CANCER MORTALITY PREDICTIONS FOR 2017 IN LATIN AMERICA

Carioli Greta[1], La Vecchia Carlo[1], Bertuccio Paola[1], Rodriguez Teresa[2], Levi Fabio[3], Boffetta Paolo[4], Negri Eva[5], Malvezzi Matteo[1]

1. *Department of Clinical Sciences and Community Health, Universitá degli Studi di Milano, Milan, Italy.*
2. *Navarra Health Service, Pamplona, Navarra, Spain.*
3. *Institute of Social and Preventive Medicine (IUMSP), Lausanne University Hospital, Lausanne, Switzerland.*
4. *Tisch Cancer Institute, Icahn School of Medicine at Mount Sinai, New York, USA.*
5. *Department of Biomedical and Clinical Sciences, Universitá degli Studi di Milano, Milan, Italy.*

Introduction

Since death certification figures are only available with a few years lag, cancer mortality predictions for the current or future years are essential to evaluate cancer prevention and management strategies, and to plan public health resource allocation, albeit with some inherent prediction uncertainty [***1***].
Over several years, for the USA [***2***] and for the European Union (EU) [***3***] predictions for cancer mortality have been published and resulted reasonably valid [***2, 4***].
We predicted the number of deaths and mortality rates for all cancers and selected major cancer sites for 2017 in seven selected Latin American countries [***5***]. Moreover, in order to select the most appropriate prediction method for these data, we compared the method used in previous publications with others, including a "hybrid" regression (a mixture of linear, log-linear, power five, and square root regression).

Materials and Methods

We retrieved official death certification data from the WHO database (WHOSIS) [***6***] for cancer of the stomach, colorectum, pancreas, lung, breast, uterus (cervix and corpus), prostate, leukaemias and total neoplasms (malignant and benign). We obtained data for the seven Latin American countries with over 85% death certification coverage and over 10 million inhabitants (Argentina, Brazil, Chile, Colombia, Cuba, Mexico, and Venezuela) [***7***], for the 1980-2014 calendar period (for Venezuela and Colombia up to 2013). We obtained resident population estimates, based on official censuses from the Pan American Health Organization (PAHO) database [***8***].
Using the matrices of certified deaths and resident population, we calculated age-specific death rates for each 5-year age-group (from 0-4 to 80+ years), sex and calendar year. We computed age-standardized rates per 100,000 person-years at all ages, with the direct method based on the world standard population. For lung cancer, we also calculated rates for the 25-44, 45-64, 65-74 and over 75 years age groups.
We based mortality data projections on an age-period joinpoint model [***9***]. A Poisson count data joinpoint regression model, allowing for up to five joinpoints, is fit to the logarithm of the number of age-specific certified deaths for each 5-year age-group to identify the most recent trend segments. We applied a linear regression model to the mortality data for each age-group over the period identified by the last segment of the joinpoint model in order to estimate the regression coefficients. We used this model to calculate the number of expected age-specific deaths for 2017 and the corresponding 95% prediction intervals (PIs). These are calculated with a standard error that takes the variability of the new observation into account [***4, 10, 11***]. Predicted age-standardized mortality rates, with corresponding 95% PIs, are calculated using the number of expected age-specific deaths and the projected population data for the period of interest from the PAHO database.
Before applying the linear regression method, we compared projections resulting from two other regression methods: log-linear and a "hybrid" regression. The latter blends the linear and log-linear regression models

along with power five and square root regressions. With the hybrid regression, the number of expected age-specific deaths for each of the previous models is calculated; we implemented an algorithm that chooses the linear transformation to be used considering the R-squared statistic values for each age-group, sex and cancer site. Thus, the resulting total number of deaths and age-standardized rate were calculated from different underlying linear transformations. In order to evaluate the results of these different methods, we used observed EU data from 1980 to 2001 as a training dataset, to which we applied the projection methods in order to predict data for the 2002-2011 period. We used observed data from 2002 to 2011 as a validating dataset. To measure the accuracy of the predicted figures and to compare the performance of the different projection methods we computed the average absolute relative deviation (AARD), i.e. the ratio between the prediction error and the observed rate. In general a prediction is considered reliable when the AARD value is less than 5% [***12***].
Moreover, for the seven selected Latin American countries, we estimated the numbers of avoided cancer deaths over the 1990-2017 period by comparing observed and expected deaths on the basis of 1990 age-specific rates.

