52)	37.9	26.5	1.4 (1.4–1.4)
Cerebrovascular diseases (I60-I69)	16.6	11.0	1.4 (1.4–1.5)
Diseases of the respiratory system (J00-J99)	19.2	19.5	1.0 (0.9–1.0)
Diseases of the skin and subcutaneous tissue (L00-L99)	4.6	2.1	2.2 (2.0–2.3)
Infections other than staphylococcal syndrome (L01-L08)	0.5	0.2	3.1 (2.5–3.7)
Decubitus ulcer (L89)	3.3	1.7	1.9 (1.8–2.1)
Leg ulcer (L97)	0.5	0.1	6.2 (5.1–7.4)
Diseases of the musculoskeletal system and connective tissue (M00-M99)	2.5	1.8	1.3 (1.2–1.4)
Infectious arthropathies (M00-M03)	0.1	0.02	2.4 (1.4–4.0)
Inflammatory polyarthropathies (M05-M14)	0.6	0.3	1.6 (1.4–1.8)
Osteomyelitis (M86)	0.3	0.1	3.8 (3.0–5.0)
Diseases of the genitourinary system (N00-N99)	14.0	5.9	2.3 (2.2–2.3)
Renal failure (N17-N19)	12.2	4.8	2.5 (2.4–2.5)
External causes of morbidity and mortality (V01-Y98)	3.9	8.6	0.5 (0.5–0.6)
Symptoms, signs and abnormal findings (R00-R99)	47.0	49.4	1.0 (0.9–1.0)

Metropolitan France, 2002

^a Age-adjusted relative risk

When diabetes was mentioned, infectious and parasitic diseases were also reported in 10% of the cases, whereas they were reported in only 7% of certificates in which diabetes was not mentioned. The age-adjusted risk of having infectious and parasitic diseases mentioned was 1.4 (1.3–1.4) for certificates with diabetes compared to certificates without diabetes

of diabetes reporting in deaths related to cardiovascular diseases as the underlying cause [25]. Diabetes may not be reported, because it did not contribute to the death, but may also be omitted because another pathology predominated, or because the certifying physician did not know about the diabetes [26].

In France, the contribution of diabetes to the overall mortality burden was 2.1% with diabetes as the underlying cause and 5.5% with diabetes among the multiple causes. These results are higher than those previously described in France: 1.2% and 3.2% respectively in 1987 [12], and 1.8% and 5.0% in 1999 [22]. This increase may have been due to a true increase in the diabetes-related burden. However, it may also have been due to improvements in diabetes diagnosis, recent changes in the diagnostic criteria for diabetes [27] or in changes in reporting and coding the causes of death [18]. In 2002, the contribution of diabetes

was only slightly lower in France than in national US mortality data [28], (2% vs. 3% in the USA, considering underlying causes), whereas the prevalence of diabetes was much higher in the USA [29] than in France [1]: 6.5% with diagnosed diabetes in the USA in 1999–2002 vs. 3.8% with treated diabetes in France in 2005. A possible explanation could once again be differences in coding the underlying cause.

The excess mortality related to diabetes in men compared to women is consistent with trends observed in French general mortality statistics, where there is an overall gender gap, although it has been narrowing since 1992 [30]. The prevalence of treated diabetes is also slightly higher in men than in women in France [1]. In the USA, an excess mortality in men with diabetes is also reported [4], with an age-standardized mortality rate 57% higher for men than women in 1971–1993. All these data

highlight the possible sex-related differences in terms of the form of the disease, diagnosis, complications and/or quality of care.

Premature mortality related to diabetes (before age 75 years) accounted for 10,042 deaths in which diabetes was listed as a multiple cause, 3% of the total number of years lost. By comparison, between 1995 and 1999, the years of potential life lost before age 65, related to cancers, accounted for 28% of the total number of years of life lost in France [31]. The absolute number of deaths related to diabetes that occurred before age 75 is low, but it may still be too high for a familiar disorder that could be better controlled and more aggressively treated [32].

