To the Editor:

Pancreatic cancer is the seventh leading cause of cancer death worldwide.1 As the 5-year survival rate sets around 8.5%, mortality from pancreatic cancer mostly overlaps its incidence which has been increasing over the past decades.2–7 In the United States, incidence increased around 0.95% a year, since 1994.4 In Europe, it is one of the few tumor types with a consistent rise in mortality.8 Common risk factors, such as obesity, smoking habits, and dietary patterns may be driving this trend, given that higher human development indexes appear to associate with pancreatic cancer mortality.4,7

We conducted an epidemiological analysis on pancreatic cancer mortality trends in Portugal over the past 25 years. Using the Portuguese National Statistical Institute public database, we identified deaths attributed to malignant pancreatic cancer (ICD10-C25; ICD98–157) on official death certificates issued between 1991 and 2015. Demographic variables analyzed included sex, age at time of death, and geographic area of residency. Age-adjusted mortality rates (AAMR) were calculated adjusting for age distribution according to the 2013 revised European standard population. Mortality trends were calculated using the Jointpoint Regression software 4.4.0.0 (Statistical Research and Applications Branch, National Cancer Institute, Bethesda, Md) tracing annual percent changes (APC) and average APCs (AAPC) from a logistic regression model. A mortality forecast was done through a univariate Autoregressive Integrated Moving Average (ARIMA) model using IBM SPSS Statistics v24 (IBM Corp, Armonk, NY).

Our findings show that pancreatic cancer-associated deaths doubled from 701 deaths in 1991 to 1415 in 2015, reflecting a mean annual increase of around 3% (APC, 2.85; 95% confidence interval [CI], 2.64–3.06; P < 0.001). The AAMR also increased throughout this period (AAPC, 0.91%; 95% CI, 0.57–1.26; P < 0.001) reaching a maximum of 12.79 per 100,000 habitants by 2015. Remarkably, the rate of increase was three times higher in the last half (AAPC2004–2015, 1.56%; 95% CI, 1.03–2.14; P < 0.001) as compared with the first half (AAPC1991–2004, 0.37%; 95% CI, −0.14 to 0.87; P = 0.145).

Age analysis confirmed a negligible mortality (0.8% of deaths) below the age of 40 years. The 75 to 79 years age group recorded the highest mean AAMR, and although it increased across all age groups above 45 years, the most noteworthy rise, nearly twice that of the remaining age groups, was registered within the 50 to 54 years age group (APC, 1.61; 95% CI, 0.65–2.59; P = 0.002).

As expected, AAMR was higher in males (mean [standard deviation (SD)], 14.12 [1.24] vs 8.88 [0.74]; P < 0.001) who showed a peak mortality at the 70 to 74 years age group (AAMR, 2.47 [SD, 0.34]) and a nonlinear increase (AAPC, 0.88; 95% CI, 0.36–1.39; P = 0.001) with an APC of around 2% a year since 2004 (AAPC2004–2015, 2.02; 95% CI, 1.22–2.83; P < 0.001). In contrast, female mortality was higher within the ≥85 age group (AAMR = 1.75 [SD, 0.25]) and AAMR increased linearly (AAPC, 0.90; 95% CI, 0.59–1.21; P < 0.001).

There were also some interesting geographical asymmetries in pancreatic cancer...
mortality. The Azores Islands (AAMR, 26.27 [SD, 4.86]) and Alentejo (AAMR, 19.29 [SD, 4.48]) displayed the highest AAMRs. Alongside Madeira Island, these regions also have the highest mortality increase over the study period, ranging from 2.52% a year for Alentejo (AAPC, 2.52; 95% CI, 1.89–3.16; P < 0.001) to 1.53% for Azores (AAPC, 1.53; 95% CI, 0.59–2.48, P = 0.003). All the remaining regions showed an AAPC below 1%. Finally, including the data from 1991 until 2017, we forecasted the annual number of deaths for the next 20 years. By 2035 annual deaths from pancreatic cancer should surpass 2000 (n = 2137; 95% CI, 1862–2413), reflecting a 51% increase (Fig. 1).

Summing up, from 1991 to 2015, annual deaths from pancreatic cancer doubled, crude mortality rates increased by 67.5% (AAPC, 2.7%), and AAMRs grew an impressive 22.8% (AAPC, 0.91%). These findings match the ones reported for other regions, suggesting that we may be facing a change toward a younger age of incidence. Another meaningful finding was a higher rate of AAMR increase among the 50 to 54 years age group. This is roughly 15 years below the age of peak incidence, suggesting that we may be facing a change toward a younger age of incidence. Lastly, if our prediction is correct, we will face a 51% increase in annual deaths during the next 2 decades. As each death by pancreatic cancer results in a mean loss of 11 years of healthy life expectancy, it appears undeniable that we need to raise a special awareness concerning pancreatic cancer in the near future.

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Pedro Marques da Costa, MD, MSci
Rui Tato Marinho, MD, PhD
Helena Cortez-Pinto, MD, PhD
Serviço de Gastroenterologia e Hepatologia Centro Hospitalar Universitário Lisboa Norte Lisbon, Portugal Faculdade de Medicina Universidade de Lisboa Lisbon, Portugal pedroavmcosta@gmail.com

Luís Costa, MD, PhD
Serviço de Oncologia Médica Centro Hospitalar Universitário Lisboa Norte Lisbon, Portugal Faculdade de Medicina Universidade de Lisboa Lisbon, Portugal

José Velosa, MD, PhD
Serviço de Gastroenterologia e Hepatologia Centro Hospitalar Universitário Lisboa Norte Lisbon, Portugal Faculdade de Medicina Universidade de Lisboa Lisbon, Portugal

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