



Review

The burden of lung cancer in Latin-America and challenges in the access to genomic profiling, immunotherapy and targeted treatments



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ABSTRACT

Lung cancer is a public health problem worldwide and Latin America (LATAM) cannot escape this reality. This malignant disease has not only a high prevalence in the region, but is also the main cause of cancer related deaths, and in other emerging countries, the incidence rates are still on the rise. Interestingly in most LATAM countries, lung cancer mortality has been decreasing in men but not in women, reflecting smoking patterns in countries such as Chile, Bolivia, and Brazil.

Despite the fact that these issues are well known to government agencies, physicians and patients in the region, current efforts still fall behind those needed in order to face this problem of epidemic proportions. Tobacco control and smoking cessation are the most important interventions against lung cancer, but even with their optimal implementation (which is far from reality at this time) the number of cases in the foreseeable future would still be significant. Beyond tobacco control, advances in our understanding of the molecular component of lung cancer have resulted in new targeted therapies and immune check point inhibitors, which have improved clinical outcomes but at a considerably higher financial cost. LATAM has not widely and speedily adopted these strategies, including new technology and approved novel drugs, due to a number of facts, and therefore only a dismal proportion of LATAMs patient population have benefited from these new advances.

A keen focus on a heterogeneous education system for caregivers in lung cancer treatment would likely help standardize care and improve future potential gains from domestic research. In this review we discuss the challenges of treatment implementation, focusing on new technologies.

1. Current status of lung cancer in Latin America

Latin America (LATAM) is a large region with 600 million people in over twenty countries. Nearly two thirds of the population is located in Brazil, Mexico, Argentina and Colombia. There are important differences in the access to lung cancer (LC) diagnostic and treatment

methods between and within countries and there are also significant disparities between urban and rural populations. A variety of socio-economic, geographic, environmental and ethnic factors strongly influence patient presentation, diagnosis and management of LC. These characteristics make the challenge of facing LC in LATAM a unique dilemma.

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Table 1
Smoking rates in selected countries from Latin America, Europe, Asia, and North America.

Country	Population Smoking Rate (%)
Chile	40
Cuba	40
Argentina	27
Brasil	17
Colombia	19
Russia	37
Estonia	36
Latvia	36
Lithuania	34
Kuwait	37
Bangladesh	37
Indonesia	36
China	33
Canada	19.9
Mexico	19.8
United States of America	16.8

In the region the most important etiology for LC is smoking. In LATAM and the Caribbean, the number of cancer cases related to tobacco is increasing for both sexes: we anticipate 541,000 new cases and 454,500 LC deaths by the year 2030 [1]. Fewer women develop LC in LATAM and the Caribbean when compared to North America, but the number of cases is increasing. Current annual deaths range from 66,000 in Mexico, to 6500 in Uruguay. Less common causes of LC include environmental pollution especially the burning of solid organic fuels, such as wood. Tobacco use plays a major influence in LC trends in the LATAM region [2–7] as shown in Table 1. This observation points to a future LC epidemic in LATAM countries that will need a long-term solution. In spite of these alarming numbers, many countries in LATAM do not have a National Cancer Institute, and many also lack widely-available programs with enough funding to address this need. Despite the fact that the etiologic agent for most cases is known, few countries in the region have effective anti-tobacco campaigns, and concomitantly there are few, if any, campaigns that target LC prevention. A concrete example of what these preventive strategies can achieve is depicted in Uruguay, where an important decrease in LC cases was recently seen, based on an effective anti-tobacco law and an increase in cigarettes cost [7]. Various countries collect significant tax revenues from tobacco products (US\$billions: 2.2 in Mexico, 1.5 in Chile, and 1.2 in Argentina yearly) but it would be a considerable mistake to believe that the tax benefit would be larger than the health costs incurred. In addition, despite the described data, the epidemiology statistics on cancer in LATAM are usually unreliable as only seven percent of the population is represented in registries when compared to 96 percent in the United States (US) alone [7]. In the fight against LC in LATAM, there are two urgently needed actions: assessing the magnitude of the problem with the improvement of cancer registries, and the financing of national cancer control programs.

