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Trends in premature mortality from diabetes mellitus in Costa Rica in the period 2000–2020

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ABSTRACT

Objectives: To analyze the temporal trends of premature mortality from diabetes in Costa Rica in the period 2000–2020, at a national level and by province, and the effect of the COVID-19 pandemic on diabetes mortality during the year 2020

Methods: We studied the temporal trends of mortality from diabetes in Costa Rica in the period between 2000 and 2020. Age-standardized mortality rates and corresponding 95% confidence intervals were calculated for each year, sex and province.

Results: We analyzed the data of 17,968 deceased persons. The mean age was 72.5 years (range 1 to 109 years), and 51.5% of the population (n = 9253) was younger than 75 years. In both men and women, we observed a significant decrease in mortality from 2000 to 2014, followed by the opposite trend from 2014 to 2020, with average yearly increases of 13.9% in men and 11.6% in women.

Conclusions: Premature mortality from diabetes has been growing from 2014. The COVID-19 pandemic changed the mortality pattern, increasing premature diabetes deaths in Costa Rica in 2020.

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1. Introduction

The worldwide prevalence of diabetes mellitus stood at 9.3% in 2019 [1]. The latest edition of the International Diabetes Federation (IDF) Diabetes Atlas shows that 537 million adults were living with the disease in 2021 [1]. According to the World Health Organization (WHO), diabetes is currently the ninth leading cause of death, and is expected to climb two places to seventh by 2030 [2]. In 2019, 1.5 million people died as a direct result of diabetes, 48% of whom were younger than 70 years of age. Between 2000 and 2016, the rate of premature mortality from diabetes increased by 5%. In high-income countries, this rate decreased between 2000 and 2010, but then rebounded between 2010 and 2016; while in low- and middle-income countries, premature death from diabetes increased during both periods [2].

In Costa Rica, according to the last two state reports of cardiovascular risk factor surveillance (prepared in 2014 and 2018), diabetes prevalence has increased in recent years, from 10.8% in 2010 to 12.8% in 2014, then to 14.8% in 2019. This most recent prevalence rate is the second highest on the American continent after that of Belize, and one of the highest in the world. The prevalence of undiagnosed diabetes increased from 2.8% in 2014 to 3.9% in 2018 [3,4].

Diabetes-attributable mortality has slowed since 2005 to a stable rate of 16 deaths per 100,000 inhabitants, and is projected to have decreased slightly by 2025. In 2017, diabetes mortality rates in Central Europe, Central America and the Caribbean were 11, 39.8 and 34.4 deaths per 100,000 inhabitants, respectively [5]. In Costa Rica, mortality from endocrine, nutritional and metabolic diseases – which include diabetes – has increased in relation to all-cause mortality in recent years, from 5.4% in 2015 (sixth leading cause of death) to 6.2% in 2017, 7.7% in 2019 and 9.9% in 2020 (fourth leading cause of death).

Data on premature mortality (mortality rate in people under 75 years of age) are of particular relevance [6,7], as they provide an overall indicator of the magnitude of deaths that occur before the average life expectancy. Premature mortality encompasses preventable mortality and treatable mortality, which reflects the quality of the healthcare system [8]. Death from type 2 diabetes is considered preventable, within the age range of 0 to 74 years [9].

Few studies have analyzed the temporal trends of diabetes mortality in Costa Rica [10], and to the best of our knowledge, none have applied an adequate methodology for detecting changes in trends over a long time period, or analyzed

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premature mortality from this disease in Costa Rica, or examined the effect of the 2020 pandemic on diabetes mortality. The main aim of this study is to analyze the temporal trends of premature mortality from diabetes in Costa Rica in the period 2000–2020, at a national level and by province, and to measure the effect of the COVID-19 pandemic on diabetes mellitus mortality during 2020.

2. Study design

2.1 Study design and participants

We studied the temporal trends of mortality from diabetes mellitus in Costa Rica in the period between 2000 and 2020, both inclusive. We included men and women of all ages who died in this period and had type 1 or type 2 diabetes specified as an underlying cause on their death certificate (International Classification of Diseases (ICD) code E10-E14). The National Institute of Statistics and Census of Costa Rica provided the data on deaths and populations [11]. Our study variables were age in years, sex, year of death and province of residence of the deceased person. We separated the population into people who had died prematurely (before 75 years of age) [6,7,12], and those aged 75 years and older, to assess whether mortality had shifted between the age groups during the study period.

2.2 Statistical analysis

We calculated age-standardized mortality rates (ASMRs) and corresponding 95% confidence intervals (CIs) for each year, sex and province, using the direct method with the 2000–2025 WHO world standard population [13]. The Pan American Health Organization (PAHO) recommends using this WHO standard to adjust rates in American countries [14]. To calculate the rates, we used SPSS v.26 [15]. We constructed maps of Costa Rica to display the data from each province for each year and both sexes, using the *tmap* library of R v.4.1.2 [16].

Joinpoint regression models were fitted to analyze temporal trends in premature mortality during the study period. Annual percentage change (APC) of the adjusted segments were estimated. Negative values of APC indicate a decrease in mortality, while positive values indicate an increase. The models were fitted assuming autocorrelated errors based on the data, and the models were selected using the permutation test, with a minimum of 0 and a maximum of 3 joinpoints [17]. For this analysis we used Joinpoint Regression Program v.4.9.0, developed by the National Cancer Institute [18]. We produced graphs showing ASMRs for the whole country and for each province, together with the segments and joinpoint estimates.

To determine the possible effect of the COVID-19 pandemic, we compared the mortality rates of 2019 and 2020. To isolate the change in 2020 from the accumulated change in previous years, we performed a sensitivity analysis, fitting two linear model between the premature mortality rates and the 2015–2020 segment: one with and one without the 2020 data. The difference between the slopes of the two models provided an estimate of the effect of the year 2020 on mortality.

3. Results

Between the years 2000 and 2020, 18,968 people died from diabetes in Costa Rica. We excluded 968 of these individuals because they had a foreign nationality, 28 because their nationality was unknown, and four because their age was not recorded. We therefore analyzed the data of 17,968 deceased persons. The average age was 72.5 years (range 1 to 109 years), and 51.5% of the people analyzed (n = 9253) were younger than 75 years of age. We found that 54% of the population (n = 9702) were women and 46% were men.

Tables 1 and 2 show the age-standardized rates of mortality from diabetes in Costa Rica for each year of the period from 2000 to 2020, by age group.

Table 1. Age-standardized mortality rates from diabetes per 100,000 population, in men, by age group, Costa Rica 2000–2020.

Year	Age 0–74 years			Age 0–54 years			Age 55–74 years			Age > 74 years		
	n	ASMR	95% CI	n	ASMR	95% CI	n	ASMR	95% CI	n	ASMR	95% CI
2000	146	12.2	(10.2–14.1)	36	2.8	(1.9–3.8)	110	69.4	(56.4–82.4)	83	228.0	(178.9–277.0)
2001	156	12.3	(10.4–14.3)	45	3.3	(2.3–4.3)	111	67.7	(55.1–80.2)	81	214.2	(167.5–260.8)
2002	148	11.5	(9.6–13.3)	33	2.3	(1.5–3.1)	115	67.9	(55.5–80.3)	69	174.8	(133.6–216.1)
2003	239	18.2	(15.9–20.5)	47	3.2	(2.3–4.1)	192	110.5	(94.9–126.2)	107	258.3	(209.4–307.3)
2004	215	15.8	(13.6–17.9)	43	2.8	(1.9–3.6)	172	95.8	(81.5–110.1)	120	277.4	(227.8–327.0)
2005	181	12.8	(10.9–14.6)	35	2.1	(1.4–2.8)	146	78.3	(65.5–91.0)	111	247.0	(201.1–293.0)
2006	172	11.6	(9.8–13.3)	37	2.2	(1.5–2.9)	135	69.6	(57.8–81.3)	111	236.2	(192.3–280.2)
2007	158	10.1	(8.5–11.7)	40	2.3	(1.6–3.0)	118	58.3	(47.8–68.9)	92	188.4	(149.9–226.9)
2008	179	11.0	(9.3–12.6)	44	2.4	(1.7–3.1)	135	63.5	(52.8–74.3)	128	253.2	(209.4–297.1)
2009	185	10.9	(9.3–12.5)	39	2.1	(1.4–2.8)	146	65.1	(54.5–75.7)	120	229.5	(188.4–270.5)
2010	200	11.3	(9.7–12.9)	48	2.5	(1.8–3.2)	152	65.1	(54.7–75.4)	142	262.0	(218.9–305.1)
2011	186	10.0	(8.5–11.4)	52	2.7	(2.0–3.4)	134	55.0	(45.6–64.3)	123	219.2	(180.5–257.9)
2012	151	7.8	(6.6–9.1)	36	1.8	(1.2–2.4)	115	44.8	(36.6–53.0)	121	208.5	(171.3–245.6)
2013	176	8.9	(7.6–10.2)	30	1.5	(0.9–2.0)	146	54.7	(45.8–63.6)	138	230.0	(191.6–268.4)
2014	189	9.3	(8.0–10.6)	36	1.8	(1.2–2.3)	153	55.7	(46.8–64.6)	124	199.8	(164.6–235.0)
2015	249	11.7	(10.2–13.2)	49	2.4	(1.7–3.0)	200	69.2	(59.5–78.8)	206	321.1	(277.2–364.9)
2016	275	12.2	(10.8–13.7)	55	2.6	(1.9–3.3)	220	71.5	(62.0–81.0)	245	369.6	(323.3–415.8)
2017	328	14.0	(12.5–15.6)	56	2.7	(2.0–3.4)	272	84.0	(73.9–94.0)	260	379.8	(333.7–426.0)
2018	307	12.5	(11.1–13.9)	63	2.9	(2.2–3.6)	244	71.7	(62.6–80.7)	245	346.1	(302.7–389.4)
2019	409	16.2	(14.7–17.8)	68	3.2	(2.4–3.9)	341	96.6	(86.3–106.9)	341	464.0	(414.7–513.2)
2020	565	21.5	(19.8–23.3)	104	4.8	(3.9–5.7)	461	124.6	(113.2–136)	482	630.1	(573.8–686.3)

ASMR; age-standardized mortality rate/100,000 population (direct method, WHO 2000–2025 world standard population); CI: confidence interval

Table 2. Age-standardized mortality rates from diabetes per 100,000 population, in women, by age group, Costa Rica 2000–2020.