Results
Overall, the AARDs from the three projection methods analyzed were quite similar, greater differences were only observed in few cases. For example, for stomach cancer, in men the AARD was 0.006 for the hybrid model, while for the linear and for the log-linear, it was respectively 0.032 and 0.014. Below the more noteworthy results: for stomach cancer, the predicted trend from the hybrid regression overlapped the observed rates perfectly. In the hybrid model, the log-linear projections seemed to be predominant. The log-linear figure in men was similar to the hybrid one, but the predicted trend overlapped the observed rates less precisely. Instead, the predictions produced by the linear regression model were less accurate. In women, the predicted trend of the hybrid model (AARD of 0.018) was similar to the linear one (AARD of 0.029), the worse projections were those of the log-linear model with wide confidence interval (AARD of 0.051). The prediction intervals tended to contain the true rates (except for the linear model in males, for which the PI was at the limit). In the case of colorectal tumour, the best predictive method in men was the log-linear model (AARD of 0.007), the predicted trend followed the observed rates closely. Similarly, the hybrid method worked well (AARD of 0.008). The linear model was less accurate (AARD of 0.02). In women the log-linear model had an AARD of 0.036; the hybrid method (AARD of 0.042) seemed influenced by the linear regression (AARD of 0.057), the worse method. Further, in women, the prediction intervals did not include the observed rates. For lung cancer, the more performing model was not the same between the sexes. In men the hybrid method provided an accurate predicted trend (AARD of 0.003), which overlapped the mortality rates perfectly and the prediction interval was narrow. However, the other two methods worked well, too (AARD of 0.015 for linear regression and of 0.007 for log-linear model). In women the best method was the log-linear (AARD of 0.009); but the prediction interval was wider than the other two methods' PIs. The hybrid method (AARD of 0.04) appeared influenced from the linear trend (AARD of 0.052), the worse one. Due to the lack of any real significant differences, we chose to continue using the linear method similarly to previous studies.
In all selected Latin American countries, total cancer mortality is predicted to decline. In men, the highest predicted rate is 132.3/100,000 for Cuba, with a percent difference of -5.4% since 2012. Argentina and Chile follow Cuba with a predicted rate of 119.8 (7% fall) and 111.2/100,000 men (6% fall), respectively. The lowest predicted total cancer rate is 64.7/100,000 men for Mexico with the largest fall in rates (-9.5%). In women, Cuba has the highest predicted rate 93.3/100,000 (-3.2%); Mexico has the lowest one, 60.6/100.000, with a decline of 8%. The greatest falls are predicted for Chile and Colombia. Women in Argentina show predicted rates for 2017 around 89/100,000, similar to those of 2012. Although favourable trends in rates, the number of deaths is predicted to increase in all countries and both sexes.

