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https://doi.org/10.21149/9932

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Abstract
Objective. To show lung cancer (LC) mortality and disability-adjusted life years (DALYs) in Mexico. Materials and methods. With the visualization tools at the Global Burden of Disease Study website, we analyzed LC mortality and disability-adjusted life years (DALYs) by state, sex, socio-demographic index (SDI), age, and risk factors between 1990 and 2016. Results. Mortality rate decreased from 13.9 to 9.1 per 100 000 between 1990 and 2016. This reduction is greater among men. However, deaths by LC rose from 5 478 to 8 470. DALYs rate also decreased. Northern states with higher SDI face a larger burden from LC but exhibited greater reductions compared with southern, less developed states. The burden of LC is concentrated among older population. Smoking is the main risk factor for LC. Conclusions. The burden by LC has decreased but is differential between states. LC threatens financially both the health system and individuals, since an important fraction of the population is not protected.

Keywords: global burden of disease; lung cancer; DALYs; Mexico

Received on: July 24, 2018 • Accepted on: October 31, 2018
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Cancer is one of the most important challenges in public health worldwide, particularly among developing countries like Mexico. Its economic and social welfare effects could be devastating for health systems. According to the World Health Organization (WHO), 71% of all deaths were caused by non-communicable diseases in 2016, and cancer is the second leading cause, with 22% of all deaths.1 Consistently with the Global Burden of Disease Study (GBD),2 cancer is a major cause of morbidity in the world, having caused 213.2 million DALYs globally in 2016. The latest Global Cancer Report (2012) establishes that there were 14.1 million new cases of cancer worldwide and 8.2 million estimated deaths.3 Of these, 19.4% are caused by lung cancer (LC). Among men, LC contributed 23.6% of all cancer-related deaths, while LC accounted for 13.8% of deaths caused by any type of cancer among women. LC has several well-known risk factors, such as tobacco smoking,4 exposure to second-hand smoke, radon and asbestos, air pollution, and others, such as arsenic in drinking water, radiation therapy to the lungs, and genetic factors.

In Latin America, Argentina shows a standardized incidence rate of LC of 20.9 new cases per 100 000 inhabitants; Chile, 13.3; Colombia, 11; Brazil, 16.3, and Peru, 10.1.5 In Mexico, the standardized incidence rate of LC is estimated at 7.5 new cases per 100 000 inhabitants, according to the International Agency for Research on Cancer.5 LC is the fifth cancer with the highest incidence rate, after breast (35.4), prostate (27.3), cervix uteri (23.3), and colorectal cancer (7.8).5 In spite of the relative importance of LC in terms of incidence, previous literature has shown that the mortality rate from LC has decreased in the last two decades, particularly among men.6-9 Although a reduction in mortality has been documented previously, it is important to note other health metrics related to the burden imposed by LC and to highlight geographic patterns. In particular, the Global Burden of Disease Study (GBD-2016) offers estimates of the burden of LC based on its impact on premature mortality and time lived with disability summarized in the number of Disability-Adjusted Life Years (DALYs).

This study aims to describe temporal and geographical patterns of mortality and DALYs rates by LC by state, sex and related risk factors in Mexico during the 1990-2016 period, according to the GBD, and to discuss their implications for the Mexican Health System.

Materials and methods

We used data from the 2016 GBD study for LC from the suite of visualization tools available online.10 The 2016 GBD study is a global initiative that generates robust historical information about the burden of disease across countries and even at a subnational level in some of them. Details about the methods used by the GBD study are reported elsewhere.11-16