Year	Age 0–74 years			Age 0–54 years			Age 55–74 years			Age > 74 years		
	n	ASMR	95% CI	n	ASMR	95% CI	n	ASMR	95% CI	n	ASMR	95% CI
2000	169	13.4	(11.3–15.4)	36	2.7	(1.8–3.6)	133	79.0	(65.6–92.5)	106	242.6	(196.4–288.8)
2001	176	13.5	(11.5–15.6)	29	2.1	(1.3–2.9)	147	84.0	(70.4–97.6)	141	308.4	(257.5–359.4)
2002	145	10.7	(8.9–12.5)	31	2.1	(1.4–2.9)	114	63.5	(51.9–75.2)	135	283.3	(235.5–331.1)
2003	250	18.1	(15.9–20.4)	37	2.5	(1.7–3.2)	213	114.7	(99.2–130.1)	229	457.5	(398.2–516.7)
2004	244	16.9	(14.8–19)	52	3.3	(2.4–4.2)	192	100.6	(86.4–114.9)	206	394.1	(340.3–447.9)
2005	194	13.0	(11.2–14.8)	40	2.4	(1.7–3.2)	154	77.9	(65.6–90.3)	179	329.7	(281.4–378.0)
2006	179	11.6	(9.9–13.3)	36	2.1	(1.4–2.8)	143	70.0	(58.5–81.5)	148	261.2	(219.1–303.3)
2007	169	10.6	(8.9–12.2)	37	2.1	(1.4–2.8)	132	62.4	(51.8–73.1)	174	294.1	(250.4–337.8)
2008	191	11.4	(9.8–13.0)	40	2.2	(1.5–2.9)	151	67.7	(56.9–78.5)	195	317.2	(272.7–361.7)
2009	191	11.1	(9.5–12.6)	37	2.0	(1.3–2.6)	154	66.9	(56.3–77.4)	219	343.6	(298.1–389.1)
2010	192	10.5	(9.0–12.0)	46	2.4	(1.7–3.1)	146	60.3	(50.5–70.1)	199	301.0	(259.2–342.8)
2011	150	7.9	(6.6–9.1)	36	1.9	(1.3–2.5)	114	44.9	(36.6–53.1)	188	274.2	(235.0–313.4)
2012	175	8.9	(7.6–10.2)	39	2.0	(1.4–2.6)	136	51.4	(42.7–60.0)	186	262.0	(224.4–299.7)
2013	171	8.4	(7.1–9.6)	40	2.0	(1.4–2.6)	131	47.8	(39.6–56.0)	189	257.8	(221.0–294.5)
2014	170	7.9	(6.7–9.1)	38	1.8	(1.2–2.4)	132	45.0	(37.3–52.8)	203	268.1	(231.2–304.9)
2015	188	8.3	(7.1–9.5)	50	2.4	(1.7–3.0)	138	45.1	(37.5–52.6)	297	379.6	(336.4–422.7)
2016	225	9.7	(8.5–11)	52	2.5	(1.8–3.2)	173	54.2	(46.1–62.3)	342	423.0	(378.2–467.9)
2017	258	10.7	(9.4–12)	45	2.1	(1.5–2.7)	213	63.3	(54.8–71.8)	386	462.1	(416.0–508.2)
2018	238	9.5	(8.3–10.7)	53	2.5	(1.8–3.1)	185	52.5	(44.9–60.1)	363	419.8	(376.6–463.0)
2019	355	13.6	(12.2–15)	65	3.0	(2.3–3.7)	290	78.8	(69.7–87.9)	514	572.6	(523.1–622.1)
2020	414	15.1	(13.6–16.6)	63	2.9	(2.2–3.6)	351	90.5	(81.0–99.9)	662	708.8	(654.8–762.8)

ASMR: age-standardized mortality rates/100,000 population (direct method, WHO 2000–2025 world standard population); CI: confidence interval

In men (Table 1), we found some fluctuations in premature mortality (< 75 years) during the study period, with rates decreasing from 12.2 deaths per 100,000 inhabitants in 2000 to 7.8 deaths per 100,000 inhabitants in 2012 and 9.3 deaths per 100,000 inhabitants in 2014, before rising again to 16.2 and 21.5 deaths per 100,000 inhabitants in 2019 and 2020, respectively.

In women (Table 2), we observed a similar pattern, with rates decreasing progressively from 13.4 deaths per 100,000 inhabitants in 2000 to 7.9 in 2011 and 2014, then increasing toward the end of the study period.

Table 3 shows the age-standardized rates of premature mortality (< 75 years) from diabetes in each province of Costa Rica, for the years 2000 (first year of study period), 2019 (pre-pandemic) and 2020 (pandemic), separated by sex, as well as the average annual percentage changes (AAPCs) calculated by joinpoint models for the whole period.

In men, the provinces with the highest rates in the year 2000 were Puntarenas and San José, with 13.5 and 13.3 deaths per 100,000 inhabitants, respectively. The provinces with the lowest rates were Limón and Guanacaste, with 7.7 and 9.8 deaths per 100,00 inhabitants, respectively. In all provinces, mortality was higher in the year 2019, particularly in Limón, where there were 20.4 deaths per 100,000 inhabitants. The changes observed in the rates are not reflected in the AAPCs for the whole period: Limón was the only province to show a significant increase with an average annual change of 2.3% between 2000 and 2020.

In women, the provinces with the highest rates in 2000 were Puntarenas and Guanacaste, with 23 and 20.1 deaths

Table 3. Premature mortality (< 75 years) from diabetes in the provinces of Costa Rica in 2000, 2019 and 2020; and average annual percent change between 2000 and 2020, by sex.

Sex	Area	Year 2000			Year 2019			Year 2020			% change	2000–2020	
		n	ASMR	95% CI	n	ASMR	95% CI	n	ASMR	95% CI	2019 to 2020	AAPC	95% CI
Men	COSTA RICA	146	12.2	(10.2–14.1)	409	16.2	(14.7–17.8)	565	21.5	(19.8–23.3)	32.7	1.5	(−0.9; 3.9)
	San José	57	13.3	(9.8–16.7)	119	14.1	(11.6–16.6)	203	23.0	(19.8–26.1)	63.1	2.4	(−0.8; 5.7)
	Alajuela	28	12.4	(7.8–17.0)	84	17.0	(13.4–20.7)	117	22.8	(18.7–26.9)	34.1	1.1	(−3.0; 5.3)
	Cartago	16	11.4	(5.7–17.1)	37	13.8	(9.3–18.2)	54	19.5	(14.3–24.8)	41.3	2.1	(−8.7; 14.2)
	Heredia	13	12.4	(5.6–19.2)	43	16.2	(11.3–21.1)	43	16.2	(11.3–21.1)	0.6	0.4	(−2.5; 3.3)
	Guanacaste	9	9.8	(3.4–16.3)	31	16.0	(10.3–21.6)	49	24.5	(17.6–31.3)	53.1	1.7	(−0.3; 3.6)
	Puntarenas	16	13.5	(6.8–20.1)	52	21.3	(15.5–27.1)	54	21.3	(15.6–27.0)	0.9	3.0	(−0.9; 7.1)
	Limón	7	7.7	(2.0–13.4)	43	20.4	(14.3–26.5)	45	19.7	(13.9–25.5)	−3.4	2.3*	(0.0; 4.7)
Women	COSTA RICA	169	13.4	(11.3–15.4)	355	13.6	(12.2–15.0)	414	15.1	(13.6–16.6)	11.0	0.8	(−2.1; 3.8)
	San José	60	11.5	(8.5–14.4)	105	10.9	(8.8–13.0)	127	12.6	(10.4–14.8)	15.6	−0.2	(−2.5; 2.2)
	Alajuela	23	9.9	(5.8–14.0)	60	11.9	(8.9–14.9)	86	16.5	(13.0–20.0)	38.7	2.5	(−7.5; 13.7)
	Cartago	18	13.5	(7.2–19.7)	35	12.3	(8.2–16.4)	40	13.4	(9.2–17.6)	8.9	−2.4	(−6.1; 1.4)
	Heredia	14	12.2	(5.8–18.6)	31	11.2	(7.2–15.1)	35	11.8	(7.9–15.8)	5.4	−0.9	(−3.4; 1.8)
	Guanacaste	18	20.1	(10.8–29.4)	31	16.8	(10.9–22.7)	35	17.7	(11.8–23.5)	5.4	−1.7*	(−3.1; −0.3)
	Puntarenas	23	23.0	(13.6–32.5)	46	21.0	(14.9–27.1)	47	20.3	(14.5–26.1)	−3.3	1.1	(−3.3; 5.6)
	Limón	13	18.4	(8.4–28.4)	47	26.4	(18.7–34.0)	44	23.7	(16.7–30.8)	−10.2	2.8	(−0.8; 6.5)

AAPC: average annual percentage change for period 2000–2020; ASMR: age-standardized mortality rates/100,000 population (direct method, WHO 2000–2025 world standard population); CI: confidence interval

