The Economist INTELLIGENCE UNIT

LUNG CANCER IN LATIN AMERICA:

Time to stop looking away

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ABOUT THIS REPORT

Lung cancer in Latin America: Time to stop looking away is an Economist Intelligence Unit report, commissioned by Roche, which examines the burden of lung cancer in Latin America and how well countries in the region are addressing the challenge. Its particular focus is on 12 countries in Central and South America, chosen for various factors including size and level of economic development: Argentina, Bolivia, Brazil, Chile, Colombia, Costa Rica, Ecuador, Mexico, Panama, Paraguay, Peru and Uruguay.

This study looks in detail at the disease burden as well as the economic and social burden of lung cancer in the region. It also introduces a major tool for stakeholders seeking to understand the policy response to lung cancer: the Latin America Lung Cancer Traffic Lights. The traffic-light system assesses national policy approaches, and to some extent outcomes, in Latin America. The Economist Intelligence Unit performed a rapid literature review to identify key issues around lung cancer in Latin America. We then held an advisory board meeting with regional experts in order to determine on which key categories, called domains, to focus. Following the advisory board's recommendations, we split the domains into three Priority Traffic Lights (those without which other progress would be impossible) and five Important Traffic Lights, which, while still crucial for successfully addressing the lung cancer challenge, were deemed less central than the Priority Traffic Lights.

The three Priority Lights are as follows: tobacco control, access, and early diagnosis. The Important Lights include the following five domains: treatment, non-curative services, non-tobacco prevention, information and advocacy, and data quality. The purpose of the traffic-light system is not to rank countries or single out countries performing less well. Rather, it will serve as the starting point for further discussion on policy progress and gaps that will be further explored in this white paper.

Our thanks are due to the following for their time and insight (listed alphabetically):

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EXECUTIVE SUMMARY

Lung cancer is Latin America's deadliest neoplasm, but frequently gets less attention than other major cancers. Until recently, the implications were small: unless caught very early—which is difficult given a lack of distinct symptoms at that stage—the prognosis was poor anyway. Medical advances, though, now hold out the hope of prolonged life, or even cures, for a growing, if still small, number of patients. It is time to look more closely at the region's response to this disease and current strengths and weaknesses of efforts to address it.

Doing so will require understanding the regional peculiarities of the lung-cancer burden. The drivers of the disease differ from those in most developed countries. While tobacco smoking remains the dominant issue, poverty—and the attendant use of indoor solid fuels for cooking and heating—appears to play an important role in certain countries, as does the natural environment, especially sometimes high levels of arsenic in groundwater. These differences in risk factors, in turn, affect the genetics of lung tumours, and therefore treatment potential. The lung-cancer challenge in Latin America, therefore, needs to be understood on its own terms.

Data deficiencies, though, inevitably impede almost any cancer-control discussion in the region. Accordingly, for this project, The Economist Intelligence unit has conducted two substantial research efforts: an economic model to estimate the direct and indirect costs of lung cancer in 12 countries in the region (known as the study countries)[1]; and a bench-marking tool to assess, in those same countries, the state of national lung-cancer control efforts across various domains. These, along with insights from 23 regional experts, collectively inform this study.

Its key findings include:

Lung cancer is not a single disease, but some forms are becoming susceptible to treatment. Lung cancer can be understood as a family of neoplasms that all strike the lung first. The main divisions are between small-cell and non-small-cell lung cancer and, in the latter sub-group, adenocarcinoma, squamous cell lung cancer and large-cell lung cancer. It is non-small-cell lung cancer that has seen the biggest medical advances in recent years with inhibitors for specific genetic mutations and immunotherapy showing great promise.

The human and economic costs are substantial. Although estimates vary, in the study countries over 60,000 people die each year from lung cancer, which represents 12% of all neoplasm deaths there. The estimated bill for diagnosis, treatment and palliative care (the direct costs) comes to US$823m in 2016 in Brazil. Rather than make individual calculations for other countries, for some of which the data would not even be available, we use a process called interpolation (see Appendix I) to estimate the total figure for the 12 study countries at US$1.35bn. Indirect costs are significant too, but substantially lower than the direct costs, at US$286m for the entire region—a figure reduced by the large proportion of those developing lung cancer who are past the relevant national retirement ages.

