Twenty-Five Years of Increasing Mortality From Pancreatic Cancer in Portugal

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; ICD9/8–157) 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 ($APC_{2004–2015}$, 1.56%; 95% CI, 1.03–2.14; $P < 0.001$) as compared with the first half ($APC_{1991–2004}$, 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 ($APC_{2004–2015}$, 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

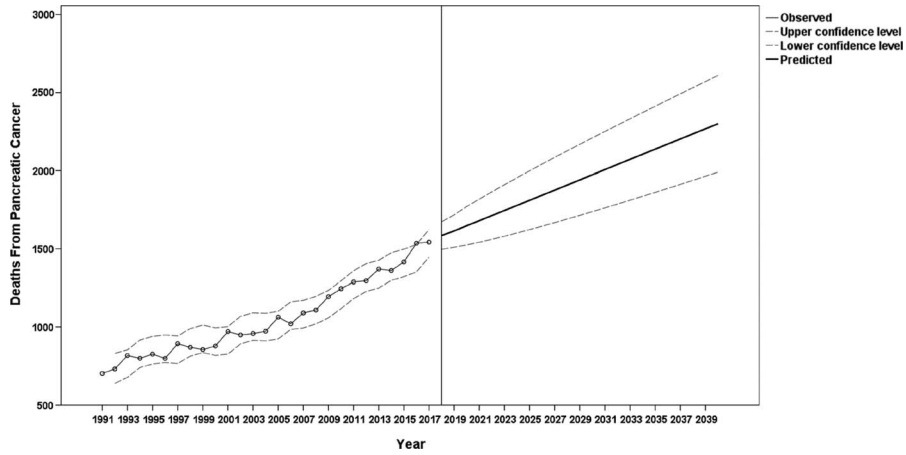

FIGURE 1. Prediction of the pancreatic cancer-associated mortality for the Portuguese population. Fitted by an ARIMA (4, 1, 0) model.

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 developed countries.[3,7] The most plausible explanation appears to be the increasing prevalence of associated risk factors.[4,6] Indeed, Alentejo and Azores show the highest prevalence of active smokers and overweight individuals in all country.[9] This might explain why, despite accounting for only 9.4% of the Portuguese population, these regions recorded both a mean AAMR and a growth rate that was nearly twice the rest of the population.

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,[10] it appears undeniable that we need to raise a special awareness concerning pancreatic cancer in the near future.

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REFERENCES

1. Ferlay JSI, Ervik M, Dikshit R, et al. *GLOBOCAN 2012 v1.0, Cancer Incidence and Mortality Worldwide: IARC CancerBase No. 11*. Lyon, France: International Agency for Research on Cancer; 2013. Available at: http://globocan.iarc.fr. Accessed: March 8, 2018.
2. Sun H, Ma H, Hong G, et al. Survival improvement in patients with pancreatic cancer by decade: a period analysis of the SEER database, 1981-2010. *Sci Rep*. 2014; 4:6747.
3. Are C, Chowdhury S, Ahmad H, et al. Predictive global trends in the incidence and mortality of pancreatic cancer based on geographic location, socio-economic status, and demographic shift. *J Surg Oncol*. 2016;114: 736–742.
4. Gordon-Dseagu VL, Devesa SS, Goggins M, et al. Pancreatic cancer incidence trends: evidence from the surveillance, epidemiology and end results (SEER) population-based data. *Int J Epidemiol*. 2018;47:427–439.
5. Ferlay J, Steliarova-Foucher E, Lortet-Tieulent J, et al. Cancer incidence and mortality patterns in Europe: estimates for 40 countries in 2012. *Eur J Cancer*. 2013;49: 1374–1403.
6. Jia X, Du P, Wu K, et al. Pancreatic cancer mortality in China: characteristics and prediction. *Pancreas*. 2018;47:233–237.
7. Wong MCS, Jiang JY, Liang M, et al. Global temporal patterns of pancreatic cancer and association with socioeconomic development. *Sci Rep*. 2017;7:3165.
8. Malvezzi M, Bertuccio P, Levi F, et al. European cancer mortality predictions for the year 2014. *Ann Oncol*. 2014;25:1650–1656.
9. Inquérito Nacional de Saúde, 2014. 2016. Available at: https://www.ine.pt/xportal/xmain?xpid=INE&xpgid=ine_publicacoes&PUBLICACOESpub_boui=263714091&PUBLICACOESmodo=2&xlang=pt. Accessed March 8, 2018.
10. Carrato A, Falcone A, Ducreux M, et al. A systematic review of the burden of pancreatic cancer in Europe: real-world impact on survival, quality of life and costs. *J Gastrointest Cancer*. 2015;46:201–211.