Total cancer mortality trends in men started to decline between 1990 and 2000, except for Cuba and Brazil. Overall, in women trends declined over the whole period considered, except for Cuba and Brazil, which showed unfavourable trends until the early-mid 2000's.
Regarding specific cancer sites (***Figure 1***), stomach cancer mortality has long been declining in both sexes; in contrast, colorectal cancer has been rising in most countries, with a tendency to level off over recent years. Pancreatic cancer rates are inconsistent. For most countries in men, lung cancer trends were moderately downwards in recent calendar periods. In women, lung cancer trends have been rising, except in Mexico. Breast cancer mortality was relatively low in most countries, except Argentina, and tended to decline over recent years. Conversely, cancer of the uterus mortality rates remain high in all Latin America, despite long term falls, particularly in Venezuela and Cuba, whose predicted rates remain around 10/100,000. Prostate cancer rates were particularly high in Cuba and Venezuela, but tended to decline moderately over the most recent years. Leukaemia mortality shows some falls over recent years.
Considering standardized mortality rates for lung cancer stratified by the age groups 25-44, 45-64, 65-74 and 75+ years, the patterns for men are favourable at all age groups and in all countries, generally larger in the young. Lung cancer rates are predicted to fall in women as well, albeit less than in men.
We estimated the number of avoided cancer deaths in men and women between 1990 and 2017, assuming the age-specific peak mortality rate in 1990 as constant. Over the 27-year period considered, a substantial amount of cancer deaths were avoided in Argentina (132,000 deaths, 88,000 in men and 44,000 in women), Chile (63,000 deaths, 16,000 in men and 47,000 in women), Colombia (83,000 deaths, 31,000 in men and 52,000 in women), Mexico (118,000 deaths, 39,000 in men and 79,000 in women) and Venezuela only for women (26,000 deaths). No appreciable reduction in cancer deaths was observed in Brazil, Cuba and Venezuelan men.

Conclusions

Regards the comparison of prediction methods, we found no measurable difference between the models under study. Most of AARDs were below the 5% threshold, thus the predictive trends for all the methods were quite satisfactory with negligible differences. However, the hybrid model projections, for any combination of cancer site and sex, were never the worst. Rather, it appeared as a compromise of the linear transformations considered, and in particular, it seemed sometimes greatly influenced by the linear or the log-linear method. Thus, when there are no strong cases for one model or another, using the hybrid model could be a good option, even if not the best. Since this hybrid method is still being refined and the results were only marginally different, we continued to use the linear regression for projection estimates also for comparability reasons.
Though there was appreciable variability across the seven Latin American countries considered, rates for all cancers and for most major cancer sites are predicted to decline to 2017.
Total cancer mortality rates in Argentina, Cuba and Chile were similar to those registered in Europe, North America and (for men) in Japan [***13***], but they were appreciably lower for both sexes in other Latin American countries considered. This reflects the historical low lung cancer (and probably other tobacco related cancers like pancreatic one) rates in these countries, due to less frequent cigarette use [***14***]. Stomach cancer predicted rates remain high in Latin America (particularly in Chile) [***13***]. This likely reflects the high prevalence of *Helicobacter Pylori* (HP) infection [***15***]. Colorectal cancer rates are much lower than in other areas of the world [***13***]; this is probably due to favourable aspects of local diet and physical activity [***16***], despite a high prevalence of overweight and obesity [***17***]. Breast cancer predicted rates decline, reflecting, as well as for the favourable predictions in prostate cancer and leukaemia rates, improved management and diagnosis [***4, 18, 19***]. Conversely, the rates for cancer of the uterus (cervix) are high, pointing the importance of prevention for this neoplasms [***20***].