[1] Argentina, Bolivia, Brazil, Chile, Colombia, Costa Rica, Ecuador, Mexico, Panama, Paraguay, Peru and Uruguay.

Tobacco is the dominant but far from the only risk. The link between smoking and lung cancer is widely understood, but this knowledge can crowd out awareness of other carcinogens. The Global Burden of Disease Study from the World Health Organisation (WHO) estimates that, in our study countries, tobacco is responsible for 64% of lung cancer. The remaining 36%, however, on its own would remain a major public health issue, on a par with cervical cancer in our study area. The main non-tobacco risks in the region are indoor and outdoor air pollution, residential radon gas, and arsenic in drinking water. The extent of these dangers is difficult to estimate because of the lack of relevant research in much of the region.

Smoking is down, but the impact on lung cancer burden depends on the metric used. Tobacco consumption in Latin America has seen a marked decrease in recent decades, with the WHO estimating that Panama's smoking prevalence fell by over half between 2000 and 2015—the biggest drop in the world—while even the worst performer in the study, Chile, saw a decline of a fifth. This will inevitably lead to fewer cases of lung cancer eventually, but when exactly is harder to say because of the various lung carcinogens in the region, their typically long latency periods, and the later rise and fall in female smoking rates compared with male ones. In most study countries, male age-standardised lung cancer mortality rates—which factor out demographic changes—have declined to some extent or stayed flat. In a few, such as Mexico, Colombia and Costa Rica, so have female ones. For the most part, however, population growth and ageing mean that the crude rates of cancer for both sexes, and case numbers, have risen or, at best, been flat. In the short term, the benefits of smoking cessation will probably appear only slowly.

Stigma impedes various elements of lung-cancer control. As one expert told this study, "in Latin America…the way we see lung cancer is that 'these guys are guilty. They did it to themselves.' There is no compassion." Various survey results tell the same story. As a result, lung cancer seems to be treated as a second-class neoplasm, with surprisingly low research funding, for example, compared with its health burden. Although high cost is also an issue, interviewees suspect that stigma may also partly explain lower willingness to fund lung-cancer treatment than that for other cancer treatments where resources are limited.

The Latin America Lung Cancer Traffic Lights: a national benchmarking tool. We publish here the results of our traffic light analysis that addresses key elements of lung-cancer control in the study countries. On our expert advisory panel's recommendation, these fall into two groups. The first are the Priority Lights: tobacco control; access; and diagnosis. The other five Important Lights are areas that are also crucial: treatment; non-curative services; non-tobacco prevention; information and advocacy; and data quality. A green light in any given area (called domains) indicates that countries are doing well by relevant global or regional standards; amber denotes an area of concern; and red a need for substantial attention.

The traffic lights give two overarching messages: substantial room for improvement overall and the need to make progress beyond tobacco control and data quality. The study countries are not doing well overall. The vast majority of lights are amber or red, with only 15% green. Experts

interviewed for this study point to the low attention given to lung cancer, and in particular a lack of government focus as the likely explanation. In fact, efforts are concentrated almost exclusively on tobacco control and data quality: all green lights but one appear in these two domains. Both are necessary, but it is short-sighted to think them sufficient.

Tobacco control is a growing strength in the region, but non-tobacco lung cancer prevention needs significant attention. Most study countries score green on tobacco control, with the rest amber. Appropriate regulation, including on smoke-free public places, and taxation on cigarettes is widespread. This progress has occurred mostly in the past decade and requires ongoing support in the face of opposition from the tobacco industry. Nevertheless, these efforts appear to be bringing about the necessarily underlying cultural change in attitudes towards smoking across the region. Prevention related to other causes of lung cancer, however, lags far behind. In much of the region, even the levels of radon-gas concentrations and arsenic in drinking water are uncertain, while air pollution limits remain above WHO recommendations.