*$p < 0.05$

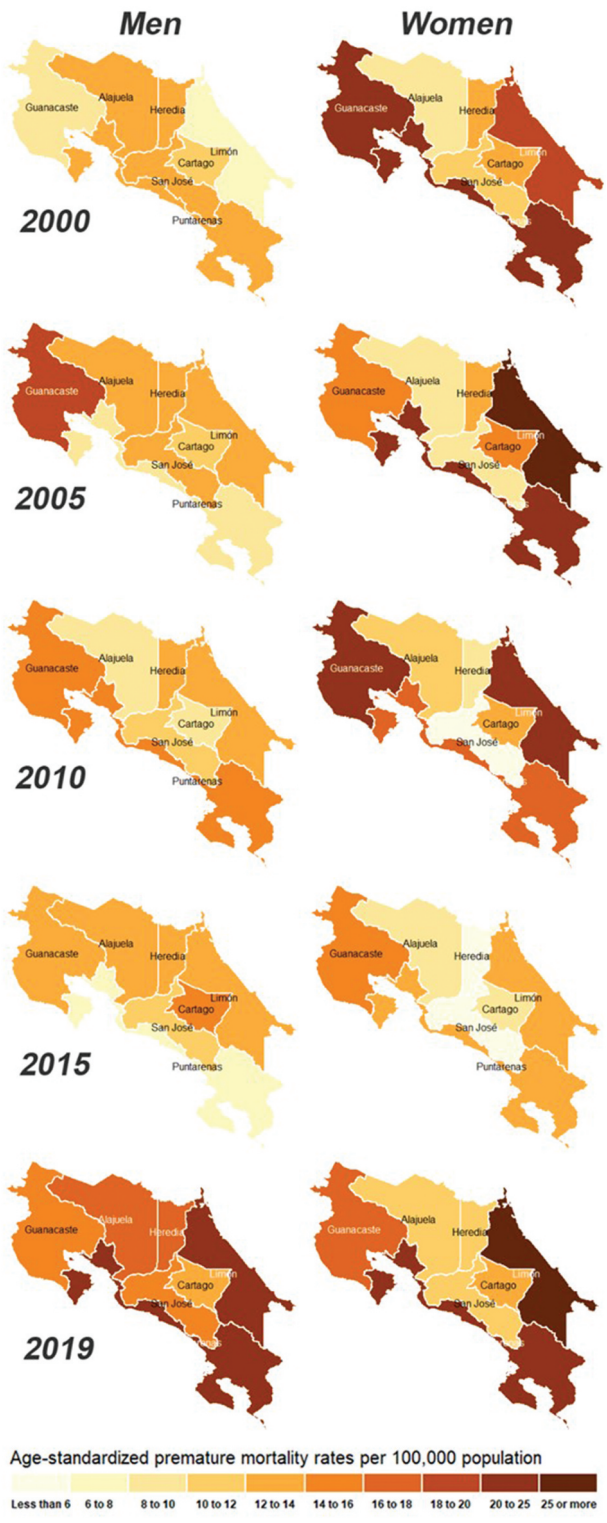

Figure 1. Age-standardized premature mortality rates from diabetes per 100,000 population by sex, Costa Rica 2000–2019

per-100,000 inhabitants, respectively; while the lowest rates – 9.9 and 11.5 deaths per 100,000 inhabitants – were found in Alajuela and San José, respectively. The changes in rates were different in women than in men, decreasing between 2000 and 2019 in all except two provinces (Limón and Alajuela). The only province where the changes observed in the ASMRs are significantly reflected in the AAPC is Guanacaste, with an average annual decrease of 1.7% during the study period.

These fluctuations in the patterns of premature mortality over the years, and the differences between the sexes, are visible in(Figure 1)

Table 4 shows the results of the joinpoint regression in the whole country and in each province, for premature mortality from diabetes in the period 2000–2020. At the national level, in both men and women, these data show a significant decrease in mortality from 2000 to 2014; followed by the opposite trend from 2014 to 2020, with average yearly increases of 13.9% in men and 11.6% in women (Figure 2). This change in trend in 2014 at the national level is approximately reflected in all provinces except Guanacaste, and in both sexes (Table 4 and Figures 3-9).

Regarding the possible effect of the pandemic, premature mortality increased by 32.7% in men and by 11% in women between 2019 and 2020. For the subgroup of people aged 55 to 74 years, the increase was 28.9% in men and 14.8% in women, and for those older than 75 years, the increase was 35.8% in men and 23.8% in women.

Among the different provinces, there was an unequal pattern of premature mortality between 2019 and 2020 in men, with the greatest increases in San José (63.1%), Guanacaste (53.1%), Cartago (41.3%) and Alajuela (34.1%), while there were no relevant increases in Heredia (0.6%), Puntarenas (0.9%) or Limón (−3.4%). In women, the changes were smaller, with the greatest increases seen in Alajuela (38.7%) and San José (15.6%); small increases in Cartago (8.9%), Guanacaste (5.4%) and Heredia (5.4%); no relevant change in Puntarenas (−3.3%); and a decrease in Limón (−10.2%) (Table 3).

The fitted linear regression model of premature mortality rates over the period 2015–2019, which shows the increase in mortality, had a slope of 0.93 in men (R^2 = 0.65) and 1.04 in women (R^2 = 0.67). These slopes reflect the average increase in mortality rate for each elapsed year. When we fitted the same model for the 2015–2020 period, we obtained slopes of 1.70 (R^2 = 0.73) and 1.27 (R^2 = 0.81) for men and women, respectively. Figure 10 The differences between the slopes represent the estimate of the effect of the pandemic on premature mortality from diabetes in Costa Rica: 0.77 deaths per 100,000 inhabitants in men and 0.23 deaths per 100,000 inhabitants in women (Figure 11).

4. Discussion

The results of our study show a significant change in the trend of premature mortality from diabetes in Costa Rica during the period 2000–2020: there was a significant decrease from 2000 to 2014, followed by a significant increase from 2014 to 2020. We observed the same pattern in most provinces and in both sexes. The possible effect of the pandemic is reflected in an increase in premature diabetes mortality between 2019 and 2020. This increase was unequally distributed among the different provinces, and was greater in men that in women (0.77 versus 0.23 additional deaths per 100,000 inhabitants).

A previous study showed that mortality from diabetes in Costa Rica is higher in women than in men in all age groups [10], but we found that this is only the case for people aged

Table 4. Trend segments and annual percentage change of premature mortality (< 75 years) from diabetes, obtained using joinpoint regression models for the age-standardized rates, by sex and province, 2000–2020, Costa Rica.

Sex	Area	Period segment	APC	95% CI	p-value	AAPC	95% CI
Men	COSTA RICA	2000 to 2014.	−3.4*	(−5.8; −0.9)	0.010	1.5	(−0.9; 3.9)
		2014 to 2020.	13.9*	(7.2; 21.1)	0.001		
	Alajuela	2000 to 2013.	−5.5*	(−10; −0.6)	0.029	1.1	(−3.0; 5.3)
		2013 to 2020.	14.4*	(4.8; 24.9)	0.005		
	Cartago	2000 to 2002	29.7	(−43.9; 199.7)	0.505	2.1	(−8.7; 14.2)
		2002 to 2012	−8.7*	(−11.9; −5.3)	0.001		
		2012 to 2015	27.3	(−31.5; 136.5)	0.406		
		2015 to 2020	1.6	(−5.0; 8.7)	0.609		
	Guanacaste	2000 to 2020	1.7	(−0.3; 3.6)	0.094	1.7	(−0.3; 3.6)
	Heredia	2000 to 2013	−3.3	(−6.5; 0.0)	0.050	0.4	(−2.5; 3.3)
		2013 to 2020	7.6*	(1.0; 14.7)	0.027		
	Limón	2000 to 2014	−0.9	(−3.1; 1.5)	0.441	2.3*	(0.0; 4.7)
		2014 to 2020	10.2*	(3.5; 17.2)	0.004		
	Puntarenas	2000 to 2016	−2.2	(−5.0; 0.7)	0.127	3.0	(−0.9; 7.1)
		2016 to 2020	27.0*	(6.6; 51.2)	0.10		
	San José	2000 to 2003	9.9	(−10; 34.2)	0.324	2.4	(−0.8; 5.7)
		2003 to 2013	−7.1*	(−9.8; −4.4)	<0.001		
		2013 to 2020	14.1*	(10.4; 18.0)	<0.001		
Women	COSTA RICA	2000 to 2003	8.9	(−9.0; 30.3)	0.325	0.8	(−2.1; 3.8)
		2003 to 2014	−6.6*	(−8.6; −4.4)	<0.001		
		2014 to 2020	11.6*	(7.1; 16.4)	<0.001		
	Alajuela	2000 to 2003	25.2	(−8.0; 70.5)	0.135	2.5	(−7.5; 13.7)
		2003 to 2006	−20.6	(−58.6; 52.4)	0.449		
		2006 to 2018	−1.4	(−4.6; 1.9)	0.354		
		2018 to 2020	41.1	(−6.6; 113.2)	0.092		
	Cartago	2000 to 2014	−6.8*	(−10.0; −3.4)	0.001	−2.4	(−6.1; 1.4)
		2014 to 2020	8.6	(−2.7; 21.2)	0.132		
	Guanacaste	2000 to 2020	−1.7*	(−3.1; −0.3)	0.020	−1.7*	(−3.1; −0.3)
	Heredia	2000 to 2015	−5.3*	(−7.4; −3.2)	<0.001	−0.9	(−3.4; 1.8)
		2015 to 2020	13.7*	(3.7; 24.6)	0.009		
	Limón	2000 to 2004	21.5*	(3.7; 42.3)	0.019	2.8	(−0.8; 6.5)
		2004 to 2014	−8.8*	(−11.9; −5.7)	<0.001		
		2014 to 2020	12.3*	(6.4; 18.6)	<0.001		
	Puntarenas	2000 to 2017	−2.7*	(−5.0; −0.2)	0.033	1.1	(−3.3; 5.6)
		2017 to 2020	25	(−6.0; 66.3)	0.117		
	San José	2000 to 2014	−5.9*	(−7.9; −3.8)	<0.001	−0.2	(−2.5; 2.2)
		2014 to 2020	14.4*	(6.9; 22.4)	0.001		

AAPC: average annual percentage change; APC: annual percentage change; CI: confidence interval* $p < 0.05$

75 years and older, and that premature mortality rates are similar in both sexes. This may be because diabetes is more prevalent in older women that in older men, and because the following risk factors are more prevalent in women aged 65 years and older than in men of the same ages [19]: hypertension (66.4% of men versus 72.8% of women), HDL of 40–50 mg/dl or lower, LDL levels of 130 mg/dL or higher, triglyceride levels of 150 mg/dL or higher, low physical activity, and obesity [20].