Although the etiology may be a common factor, there is a diversified health system strategy when delivering LC care in LATAM countries. There are wide disparities in access to diagnosis, staging procedures, surgery and chemotherapy. Most patients in the region are diagnosed when they are in advanced or metastatic stages (70%), because there are few established early detection/screening programs for LC. This is particularly the case in the rural setting, where these programs are practically non-existent [8]. In addition to the diagnosis problems, patients also must wait as long as 6 months for treatment after the initial diagnosis. Treatment access is limited, exemplified in the fact that currently six countries in Latin America and the Caribbean lack radiotherapy. Health expenditure as a percentage of GDP varies widely and is lower than in developed nations, with new drugs such as targeted agents and immunotherapy being unaffordable to most patients. There is also a lack of support in the implementation of new molecular

profiling technologies and targeted therapy [9]. There appear to be several reasons LATAM is far behind its counterparts in the US and Europe. Costs are a major barrier to bring new, expensive, technologies. Bringing next generation sequencing to LATAM has been limited due to minimal operations and investment in the region. A similar situation arises in the case of personalized treatments, such as immunotherapy and targeted therapy, where it takes an extended time for new agents' approval, only to find a restricted use due to the high cost, despite oncologists prescribing the therapy. The rising number of cancer cases is therefore many times met with poorly funded health care institutions, which also lack a structured systematic approach for studying LC patients. Under these challenging circumstances, palliative care and pain relief is the only option for many patients. Even with palliative care, there are large disparities to access optimal palliative care across countries. Our best initial approach in LATAM must unequivocally consider an improvement in prevention programs as well as access to healthcare.

2. The economic impact of cancer in Latin America

In 2020, an estimate of more than 1.7 million people will develop cancer in LATAM and the Caribbean, and more than 1 million will die from the disease as well. There is no adequate care for many populations based on socioeconomic, geographic, ethnic, and other factors as discussed previously. The dangers and costs from lack of action are enormous [8]. Of all new cancer cases reported, approximately 60% appear in low and middle-income countries (LMICs), such as those in LATAM, and nearly two-thirds of cancer related deaths happen in these nations. These statistics show that LMICs are less able to meet the needs of patients compared to richer nations. Indeed, in 2009 it was reported that approximately half of the total cost of cancer was attributable to treatment, whereas productivity loss accounted for one-quarter of the costs [8]. This report suggested that LMICs contributed only 6.2% of the total spent on cancer globally, but were responsible for an overwhelming 89% of the global cancer expenditure gap, which is the difference between the estimated cost incurred in each country and the cost incurred should the country match a global cancer expenditure standard.

The estimated total economic burden of cancer in the region is over US \$4 billion [8]. The cost of cancer care in South America represented 0.125% of gross national income per capita (ranging from 0.06% in Venezuela to 0.29% in Uruguay) as compared with 0.51%, 0.6%, and 1.02% for the United Kingdom, Japan, and the US, respectively. In India, cost per case as a percentage of gross national income per capita was 0.05%, and in China, it was 0.11% [8]. In the Americas, including the United States and Canada, there were approximately 2.8 million new cancer cases in 2009, with an estimated cost of \$153 billion for the first year after diagnosis. This figure however, does not include the cost of cancer screening and prevention, lost income due to cancer mortality, or future treatment costs. The costliest cancer was lung (\$31 billion per year), followed by prostate (\$18 billion), and breast (\$17 billion) [10].

A publication recently calculated the economic burden of cancer per patient including the direct medical expenses, nonmedical expenses (such as transportation and home care) and productivity losses in South America (\$7.92), China (\$4.32) and India (\$0.54) [11]. These values pale in comparison to the expense per patient in the UK (\$183), Japan (\$244) and USA (\$460). Adjusting by income at current exchange rates, the amount spent on cancer care is equivalent to 0.12% of the per capita gross national income (GNI) in South America, 0.05% in India and 0.11% in China. In the UK, Japan and USA, the corresponding expenses were 0.51%, 0.6% and 1.02% of GNI, respectively. While we would like to present statistics similar to the ones we mentioned from Asia or the US, published specifics on economic impacts in LATAM are few.

The lack of specific data for LATAM highlights the need for regional studies to help policy makers plan for prevention programs as well as

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