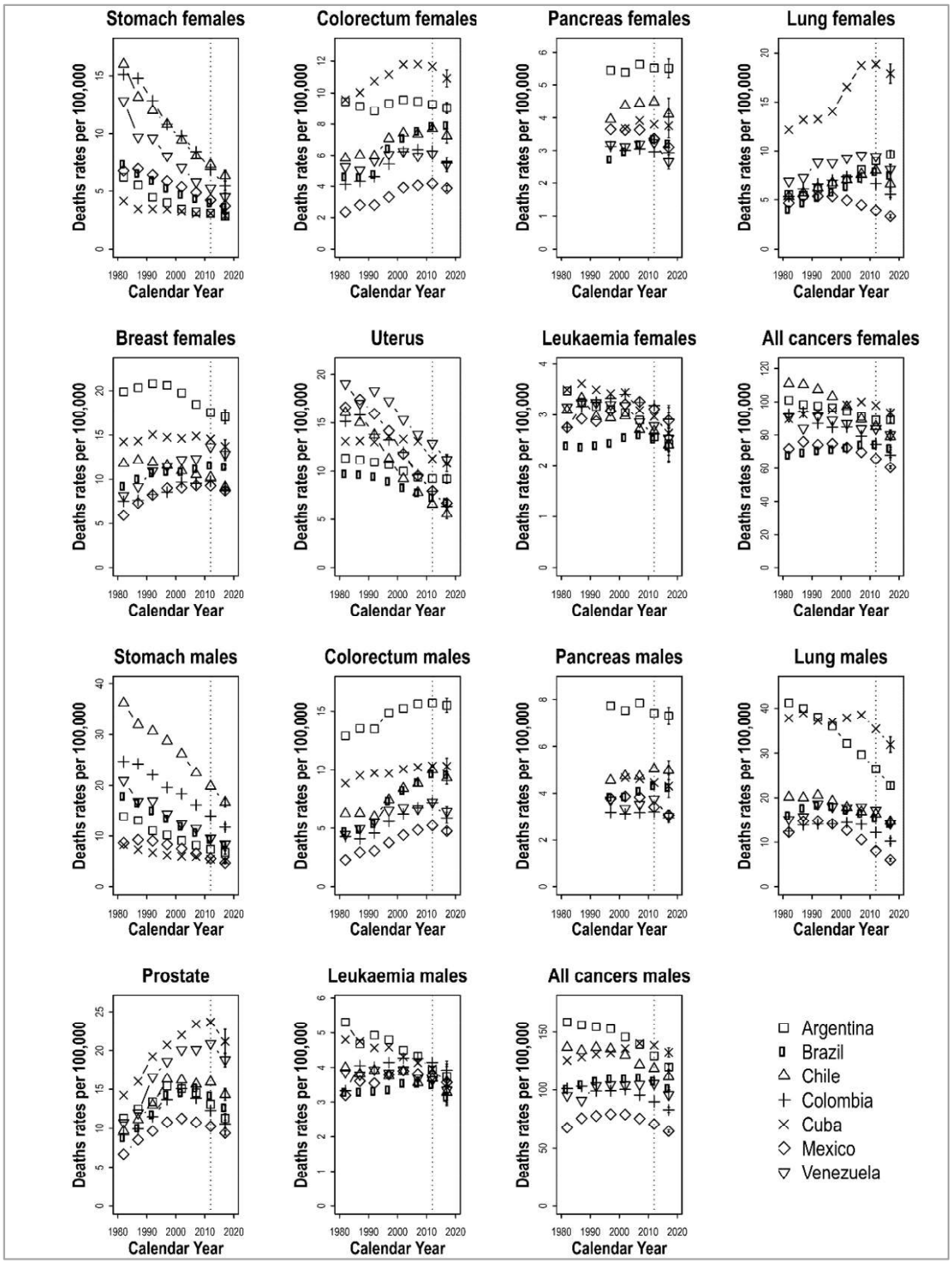

Figure 1. Age-standardized (world population) cancer mortality rate trends for men and women in quinquennia from 1980-84 to 2010-14 and predicted rates for 2017 with 95% PIs for stomach, colorectum, pancreas, lung, breast, uterus, prostate, leukaemias, and all cancers in the 7 selected Latin American countries.

The total number of avoided deaths in the selected Latin American countries was over 420,000, except Brazil, Cuba and Venezuelan men. This suggests the urgency of improving cancer prevention and management in these countries.
The number of avoided deaths may be underestimate, assuming that cancer deaths certification accuracy has improved over the last three decades. However, we considered only major cancer sites that are relatively easy to diagnose (except pancreas) and hence certify, and we included only countries with acceptable indicators of deaths certification validity in the WHO database.
An inherent limitation of predictions is their inability to model sudden changes or fluctuation in slope. Hence, caution in interpretation should be used and prediction estimates should be considered only as general indications for epidemiology and health planning.
These limitations taken into account, we predicted declines, though modest, in cancer mortality to 2017 in Latin America, with the exception of Cuba.