The trends in mortality from diabetes in Costa Rica in this study are consistent with the findings of previous studies [10,19–21], which showed an increase in mortality from 2014, although they did not apply models that could reveal changes in trends. By using joinpoint regression models, we have shown a statistically significant change in trend in 2014, when the significant average annual decreases of −3.4% in men and of −6.6% in women over the previous four years changed to important average annual increases of 13.9% in men and 11.6% in women over the following six years, until 2020.

We hypothesize that the increase in mortality from 2014 may be due to:

- Increased prevalence of diabetes. The high prevalence of diabetes in Costa Rica has increased by 2% every four years, reaching 14.8% in 2018 [3,20].
- High prevalence of risk factors. In Costa Rica, the prevalence of overweight and obesity increased from 62.2% in 2014 (68.5% in the urban population) to 70.7% in 2018 [3,20,22] While the rate of low physical activity improved from 2014 (44.5%) to 2018 (36.1%), it is still high, and the improvement has not been reflected in lower obesity rates [23,24], possibly owing to continued poor diet and sedentary lifestyle. Research has found that the factors most closely associated with mortality from diabetes are overweight/obesity, responsible for 30.8% of these deaths; and poor diet (low in whole grains, fruits, nuts and seeds, and high in sugary drinks and red meats), which causes 24.7% of diabetes deaths [5]. The prevalence of hypertension and dyslipidaemia also increased slightly between 2014 and 2018 [25].
- Poor control and monitoring of the disease. Several studies have reported poor control of the disease, with suboptimal levels of blood glucose, blood pressure and lipids [26–28]. Poor control is the main cause of vascular complications and death. This may be because people with diabetes do not adhere to their treatment plan, are not diagnosed, do not receive clinical education, or have problems accessing healthcare and adequate treatments.

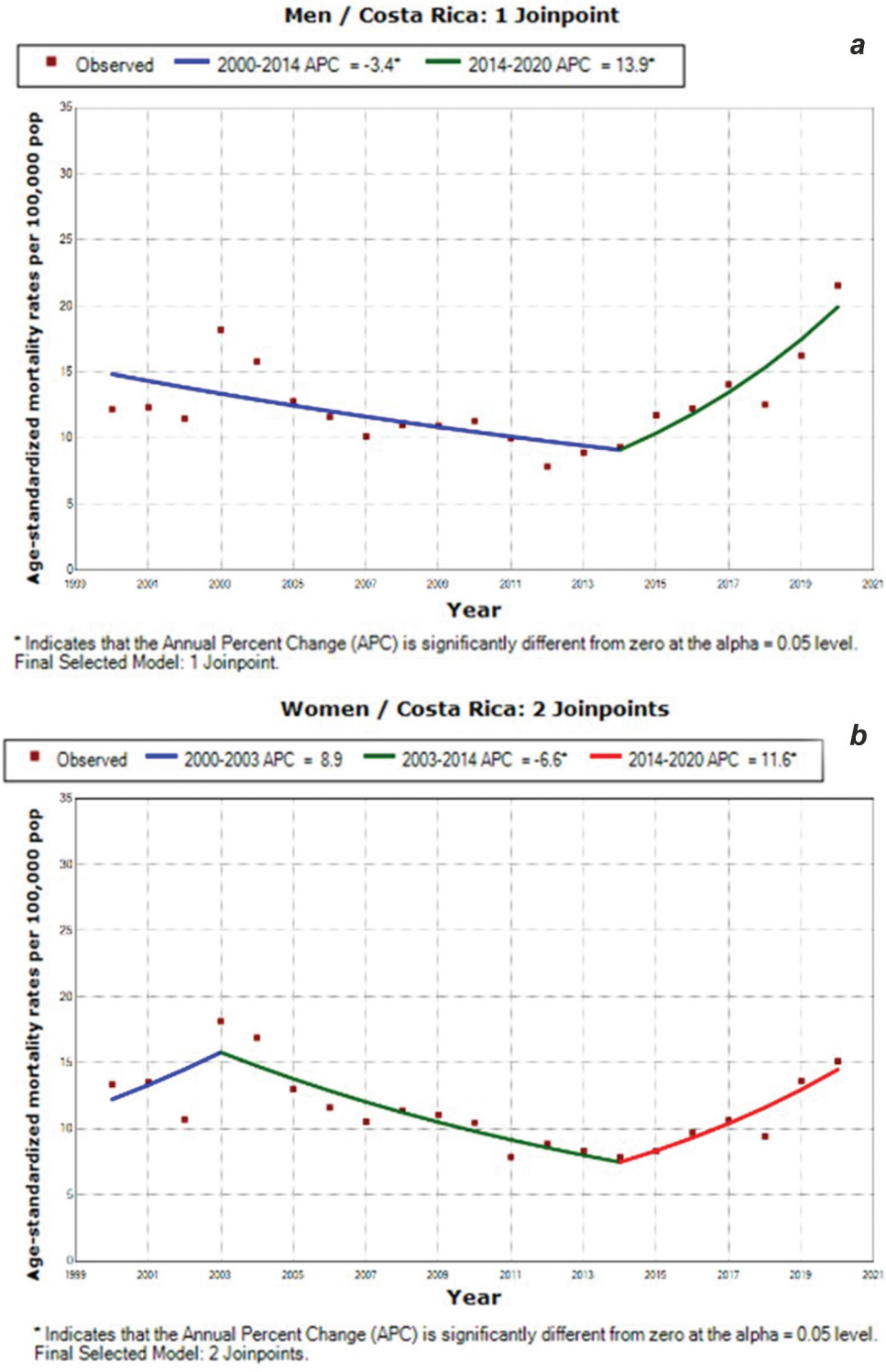

Figure 2. Trends in premature mortality from diabetes in Costa Rica by sex, 2000–2020 (A: men; B: women)

- Clinical complications. In 2016, one study estimated that 13.8% of people with diabetes in Costa Rica had macrovascular complications, and 15.2% had microvascular complications [28]. People with type 2 diabetes were 2.8 times more likely to die from cardiovascular complications, and 15.9 times more likely to die from renal complications, than people without type 2 diabetes [29]. Hospitalizations due to complications of diabetes, although with age differences by sex, show an increase in both groups since 2013 [29].
- Access to treatment. The latest international clinical practice guidelines on the management of type 2 diabetes recommend oral hypoglycemic agents such as metformin as first-line therapy [30,31]. Where this option

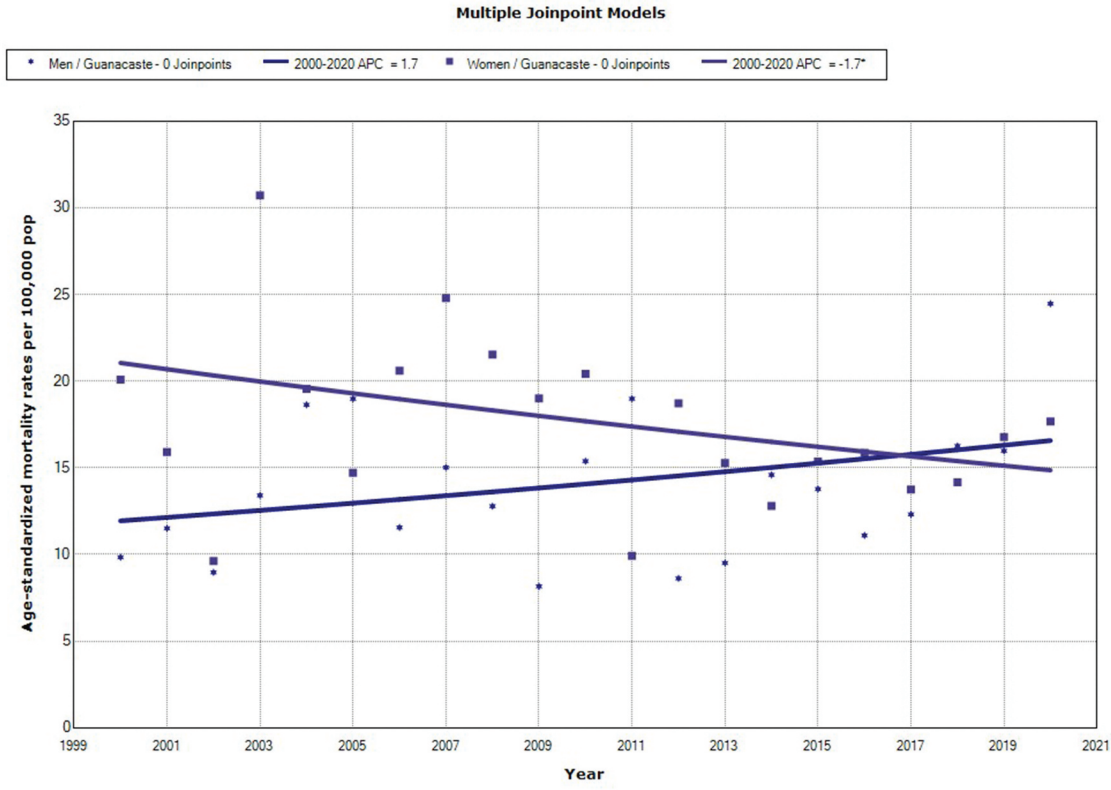

Figure 3. Trends in premature mortality from diabetes in Guanacaste by sex, 2000–2020