In France, the prevalence of diabetes in people aged under 20 in 1998 was estimated to be 0.95/1,000 ($n = 14,300$), based on treatment reimbursement claims [33]. The number of diabetes-related deaths before age 18 is correspondingly low: 25 certificates mentioned diabetes during 2000–2002, but only in 10 was death considered to be directly related to diabetes. In a cohort of 1,854 English children with diabetes followed up from 1978 to 1993 [34], 26 deaths were identified: 58% were attributed to diabetes or its complications, and 42% unrelated. Another study in England and Wales reported 83 deaths directly related to diabetes between 1990 and 1996, for an estimated 150,600 young people with type 1 diabetes who were under 20 years of age [35]: 83% of these deaths were related to diabetic ketoacidosis or hypoglycaemia. While the number of childhood deaths directly associated with diabetes is low in our study, it is mainly related to acute diabetes complications, and therefore probably still preventable.

We observed large geographic disparities in diabetes-related mortality rates, with particularly high rates in the North-East and low rates in the West. These geographic differences are similar to those observed for overall mortality in France [36], as well as to the geographic differences in the prevalence of diabetes [33] and obesity [37]. It may also reflect social category, nutritional behaviour, health care access and environmental or cultural factors [38] that we cannot explore further here.

According to Eurostat [39], in 2003, standardized mortality rates for diabetes as an underlying cause ranged between 28.6/100,000 in Portugal, 16.5 in Germany, 7.1 in the United Kingdom and 5.2 in Greece. These large differences between countries may reflect differences in the burden of diabetes. Among the 24 countries with available data, France ranked in the middle (13th), with a rate of 12.4/100,000, which matched the prevalence of diabetes [40].

In France, as in other European countries, coronary events are the main cause of death in the general population [41], although France has the lowest European death rate related to coronary diseases, along with Spain and Italy

[42]. In our analysis, diseases of the circulatory system are also the most frequent cause when diabetes is reported, and are more frequent when diabetes is reported (76%) than when it is not (46%). Similarly, in the Framingham study [43], adults with diabetes have approximately twice the risk of cardiovascular events as those without diabetes. It demonstrates the need to improve the cardiovascular risk profile of people with diabetes, since it is estimated that one in three people with diabetes has at least three cardiovascular risk factors other than diabetes [44].

Other causes of death more frequently associated with diabetes are related to known microvascular complications of diabetes (foot ulcers, amputations, renal failure), to septicaemia, and to mental and behavioural disorders due to alcohol. A similar finding was previously reported in a French cohort of 7,180 working men aged 44–55 [45]. Over a period of 15 years, 838 deaths occurred, and the risk of death due to alcohol and cirrhosis in the men with diabetes was higher ($RR = 13.3$ [5.4–30.8]) than in those with normal blood glucose. Conversely, neoplasms, tuberculosis and external causes of mortality (including transport accidents) were less often associated with diabetes, which may reflect the fact that diabetes did not contribute to these deaths. In the Nhanes I cohort [4], while ischaemic heart diseases and cerebrovascular diseases were more frequently listed as causes of death for people with diabetes than in those without it, neoplasms were also less frequently listed.

Historical data provide slightly different figures for France. In 1987, among the death certificates in which diabetes was mentioned as a multiple cause of death according to the previous coding system [12], 63% also reported a disease of the circulatory system, 20% ischaemic heart disease, 19% a cerebrovascular disease and 6% a disease of the genitourinary system versus 76%, 26%, 17% and 14% respectively in the present analysis. These differences may reflect an increase in the reporting of cardiovascular disease and renal failure, and a slight decrease in reporting of cerebrovascular deaths, in association with diabetes. This could be due to changes in the clinical history of diabetes, but also to changes in certification and coding practices.

One limitation of our study is the quality and amount of information reported in each death certificate, and the changes of coding and recording. While recent changes have improved the quality and comparability of data in European countries [9], they have also made it more difficult to perform time-trend comparisons.

To conclude, in France where the prevalence of diabetes is about 3.8% and increasing, the diabetes-related burden on total mortality is high, especially for men. In young people, mortality related to diabetes is rare but still preventable. Although France may be considered to be a

country with a low incidence of cardiovascular diseases, macrovascular complications are the main cause of death associated with diabetes, which highlights the need to reduce the cardiovascular risk profile of people with diabetes living in France. Other factors contributing to the death process of people with diabetes are neuropathy (foot ulcers) and renal disease, for which specific interventions are also warranted.

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