

Editorial

Trends in Mortality From Diabetes in Spain: On the Right Way



Tendencias de la mortalidad por diabetes en España: por el buen camino

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For decades, the incidence and prevalence of diabetes has been increasing in countries throughout the world. This situation is clearly reflected in the recently published data from the NCD-RisC (Non-Communicable Diseases Risk Factors Collaboration) study, showing that the number of individuals with diabetes quadrupled between 1980 and 2014, particularly in developing countries.¹ Spain has not escaped this upward trend. The Di@betes study reported an age- and sex-adjusted total prevalence of 13.8%, and almost half the affected individuals (6%) were unaware of their condition.^{1,2} Furthermore, the expectations for the future are not reassuring: The International Diabetes Federation has estimated that this disease will affect 642 million adults aged 18 to 79 years in 2040 (this same organization established the value at 415 million in 2015), and approximately 90% of them will have diabetes type 2.³ These figures are a cause for concern among the various health systems, since 7% to 14% of their current budget is allocated to the treatment of this disease. Recent studies in Europe⁴ have shown that patients with diabetes consume twice the amount of health care resources as the nondiabetic population, and the cost increases as patients develop chronic complications. There are several reasons for the rise in the incidence and prevalence of this condition, such as increases in the dual epidemic of excess weight and obesity⁵ and in sedentary lifestyles, as well as population aging. One key factor related to the higher prevalence is the improvement in survival prompted by various therapies that enable better glycemic control, and especially, control of cholesterol levels and hypertension. Diabetes is associated with considerable morbidity and mortality, mainly of cardiovascular origin. More than 75% of hospitalizations and more than 50% of deaths in this population are due to cardiovascular causes, as has been extensively reported. The Steno-2 study showed that intensive, multifactorial management of hyperglycemia, hypercholesterolemia, and hypertension, together with antiplatelet therapy, result in effective reductions in vascular complications and mortality in the type 2 diabetes population, with decreases of 57% in cardiovascular deaths and 46% in overall mortality. In a recent update of that study, intensive treatment during the first

7 or 8 years was associated with a mean increase in life expectancy of 7.9 years after a follow-up period of 21 years.⁶

In Spain, it is essential to have data on the temporal trends of diabetes-related mortality to establish health care policies that will improve the health of the population and limit or prevent inequalities between the country's autonomous communities. In this line, the article by Orozco-Beltrán et al.⁷ in *Revista Española de Cardiología* updates a previous study by the same group⁸ that analyzed the geographic distribution of mortality due to type 1 and 2 diabetes during the period 1981 to 1986. The findings showed a north-south gradient, with a clear concentration of higher mortality in the south and southeast areas of Spain. In their current study, the authors used data provided by the National Institute of Statistics on the population and deaths, and analyzed a longer time span (1998–2013), divided into 5-year periods (1998, 2003, 2008, and 2013). The specific rates were calculated by age and sex, and the standardized mortality rates by provinces, using a different statistical method. Specifically, the authors used joint-point models to carry out a more rigorous analysis of the trends occurring in each successive period, which enabled identification of the years (points) when a significant change in trend was produced. The data show that the gradient of higher mortality in the southern parts of the country is gradually disappearing (although it was maintained during the 1998–2003 period) and the inequality between provinces is declining. They also found a clear and encouraging reduction in mortality (around 37%), with uneven results by sex: 25% in men and 41% in women. Regrettably, there were exceptions in all the periods analyzed: Ceuta, Melilla, and the Canary Islands (which, in this respect, are not exactly “the Fortunate Isles”). As was seen in the DARIOS⁹ study, the prevalence of obesity, hypertension, dyslipidemia, metabolic syndrome, and insulin resistance, and the incidence of dialysis and lower limb amputations, was higher in the Canary Islands than in the rest of Spain. However, none of the above would be attributable to a deficiency of medication use or of specialized health care services. Several factors would have to be analyzed, such as differences in lifestyle, but one important factor to take into account is the differing genetic traits of the Canarian population. This factor would also apply to Ceuta and Melilla, whose populations contain an elevated percentage of individuals of Magreb origin.

One understandable limitation of the study is the failure to describe known factors that can affect mortality risk, such as the duration of diabetes or the presence of microvascular complications.¹⁰ The risk of cardiovascular events increases linearly with

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the number of microvascular complications, independently of conventional risk factors. Other limitations are the lack of data on the use of drugs known to reduce mortality risk (eg, statins) and on the degree of glycemic control. A Swedish population study¹¹ including all type 1 diabetes patients in the country found that the risk of cardiovascular death was double that of the general population in patients with good glucose control, but it was 8 to 10 times higher in patients with poor control. It would also have been of interest to separate patients with type 1 diabetes from those with type 2. The prevalence of obesity, hypertension, and dyslipidemia differ in these 2 conditions, and therefore, these factors may differentially affect the mortality rates.

Recently, the trends associated with chronic complications of diabetes between 1990 and 2010 were analyzed in the United States.¹² During the 20 years studied, there was a 68% decrease in myocardial infarctions, 53% in stroke, 52% in lower limb amputations, and 29% in kidney failure. Furthermore, several studies carried out exclusively in developed countries have reported a reduction over the last decades of 15% to 10% every 10 years,¹³ despite increases in the incidence and prevalence of this condition. There are several explanations for this decrease: reductions in mortality due to ischemic heart disease and ischemic stroke, reductions in smoking, increasingly earlier establishment of the diabetes diagnosis, and implementation of therapeutic measures set down in various clinical practice guidelines that provide increasingly more effective control of hyperglycemia, hypercholesterolemia, and hypertension. In the last 8 years, several glucose-lowering drug classes have arrived on the market, such as IDPP-4 (dipeptidyl dipeptidase-4 inhibitors), arGLP-1 (analogs of the glucagon-1-like peptide receptor), and most recently, iSGLT2 (sodium-glucose cotransporter inhibitors), some of which have the added effect of reducing cardiovascular and overall mortality. These treatments are expected to have a further beneficial impact in future mortality analyses, considering the recent results obtained with the iSGLT2, empagliflozin, in the EMPA-REG OUTCOME trial¹⁴ (cardiovascular mortality, -38% [$P < .001$] and overall mortality, -32% [$P < .001$]) and with the arGLP-1, liraglutide, in the LEADER trial¹⁵ (cardiovascular mortality, -22% [$P = .007$] and overall mortality, -15% [$P = .02$]).

Nonetheless, we cannot forget that a key factor related to the excess mortality due to diabetes throughout the world is socioeconomic inequality. It is known that the poorer the socioeconomic conditions, the higher the cardiovascular mortality rate and the greater the prevalence of cardiovascular risk factors.^{16,17} This aspect may have had an effect on the results found in the study by Orozco-Beltrán et al. Socioeconomic inequality can only be resolved by adequate policies that enable changes in the health service structure, provide sufficient resources, develop adequate coordination at all levels of the health system and, in the case of diabetes, effectively implement

the related National Health System strategy, designed in 2006 and updated in 2012, so that we can continue to go forward in the right direction.

CONFLICTS OF INTEREST

J.M. Cabezas-Agrícola has received honoraria for conferences from Sanofi, Novo Nordisk, Lilly, Astra-Zeneca, Boehringer-Ingelheim, Esteve, Almirall, Ipsen and Novartis.

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