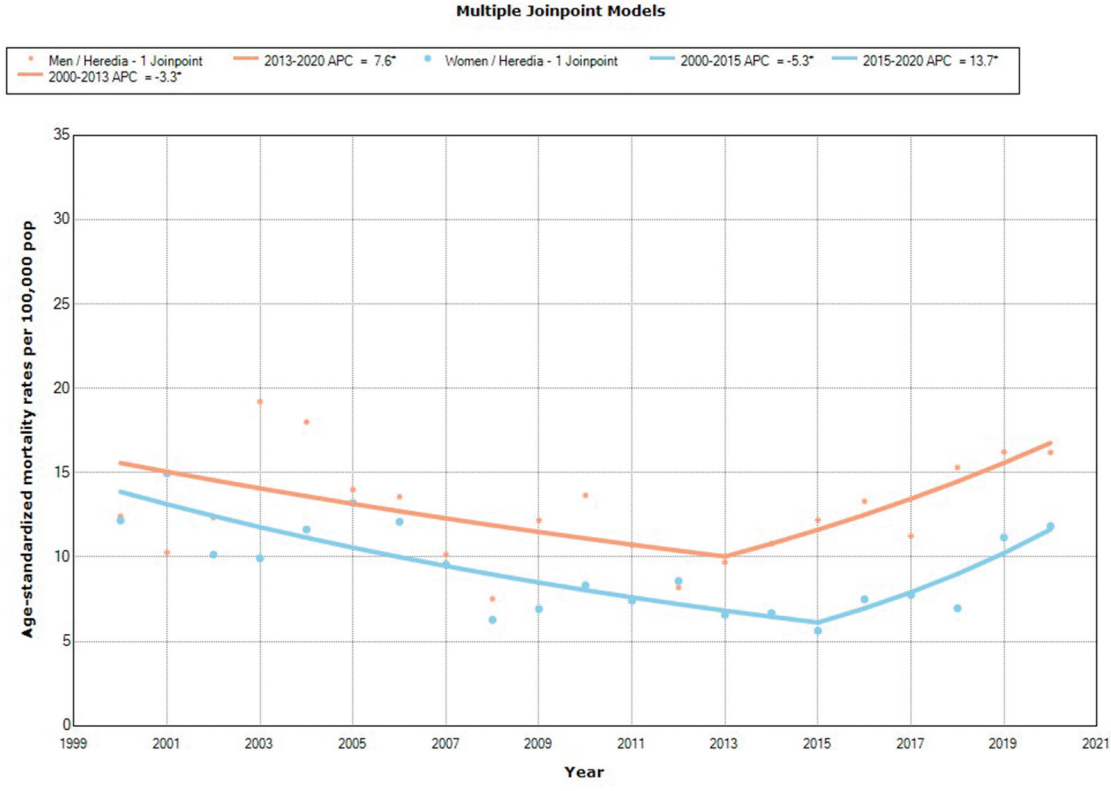

Figure 4. Trends in premature mortality from diabetes in Heredia by sex, 2000–2020

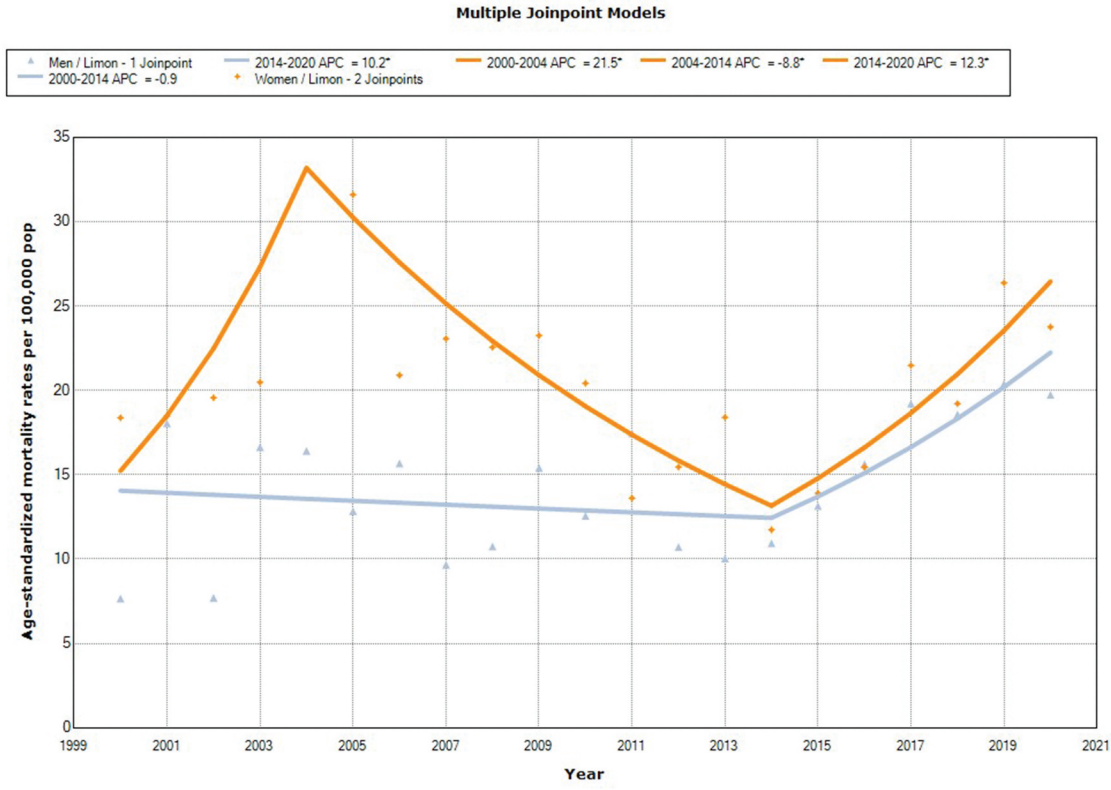

Figure 5. Trends in premature mortality from diabetes in Limón by sex, 2000–2020

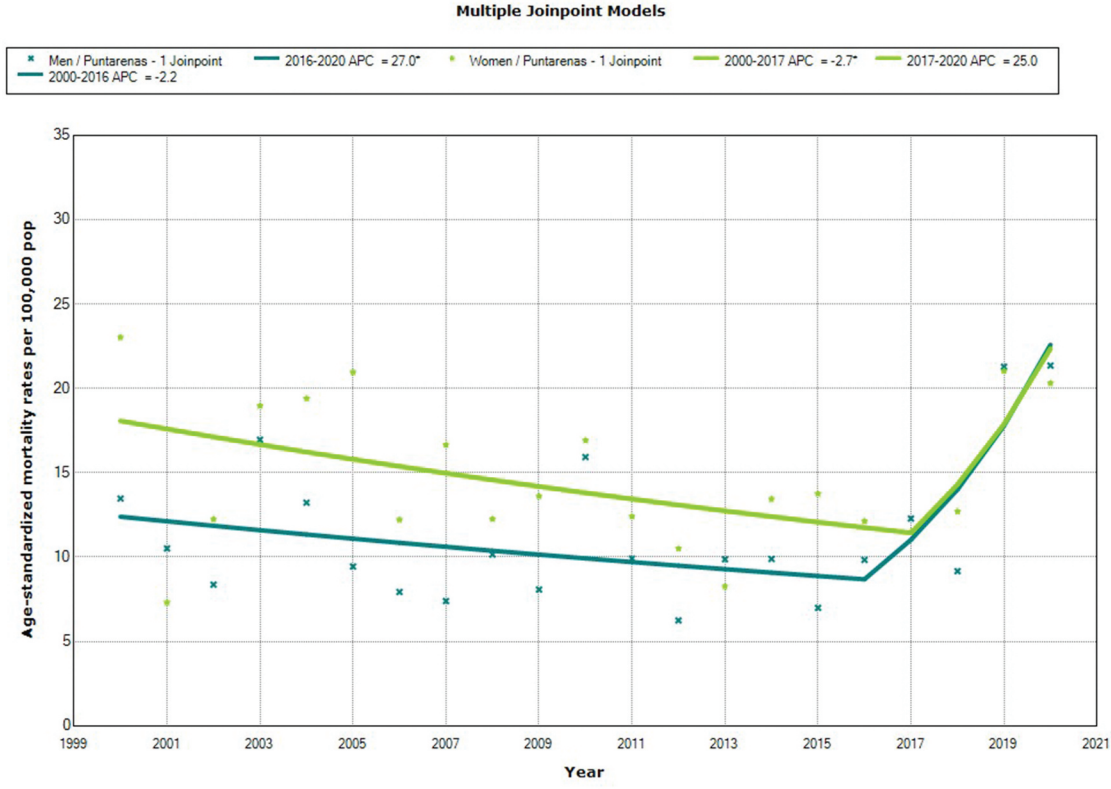

Figure 6. Trends in premature mortality from diabetes in Puntarenas by sex, 2000–2020