We describe the magnitude and trend from 1990 to 2016 of the age-standardized LC mortality and DALYs by sex, state, sociodemographic index (SDI) tertile at state level, and by age group for Mexico. DALYs are defined as the sum of years of potential life lost due to premature mortality and the years of life lost due to disability attributable to LC,17 while SDI is a proxy of economic development that takes into account the income per person, the educational attainment, and the total fertility rate, being the composite average of these measures.18 Higher values of SDI mean a higher level of development. SDI was also estimated by the Institute of Health Metrics and Evaluation, the institution that performed the GBD. We performed a descriptive regression with the mortality and DALYs rates as dependent variable and SDI tertiles and year as explanatory variables. Federal states in the lowest SDI tertile are: Chiapas, Guanajuato, Guerrero, Hidalgo, Michoacán, Oaxaca, Puebla, San Luis Potosí, Tabasco, Veracruz, and Zacatecas. The highest SDI tertile includes the northern states of Baja California, Baja California Sur, Chihuahua, Coahuila, Nuevo León, Sonora, and Tamaulipas, along with Colima, the Federal District, and the state of Mexico.

We also analyzed the burden attributable to the following risk factors: smoking, secondhand smoke, ambient particulate matter pollution, occupational carcinogens, and household air pollution from solid fuels at state level. This information was also generated by the GBD Study.10

Results

According to the GBD, Mexico presents a sharp decline in the age-standardized mortality rate due to LC, from 13.92 deaths per 100 000 inhabitants [uncertainty interval (UI) 95%: 13.57, 14.26] in 1990 to 9.18 deaths per 100 000 [UI95%: 8.82, 9.58] in 2016. This decline is primarily driven by a 41% decrease of the mortality rate among men, which fell from 21.8 deaths per 100 000 inhabitants [UI95%: 21.19, 22.48] in 1990 to 12.88 deaths per 100 000 inhabitants [UI95%: 12.23, 13.73] in 2016. In contrast, women exhibited a lesser decline, from 7.6 deaths per 100 000 inhabitants [UI95%: 7.33, 7.90] in 1990 to 6.04 deaths per 100 000 inhabitants [UI95%: 5.71, 6.36] in 2016—a decrease of 20.5%. However, the absolute number of deaths from LC increased from 4 785 in 1990 to 8 470 in 2016. In this case, females showed a greater relative increase from 1 654 in 1990 to 3 031 in 2016 (83.3%) than men: 3 824 in 1990 to 5 438 in 2016 (42.2%) (figure 1).
The mortality rate from LC decreased throughout the country. Nevertheless, it is remarkable that in 1990 northern states, such as Sonora, Baja California, Baja California Sur, Sinaloa, and Coahuila show a higher mortality rate than the rest of the states (figure 2, panel A). In 2016, only Chihuahua left the highest quintile of mortality rate from LC (figure 2, panel B). For the DALYs rate, the reduction pattern is similar to that of Panel A, with the Northern states (Sonora, Baja California, Baja California Sur, Sinaloa, and Coahuila) showing the highest DALY’s rate in Mexico (figure 2, panel C). All states exhibit a significant decrease in both rates in 2016 compared to 1990, except for Guerrero, Chihuahua, Durango and Nuevo León show the biggest reductions (59.8, 48.9, 47.7 for deaths and 59.1, 50.5, 51.0 for DALYs, respectively). See Appendix 1 for detailed figures, at https://goo.gl/cP9BBP

As for the age group, the mortality rate is higher in advanced ages. Conversely, in all age groups the mortality rate has diminished. In 1990 the mortality rate in the older group (>70 years old) decreased 27.2% with respect to 2016 (going from 107.67 per 100 000 inhabitants in 1990 to 78.34 in 2016). The DALYs rate by age group shows the same general decreasing pattern. The DALYs rate was of 1 385.35 per 100 000 in 1990 and 975.82 per 100 000 for the >70 years old group. Both the mortality and DALYs rate by LC among the youngest age group are small compared to older groups (figure 4). The age-standardized DALYs rate also fell during the 1990-2016 period from 285 DALYs per 100 000 in 1990 per 100 000 inhabitants per year on average [U95%: -0.53, -0.36], compared to a reduction of 0.12 deaths per 100 000 per year on average [U95%: -0.15, -0.09]. The states in the highest SDI tertile had a DALYs rate of 461 per 100 000 inhabitants in 1990 [U95%: 357.8, 564.2], whilst the states within the lowest SDI tertile faced a DALYs rate of 211 [U95%: 182.5, 239.5] in 1990 on average. As in the case of the mortality rate, the greatest reduction occurred the states in the third SDI tertile: -9.3 DALYs per 100 000 inhabitants per year [U95%: -11, -7.5], versus a reduction of 2.8 DALYs per 100 000 per year [U95%: -3.4, -2.2] (figure 3).