References

[**1**] Qiu Z, Hatcher J, Wang M. Review ancer projection methods for canadian partnership against cancer analytic network. Alberta Health Services for the Canadian Partnership Against Cancer.
[**2**] Siegel RL, Miller KD, Jemal A. Cancer Statistics 2017. CA Cancer J Clin 2017;67:7-30.
[**3**] Malvezzi M, Carioli G, Bertuccio P, et al. European cancer mortality predictions for the year 2017, with focus on lung cancer. Ann Oncol 2017;28:1117-23.
[**4**] Malvezzi M, Carioli G, Bertuccio P, et al. European cancer mortality predictions for the year 2016 with focus on leukaemias. Ann Oncol 2016; 27: 725-731 doi 710.1093/annonc/mdw1022.
[**5**] Carioli G, La Vecchia C, Bertuccio P, et al. Cancer mortality predictions for 2017 in Latin America [In press]. Ann Oncol 2017; doi: 10.1093/annonc/mdx1301.
[**6**] World Health Organization Statistical Information System. WHO mortality database Available from: http://www.who.int/healthinfo/statistics/mortality_rawdata/en/index.html (Last accessed October 2016).
[**7**] Mathers CD, Fat DM, Inoue M, et al. Counting the dead and what they died from: an assessment of the global status of cause of death data. Bull World Health Organ 2005;3:171-77.
[**8**] Pan American Health Organization (PAHO). Health Information Platform for the Americas. Available from: http://www.paho.org/data/index.php/en/indicators/demographics-core/308-poblacion-nac-en.html (Last accessed February 2017).
[**9**] Kim HJ, Fay MP, Feuer EJ, et al. Permutation tests for joinpoint regression with applications to cancer rates. (Erratum in: Stat Med 2001;20: 655). Stat Med 2000;19:335-51.
[**10**]. Faraway JJ. Linear Models with R. Texts in statistical science. vol. 63. Boca Raton:Chapman & Hall/CRC. 2005.
[**11**] Verzani J. Using R for Introductory Statistics. Chapman & Hall,2005.
[**12**] Lee TC, Dean CB, Semenciw R. Short-term cancer mortality projections: a comparative study of prediction methods. Stat Med 2011;30:3387-402.
[**13**] Hashim D, Boffetta P, La Vecchia C, et al. The global decrease in cancer mortality: trends and disparities. Ann Oncol 2016;27:926-33.
[**14**] Shafey O, Dolwick S, Guindon G. Tobacco control country profiles 2003. Atlanta, Georgia: American Cancer Society, World Health Organization, International Union Against Cancer, 2003.
[**15**] Peleteiro B, La Vecchia C, Lunet N. The role of Helicobacter pylori infection in the web of gastric cancer causation. Eur J Cancer Prev 2012;21:118-25.
[**16**] Ortiz-Hernandez L, Ramos-Ibanez N. Sociodemographic factors associated with physical activity in Mexican adults. Public Health Nutr 2010;13:1131-38.

[**17**] Garmendia ML, Ruiz P, Uauy R. [Obesity and cancer in Chile: estimation of population attributable fractions]. Rev Med Chil 2013;141:987-94.
[**18**] Amadou A, Torres-Mejia G, Hainaut P, et al. Breast cancer in Latin America: global burden, patterns, and risk factors. Salud Publica Mex 2014 56:547-54.
[**19**] Cuzick J, Thorat MA, Andriole G et al. Prevention and early detection of prostate cancer. Lancet Oncol 2014;15:484-92.
[**20**] Luciani S, Cabanes A, Prieto-Lara E, et al. Cervical and female breast cancers in the Americas: current situation and opportunities for action. Bull World Health Organ 2013;91:640-49.