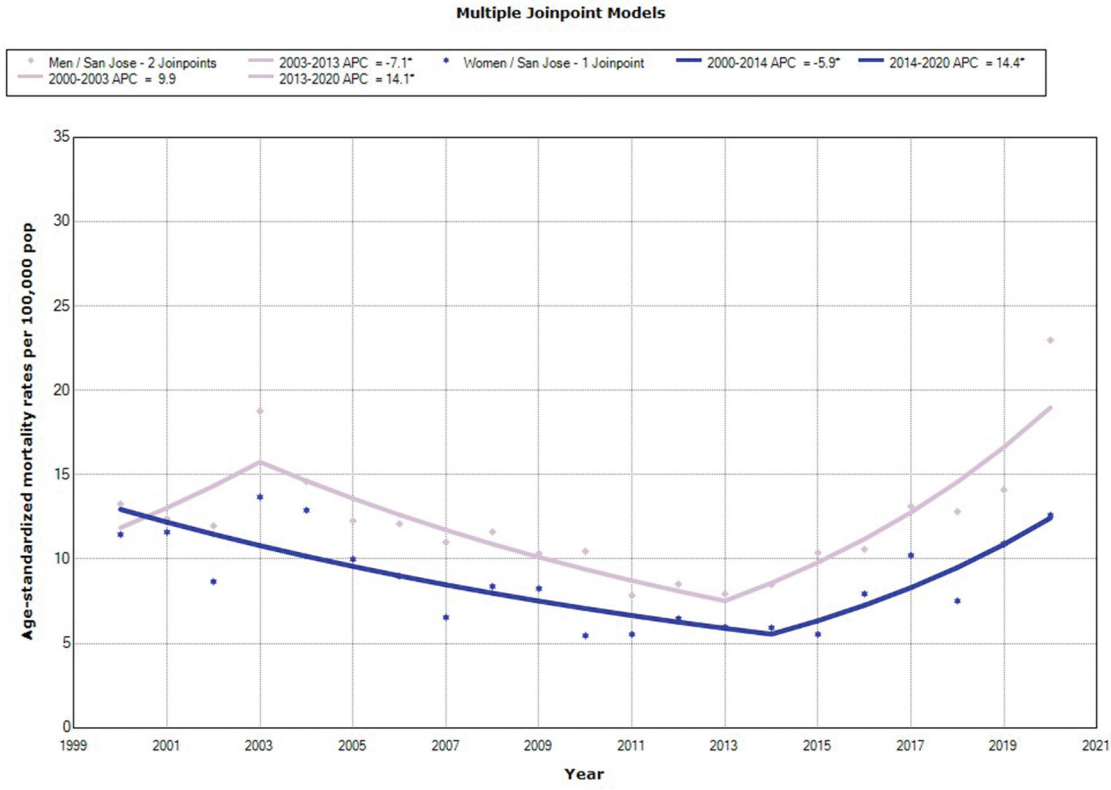

Figure 7. Trends in premature mortality from diabetes in San José by sex, 2000–2020

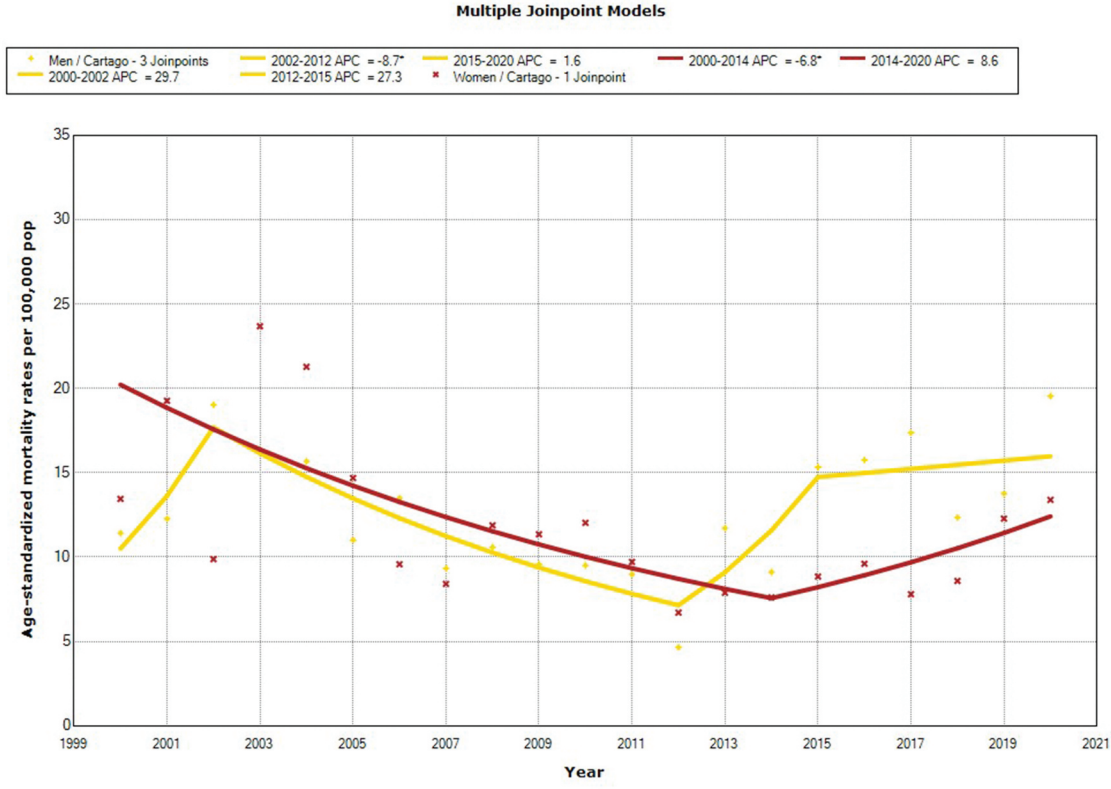

Figure 8. Trends in premature mortality from diabetes in Cartago by sex, 2000–2020

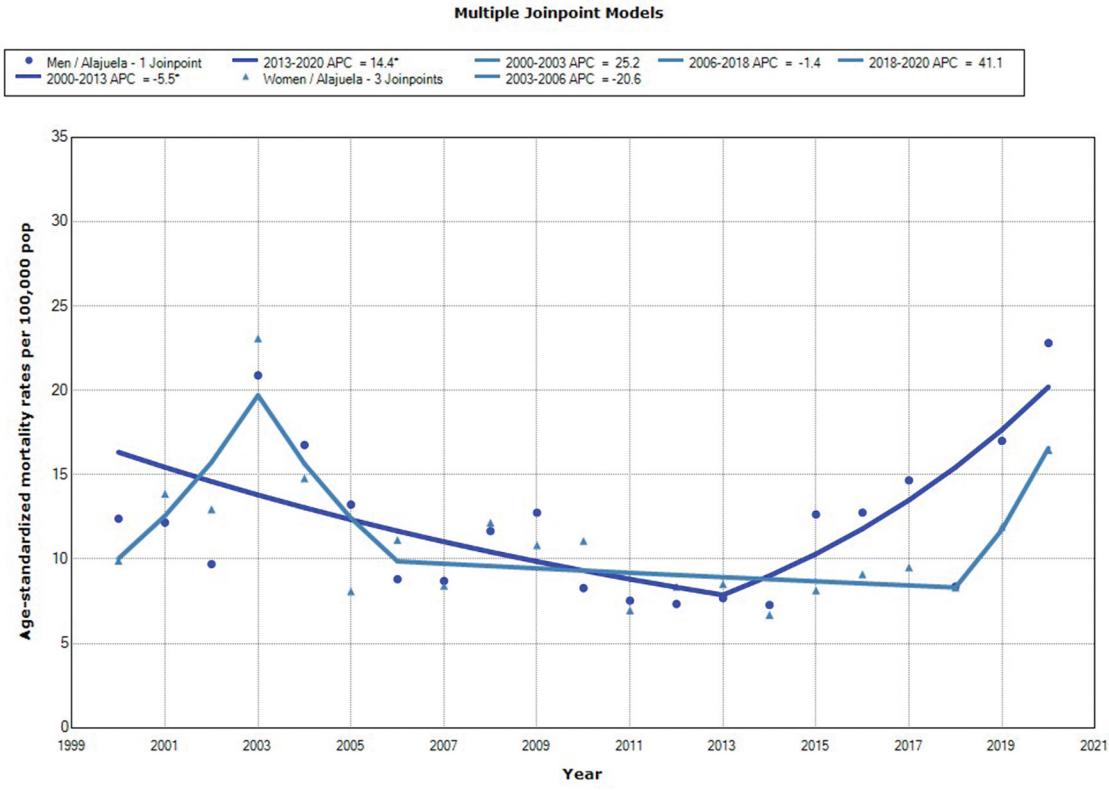

Figure 9. Trends in premature mortality from diabetes in Arajuela by sex, 2000–2020

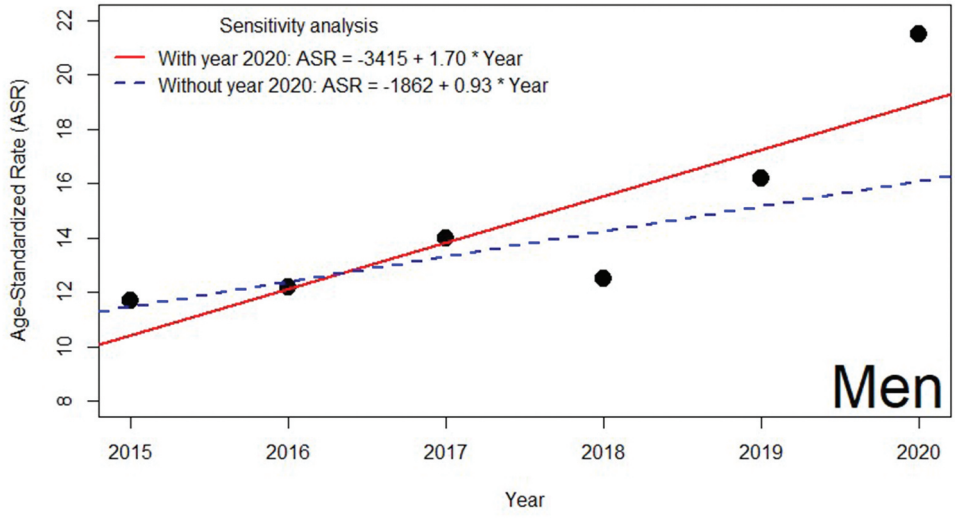

Figure 10. Sensitivity analysis of the effect of the year 2020 on premature mortality from diabetes in Costa Rica, for men

does not have an adequate effect, guidelines recommend adjuvant therapy with a combination of other drugs that have novel active ingredients [32–34], that are not included in the basic social security healthcare plan in Costa Rica, and if diabetes patients do not improve with metformin, they can only receive glibenclamide, gliclazide or insulin as adjuvant therapy [35]. Lack of access to certain treatments in the event of poor control of the disease, combined with the increased prevalence of risk factors and poor control and monitoring of the disease, and the decrease in health spending from 2014 may be one of the causes of the premature mortality rise.