As for the age group, the mortality rate is higher in advanced ages. Conversely, in all age groups the mortality rate has diminished. In 1990 the mortality rate in the older group (>70 years old) decreased 27.2% with respect to 2016 (going from 107.67 per 100 000 inhabitants in 1990 to 78.34 in 2016). The DALYs rate by age group shows the same general decreasing pattern. The DALYs rate was of 1 385.35 per 100 000 in 1990 and 975.82 per 100 000 for the >70 years old group. Both the mortality and DALYs rate by LC among the youngest age group are small compared to older groups (figure 4). The age-standardized DALYs rate also fell during the 1990-2016 period from 285 DALYs per 100 000 in 1990.
to 178 per 100,000 in 2016. However, the relative importance of DALYs due to LC among all causes DALYs has increased from 0.46% in 1990 to 0.6% in 2016.

Finally, regarding the mortality by risk factor, we found that smoking remains the leading risk factor, with 3,478 deaths by LC in 2016. The estimated number of deaths from LC due to occupational carcinogens was 1,314 in 2016. Ambient particulate matter produced 911 deaths in 2016. By state, Sonora, Baja California Sur and Sinaloa showed the largest number of deaths. In these three states, smoking was the main risk factor for death from LC. In every state, smoking was the main cause of disability due to LC. As for the DALYs, we found the same pattern with respect to Sonora, Baja California Sur and Sinaloa as the states with the highest burden by LC (figure 5).

**Discussion**

This study presents an update of mortality due to lung cancer in Mexico. In addition, we showed estimates for DALYs, a more comprehensive metrics for burden of disease. We depicted geographic patterns by severity of the burden of disease and sociodemographic development. We also included estimates of mortality and DALYs from lung cancer by age group and risk factor.

The LC mortality rate has decreased in Mexico in the last decades. The greatest decline was among men.
However, the number of deaths caused by LC has been increasing, mainly due to population growth. These results are congruent with previous literature about LC in Mexico. With respect to geographic areas, the GBD study coincides with other studies about the greater LC mortality rate in northern states, which also have a higher SDI.

By age group, LC mortality rate is higher at advanced ages (>70 years), but the DALYs rate is greater among younger age groups. In addition, the greatest DALYs rate among the 50-69 years age group can be related to longer survival periods and to more life-years lost. In turn, these longer survival periods could be related to better general health status but also to better treatments for LC in Mexico.

There is no single explanation for such declines in the LC mortality rates, since several important risk factors intervene in developing the disease after a long time exposure, i.e. it is necessary to wait several decades from the time of the exposure to the onset of
the disease. With respect to smoking, the prevalence has remained stable in the last years, although there may have been a reduction among men according to other sources. However, further cohort analyses are necessary to determine if older cohorts were more exposed to tobacco smoking than the younger ones. In addition, it is necessary to evaluate the existing policies that aim to reduce tobacco smoking. Mexico ratified the Framework Convention on Tobacco Control in 2004. However, the implementation of tobacco control policies has stagnated: the last increase in tobacco taxes took place in 2011; most states have not implemented smoke-free environments, cessation interventions are not widespread among smokers, and complete banning of advertising has not been implemented.

Also, exposure to asbestos is an important factor, yet little is known about it in Mexico. Air pollution remains a very important risk factor that has not decreased over time in Mexico. In the same line, the use of biomass as fuel in the household has not declined importantly over time and it is projected that there will be no relevant decreases in the near future. However, the states in the south of the country tend to use more biomass as fuel.

Therefore, research on these important risk factors for LC is required. In this sense, specific interventions aiming to reduce the exposure to risk factors are necessary in order to reduce the burden of LC in the medium and long terms.

The health system response deserves special attention. In Mexico, an important fraction of the population (almost 55 million people out of an estimated population of 122 million in 2016) is covered by the Popular Health Insurance (Seguro Popular). Despite the coverage of several oncological conditions by this health insurance, there are still certain diseases and interventions that remain without financial protection, such as LC. LC remains as an important financial threat to the health system, since its treatment is expensive and consumes an important proportion of the available resources. However, it is worth mentioning that LC, with 0.7% of DALYs, is the second cancer that causes most DALYs in Mexico, only after leukemia (0.82% of DALYs). These cancers are followed by stomach, colorectal, cervix, liver, prostate, non-Hodgkin lymphoma, ovaries and kidney cancers. LC, stomach, liver and kidney cancers are not covered by the Seguro Popular.
Accordingly, the effectiveness of interventions against LC should be better assessed, because their role in reducing mortality from LC at productive ages such as the 50-69 years age group in Mexico could be relevant. Access to health care, measured by the Healthcare Access and Quality Index (HAQ) is highly correlated with the SDI at the state level (correlation 0.93, \( p<0.01 \)), and states with lower access to health care have lower reductions in the burden of disease due to lung cancer between 1990 and 2016, compared to states with a higher HAQ (data not shown).

It is also necessary to strengthen such initiatives as the National Cancer Registry, created by decree in 2017. A cancer registry would be a valuable tool to identify and follow up incident and prevalent cases, to better explain the etiology in Mexico and to have better estimates of the demand of healthcare services with respect to cancer in general and LC in particular. However, further research on the diagnosis and registry of LC cases is necessary, in order to determine if the seemingly low relative mortality rates from LC in the south of the country are due to poor access to health care services.

*Source: Institute for Health Metrics and Evaluation.*

**FIGURE 5. DEATHS AND DALYS DUE TO LUNG CANCER BY RISK FACTOR, BY FEDERAL STATE. GLOBAL BURDEN OF DISEASE STUDY 2016.**
As strengths of our study, we showed updated mortality and DALYs rates due to LC, and provided information about subnational burden of disease patterns that may be related to differential exposure to risk factors. We also highlighted that a significant fraction of the population is not insured against LC, and, therefore, studies on the financial burden on the health system caused by smoking-attributable diseases could overestimate the financial burden of LC in particular. We consider that the distribution of the financial costs among healthcare providers/payers and out of pocket expenditures made by the patients and their families should be assessed in order to determine equity implications. Since we relied on the GBD Study, certain considerations are necessary. Criticisms to the GBD indicate that its estimates often tend to vary largely, depending on a set of parameters and on the data and models utilized to provide estimates of such metrics as the DALYs. In countries and territories with low availability of high-quality information this could be a major concern. However, health information in Mexico is generally considered of good quality, and therefore the estimates may be reliable.

In conclusion, analyzed data suggests that LC mortality and DALYs rates in Mexico have decreased over time, although the absolute numbers of deaths have increased, especially in the northern region. However, greater reductions in the burden of disease from lung cancer were seen in the more developed states, compared with the less developed ones. The epidemic is focused in advanced age groups. LC may impose an increasing financial burden on the health system since an important fraction of the population is not protected against out-of-pocket expenditures to afford LC healthcare. Therefore, it is a financial threat to low income populations. Specific public policies to reduce the most important risk factors should be implemented and strengthened to reduce the exposure to smoking, occupational carcinogens, and air pollution.

Declaration of conflict of interests. The authors declare that they have no conflict of interests.

References