- Decrease in healthcare spending. Healthcare spending in Costa Rica reached a maximum level of 8.12% of the gross domestic product (GDP) in 2011, before decreasing to 7.68% in 2013, then 7.59% in 2015, and 7.05% in 2017. It did rise slightly to 7.29% in 2019 [36].

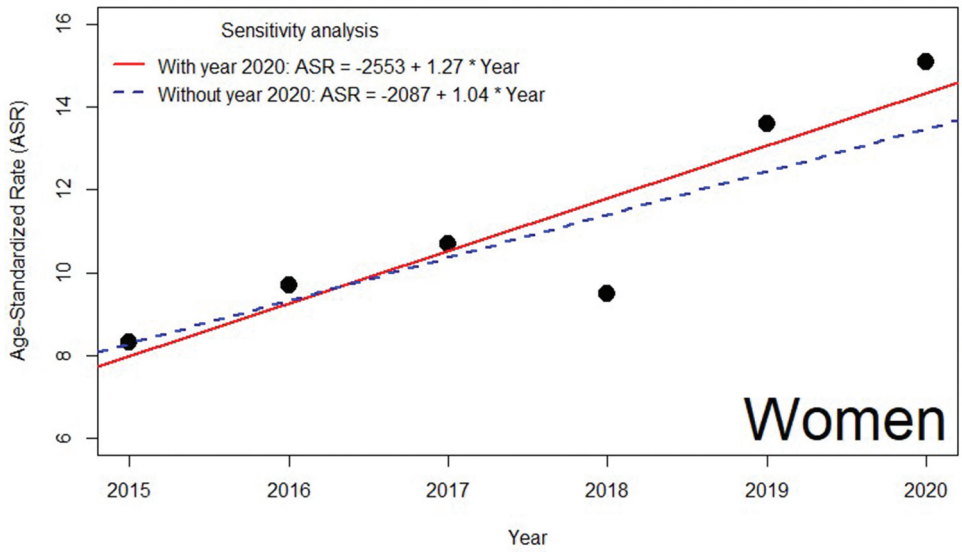

Figure 11. Sensitivity analysis of the effect of the year 2020 on premature mortality from diabetes in Costa Rica, for women

In summary, the alarming increase in overweight and obesity in the population from 2014, due to inadequate diet and sedentary lifestyle, are possible causes of the large increase in diabetes prevalence. The high prevalence of hypertension and dyslipidaemia in people with diabetes, and poor control of the disease caused by underdiagnosis, lack of access to novel treatments and decrease in public spending, can lead to considerable complications. All these factors together may explain the increase in premature mortality from diabetes in Costa Rica between 2014 and 2020, at the national level and in the individual provinces.

To reduce the premature mortality, it would be important for public institutions to increase their investments in health promotion, disease prevention, both primary and secondary, to modify and control the risk factors associated with both developing DM and reducing complications associated with it.

Effect of the COVID-19 pandemic on premature diabetes mortality

All-cause mortality in Costa Rica was 5.2 deaths per 1000 inhabitants in 2019 and 2020 [37], but the distribution of causes of death altered during the COVID-19 pandemic, with fewer deaths from vascular diseases, respiratory diseases, gastrointestinal diseases and external causes; and more deaths from infectious diseases (burden attributable to COVID-19) and from endocrine, nutritional and metabolic diseases. The proportion of all-cause mortality attributable to diabetes increased from 1.6% in 2019 to 2.9% in 2020 [11].

With the COVID-19 pandemic, the crude all-cause mortality rate in Costa Rica increased slightly from 515 deaths per 100,000 inhabitants in 2019 to 522 deaths per 100,000 inhabitants in 2020 [37]. The country reported 2185 COVID-19-related deaths in 2020 [6], meaning COVID-19 was responsible for 8.5% of all-cause mortality and constituted the leading cause of death that year. Diabetes death is likely to have increased in parallel, since previous studies have shown that diabetes increases the risk of death from COVID-19 [21,38,39,40,41].

We have shown an excess of premature mortality from diabetes attributable to the COVID-19 pandemic in women, by eliminating the upward trend from 2015 to 2019 as have been detailed in methods section. Part of the reason for this finding may be that diabetes increases the risk of death from COVID-19 [21,38,40,41]. Higher levels of glucose in the blood reduce immunity and increase SARS-Cov-2 replication, and diabetes leads to greater oxidative stress, higher proinflammatory cytokine production, and more hyperglycemic episodes [42]. However, a recent study has shown that diabetes is not an independent predictor of hospital admission in people aged over 50 years who have COVID-19, and that hypertension plays a greater role [43]. There is also evidence to suggest that COVID-19 may cause new-onset diabetes [44,45], through more studies are needed to confirm this effect.

The provinces in Costa Rica with the greatest increases between 2019 and 2020 in premature mortality from diabetes were San José, Guanacaste, Cartago and Alajuela in men; and Alajuela and San José in women. Although there is information on population density by canton and district, in Costa Rica a threshold has not been established to differentiate between urban and rural areas according to their density, so it has not been possible to carry out an analysis with rural/urban disaggregation, because has the corresponding populations to be able to calculate the mortality rates in this disaggregation(45).We found no clear link between these patterns and indicators such as population density. A previous study found a higher concentration of people with diabetes in San José, the Costa Rican province with the largest population and the most class A hospitals. This fact might be related with higher premature mortality rates in the most populated areas [19].

Another factor that may have influenced diabetes mortality during the pandemic was the general prioritization of COVID-19 patients over people with chronic diseases. In 2020, the number of appointments for type 2 diabetes Mellitus decreased by 8% [46].

Our study has some limitations. Firstly, we analyzed mortality from diabetes as an underlying cause, and the changes in the process of certification or coding could have affected the data we analyzed, although this is a standardized scheme that has provided consistent results over the years. It is possible that mortality from diabetes is underestimated in death registers [47], but this factor should not affect the reported trends. Secondly, we did not have access to individualized data of the deceased (e.g. duration of illness, degree of control, physical characteristics and lifestyle), which we could have used to adjust models and explain the observed trends in greater detail. Thirdly, we assumed a linear increase in mortality from 2014 to estimate the mortality attributable to the COVID-19 pandemic in 2020, and this assumption will have to be confirmed with future data. One strength of this study is that our data were provided by the national statistics institute of Costa Rica, meaning we were able to analyze an exhaustive population sample for every year of the study period.

We can conclude that premature mortality from diabetes mellitus increased significantly between 2014 and 2020 in Costa Rica, possibly owing to several interacting causes such as poor diet, the alarming increase in overweight and obesity, decreased public spending, and poor control of the disease. The COVID-19 pandemic changed the pattern of mortality, increasing the number of premature deaths from diabetes in Costa Rica in 2020.

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References

1. Diabetes Atlas. International Diabetes Federation [accessed 2022 May 9] Available from: https://diabetesatlas.org
2. Diabetes Mellitus. World Health Organization accessed 10 Nov 2021]. Available at 2021 Nov 10: https://www.who.int/news-room/fact-sheets/detail/diabetes.
3. Vigilancia de los factores de riesgo cardiovascular, segunda encuesta 2014 Accessed 22 may 2022. Caja Costarricense del Seguro Social[Surveillance of cardiovascular risk factors, second survey 2014. Costa Rica Social Security Box .https://repositorio.binasss.sa.cr/repositorio/bitstream/handle/20.500.11764/628/encuesta2014.pdf?sequence=1&isAllowed=y
4. Vigilancia de los factores de riesgo cardiovascular, segunda encuesta 2018 Accessed 16 jun 2022. Caja Costarricense del Seguro Social [Surveillance of cardiovascular risk factors, second survey 2018. Costa Rica sSocial Security Box. https://www.binasss.sa.cr/informeservicios2019.pdf
5. Lin X, Xu Y, Pan X, et al. Global, regional, and national burden and trend of diabetes in 195 countries and territories: an analysis from 1990 to 2025. Sci Rep. 2020 Sep 8;10(1):14790. PMID: 32901098; PMCID: PMC7478957.
6. Mackenbach JP, Kulhánová I, Menvielle G, et al. Eurothine and EURO-GBD-SE consortiums. Trends in inequalities in premature mortality: a study of 3.2 million deaths in 13 European countries. J Epidemiol Community Health. 2015 Mar;69(3):207–217
7. Regidor E, Santos JM, Ortega P, et al. Decreasing income inequality and emergence of the association between income and premature mortality: Spain, 1970-2010. Health Place. 2014May; 27: 30–37Epub 2014 Feb 13. PMID: 24530650
8. Holland WW. European Community atlas of avoidable death. 2nd ed. Oxford: Oxford University Press; 1991.
9. Avoidable mortality: OECD/Eurostat lists of preventable and treatable causes of death, 2022 [accessed 2022 May 9]. Available at: https://www.oecd.org/health/health-systems/Avoidable-mortality-2019-Joint-OECD-Eurostat-List-preventable-treatable-causes-of-death.pdf
10. Jiménez-Montero JG, Villegas-Barakat M. Changes in DM mortality rate in Costa Rica 2007-2017. DM Res Clin Pract. 2021 Apr;174:108749
11. Estimaciones y proyecciones de población por sexo y edad 1950-2050. defunciones. instituto nacional de estadística y censos [population estimates and projections by sex and age 1950-2050. Deaths. National Institute of Statistics and Censuses] [accessed 2022 May 9]. Available at: https://www.inec.cr/poblacion/defunciones
12. Gómez-Martínez L, Orozco-Beltrán D, Quesada JA, et al. Trends in premature mortality due to heart failure by autonomous community in Spain: 1999 to 2013. Rev Esp Cardiol (Engl Ed). 2018 Jul;71(7):531–537.
13. Ahmad O, Boschi-Pinto C, Lopez A, et al. Age standardization of rates: a new who standard. GPE Discussion Paper Series: No. 31 EIP/GPE/EBD World Health Organization 2001 [accessed 2022 May 9] Available at: https://qmplus.qmul.ac.uk/pluginfile.php/154532/mod_book/chapter/3129/Age%20standardization%20of%20rates.pdf
14. Indicadores de salud. Aspectos conceptuales y operativos Organización Panamericana de la Salud [Health indicators. Conceptual and operational aspects Pan American Health Organization] [accessed 2022 May 9]. Available at: https://www3.paho.org/hq/index.php?option=com_content&view=article&id=14405:health-indicators-conceptual-and-operational-considerations&Itemid=0&lang=es
15. IBM Corp. IBM SPSS Statistics for Windows [Internet]. Armonk NY: IBM Corp; 2017 Accessed 10 jun 2022. Available from: https://hadoop.apache.org.

16. R Core Team. R: a Language and Environment for Statistical Computing [Internet]. Vienna Austria; 2016 Accesed 14 feb 2022. Available from: https://www.R-project.org
17. Kim HJ, Fay MP, Feuer EJ, et al. Permutation tests for joinpoint regression with applications to cancer rates. Stat Med. 2000Feb15;19 (3):335–351. Erratum in: Stat Med 2001 Feb 28;20(4):655. PMID: 10649300.
18. Joinpoint Regression Program, Version 4.9.1.0. Statistical Methodology and Applications Branch. United States: Surveillance Research Program National Cancer Institute; 2022.
19. Cubero-Alpízar C, P R-VL. Comportamiento de la diabetes mellitus en Costa Rica[Behavior of diabetes mellitus in Costa Rica] Horizonte Sanitario . Horizonte Sanitario. 2017;16(3). 10.19136/hs.a16n3.1871.
20. Informe de resultados de la Evaluacion de la prestación de Servicios de Salud 2019 Accessed 4 apr 2022. Monitoreo 2020. Caja Costarricense de Seguro Social. Direccion de Servicios de Salud San Jose. https://www.binasss.sa.cr/informeservicios2019.pdf
21. Schiller M, Solger K, Leipold S, et al. DM-associated nephropathy and obesity influence COVID-19 outcome in type 2 DM patients. J Community Hosp Intern Med Perspect. 2021 Sep 20;11 (5):590–596. PMID: 34567446; PMCID: PMC8462845.
22. Gómez Salas G, Quesada Quesada D, Monge Rojas R Perfil antropométrico y prevalencia de sobrepeso y obesidad en la población Urbana de Costa Rica entre los 20 y 65 años agrupados por sexo: resultados del Estudio Latino Americano de Nutrición y Salud [Anthropometric profile and prevalence of overweight and obesity in the urban population of Costa Rica between 20 and 65 years of age, grouped by sex: results of the Latin American Study of Nutrition and Health]. Nutr Hosp. [Internet]. 2020 Jun cited 2022 Apr 16;37(3): 534–542. Available at: http://scielo.isciii.es/scielo.php?script=sci_arttext&pid=S0212-16112020000400017&lng=es. Epub -2020 Nov 30
23. Pabón CA, Hubley E, Spurrell G, et al. Obesidad: análisis de la prevalencia de obesidad y sobrepeso en una población de adultos con bajos ingresos en Costa Rica [Obesity: analysis of the prevalence of obesity and overweight in a population of low-income adults in Costa Rica. Science and Health Magazine Integrating Knowledge. 2021;5(2):46–62.
24. World Obesity Atlas 2022, World Obesity Federation (London) [accessed 2022 May 9] Available at: https://www.worldobesity.org/resources/resource-library/world-obesity-atlas-2022
25. Perales-Torres AL, Castillo-Ruíz O, Castañeda Licón MT, et al. La DM y la alimentación determinantes en la progresión de aterosclerosis [DM and type of diet as determinant factor in the progression of atherosclerosis]. Arch Cardiol Mex. 2016 Oct-Dec;864:326–334.
26. Lopez Stewart G, Tambascia M, Rosas Guzmán J, et al. Control of type 2 diabetes mellitus among general practitioners in private practice in nine countries of Latin America. Rev Panam Salud Pública. 2007Jul;22(1):12–20. PMID: 17931483.
27. Brenes-Camacho G, Rosero-Bixby L. Metabolic control in a nationally representative diabetic elderly sample in Costa Rica: patients at community health centers vs. patients at other health care settings. BMC Int Health Hum Rights. 2008 May 14;8:5. PMID: 18447930; PMCID: PMC2396151.
28. Chen-Ku CH, Gonzalez-Galvez G, Vásquez M, et al. Vascular complications in patients with type 2 DM: prevalence and comorbidities in 6 countries of Latin America. (A cohort of the discover study program). Endocr Pract. 2019Oct;2510:994–1002.Epub 2019 Jun 6. PMID: 31170372
29. Carrillo-Larco RM, Barengo NC, Albitres-Flores L, et al. The risk of mortality among people with type 2 DM in Latin America: a systematic review and meta-analysis of population-based cohort studies. DM Metab Res Rev. 2019 May;35(4):e3139
30. Garber AJ, Handelsman Y, Grunberger G, et al. Consensus statement by the American association of clinical endocrinologist and American College of Endocrinology on the comprehensive type 2 diabetes management algorithm- 2020 executive summary. Endocr Pract. 2020Jan;261:107–139.PMID: 32022600
31. American Diabetes Association. Pharmacologic Approaches to Glycemic Treatment: standards of Medical Care in Diabetes-2020. Diabetes Care. 2020;43(1):S98–S110.
32. See S, Care DS, S S. Pharmacologic approaches to glycemic treatment: standards of medical care in diabetes–2020. Diabetes Care. (2020). 9;43(June):S98–S110.
33. Morales-Olvera D, Obregón-Aguilar A, Pérez-Mendoza MT, et al. iSGLT2 y su potencial efecto nefroprotector en pacientes con diabetes mellitus 2 [iSGLT2 and its potential nephroprotective effect in patients with diabetes mellitus 2]. Med Interna Méx. 2022;33(4):503–510.
34. Chen-Ku CH, Grimaldo de sucre P, Vinocour M, et al. diabetes second-line medication prescription patterns in costa rica and panama: evidence from the discover registry. Cureus. 2021 Jun 30;13(6):e16060. PMID: 34354876; PMCID: PMC8328805.
35. Arellano-Moya DA, Quirós Torres M. Novedades farmacológicas disponibles en Costa Rica para el manejo terapéutico de la DM Mellitus tipo 2 [Pharmacological novelties available in Costa Rica for the therapeutic management of DM Mellitus type 2. Acta Académica, 67 (November), 107–144
36. Global Health Expenditure Database 2020. World Health Organization [accessed 2021 Nov 10. Available at: https://apps.who.int/nha/database
37. Death rate, crude (per 1,000 people) - Costa Rica World Bank Development Indicators. [accessed 2022 May 5]. Available at: https://data.worldbank.org/indicator/SP.DYN.CDRT.IN?locations=CR
38. Wu ZH, Tang Y, Cheng Q. Diabetes increases the mortality of patients with COVID-19: a meta-analysis. Acta Diabetol. 2021Feb;58(2):139–144. Epub 2020 Jun 24. PMID: 32583078; PMCID: PMC7311595.
39. Schiller M, Solger K, Leipold S, et al. DM-associated nephropathy and obesity influence COVID-19 outcome in type 2 DM patients. J Community Hosp Intern Med Perspect. 2021 Sep 20;11 (5):590–596. PMID: 34567446; PMCID: PMC8462845.
40. Calixto-Calderón B, Vázquez-González MF, Martínez-Peláez R, et al. Pre-existing comorbidity, the highest risk factor for poor prognosis of COVID-19 among the Mexican population. Nova scientia. 2022;13(1).
41. Tamura RE, Said SM, de Freitas Lm, et al. Outcome and death risk of diabetes patients with Covid-19 receiving pre-hospital and in-hospital metformin therapies. Diabetol Metab Syndr. 2021 Jul 13;13(1):76. PMID: 34256824; PMCID: PMC8275913.
42. Sen S, Chakraborty R, Kalita P, et al. DM mellitus and COVID-19: understanding the association in light of current evidence. World J Clin Cases. 2021;9(28):8327–8339.
43. Orozco-Beltrán D, Merino-Torres JF, Pérez A, et al. Does Not Increase the Risk of Hospitalization Due to COVID-19 in Patients Aged 50 Years or Older in Primary Care—APHOSDIAB—COVID-19 Multicenter Study. J Clin Med. 2022;11(8):2092.
44. Shrestha DB, Budhathoki P, Raut S, et al. Diabetes de nueva aparición en COVID-19 y resultados clínicos: una revisión sistemática y metanálisis. Mundo J Virol. 2021;10(5): 275–287
45. Samper M, González H, "Caracterización de los espacios rurales en Costa Rica y propuestas de alternativas metodológicas para su medición"["Characterization of rural spaces in Costa Rica and proposals for methodological alternatives for their measurement"Documentos de Proyectos (LC/TS.2020/131; LC/MEX/TS.2020/33), Ciudad de México, Comisión Económica para América Latina y el Caribe (CEPAL), 2020.
46. Barrantes-Arroyo A, Cortés-Ruiz A, Molina-Granados JM, et al. Afectación de los servicios de atención primaria en salud por la pandemia de COVID-19 en Costa Rica: el recuento de las interrupciones. Gestión En Salud Y Seguridad Social [Affectation of primary health care services by the COVID-19 pandemic in Costa Rica: the count of interruptions. Management in Health and Social Security,1 (2), 14–24.
47. Laclé-Murray A. Causes of death in a diabetic population of costa rica and the quality of their death certificates. Acta méd costarric 2022 Apr 17; 54(1): 23–30.