Access challenges remain a substantial barrier. Last year's publication accompanied the release of the Latin America Cancer Control Scorecard (LACCS), which covered the same countries discussed here, and looked in detail at the challenges of accessing cancer diagnosis and treatment for those with limited financial means or living away from major cities.[2] These remain, with public care behind private to a worrying extent. Worse still, public care is not always affordable. Some government programmes that cover the high costs of other cancers do not do so for lung cancer, notably Mexico's Seguro Popular and Chile's Régimen de Garantías Explícitas en Salud. Access challenges and mediation costs, both general and specific to lung cancer, help explain why payment for lung cancer drugs is a frequent theme in the growing patient litigation around rights to healthcare.

Diagnosis occurs too late, but screening remains controversial. Early diagnosis of lung cancer saves lives but is difficult. In Japan, for example, 58% of patients with the disease are found at stage III or IV. In our study countries, this figure is much worse, with most around 85% and Mexico at 99%. Screening has helped with downstaging of other neoplasms, and a major US study indicated it could cut lung cancer mortality by 21%. Pilot screening projects have occurred in Brazil, and one is taking place in Mexico. Generally, however, health systems are reluctant to adopt this approach because of cost, uncertainty over its applicability to regional populations, and lack of health-system preparedness. Unfortunately, very few other initiatives exist to detect lung cancer earlier. Accordingly, this is one of the areas where the study countries as a group do worst.

Treatment has some strengths, but lack of resources impedes better care. Lung-cancer treatment varies widely by country: some, such as Uruguay and Argentina, have better provision, even for those with limited financial means, while others, notably Paraguay and Bolivia, provide only the very basics. Most study countries have national treatment guidelines, although it is surprising that Chile lacks them. Putting the guidelines into practice is another matter, with health-system fragmentation and limited resources impeding, or reducing, the availability of multidisciplinary care. Not surprisingly, a few leading systems are able to begin treatment as quickly as those in developed

[2] The Economist Intelligence Unit, *"Cancer Control, Access and Inequality in Latin America: A tale of light and shadow"*, 2017.

countries, but others lag far behind, with Mexico taking on average four and a half months from diagnosis to treatment.

Too often care stops with the end of curative interventions. The study countries are weak on care that goes beyond curative intervention, even though, in theory, every patient could benefit. Palliative care, broadly speaking, should have two roles with lung cancer: helping with symptom management from the time of diagnosis, and continuing to provide such relief until death if curative care fails. In the study countries only Argentina, Chile, Costa Rica, Panama and Uruguay have the capacity to provide this. Meanwhile, as lung cancer transforms in some cases from a terminal to a chronic condition, survivorship care will become a growing concern. Just Colombia and Mexico, however, have guidelines encouraging pulmonary rehabilitation, a likely essential element of any future survivorship programme.

There are few awareness-raising efforts and patient advocacy groups. Lung-cancer awareness is very low in the region with, for example, half of Brazilians and Argentinians unable to name a single correct symptom. Unfortunately, most study countries are doing too little to improve knowledge. Despite the region's strength in tobacco control, five study countries did not conduct national anti-smoking campaigns in 2014 or 2016 (as recorded by the Tobacco Atlas), including Chile and Bolivia, where smoking prevalence remains high. Broader lung-cancer awareness activity, meanwhile, was rare, with only four countries showing evidence of substantial efforts in recent years. The awareness-raising that does occur is usually the work of patient advocacy groups, but there are few in the region.

Data quality continues to improve but lags on lung cancer. As reported in our LACCS study, registry quality is getting better across Latin America, which helps to explain the high number of green lights in this domain. Unfortunately, lung-cancer data quality lags that of other neoplasms, with more than twice as many registered cases coming from death records on average. Unfortunately, mortality data are also often weak in the region, with only five countries getting full marks. On the plus side, in the absence of a specific lung-cancer registry, researchers are engaging in substantial data sharing through the Latin American Consortium for the Investigation of Lung Cancer.

CHAPTER 1: LATIN AMERICA'S LUNG CANCER CHALLENGE

I. The high human cost

Lung cancers kill more people in Latin America than any other kind. Varying estimates paint the same picture. According to the International Agency for Research on Cancer (IARC), in 2012 (its latest data) just above 60,000 people died from lung cancer in the countries included in this study. The WHO's Global Burden of Disease (GBD) figures, using a different methodology, put the 2016 figure at just above 65,500. In both cases, this represents more than 10,000 more lives lost than the next most lethal cancer and around 11-12% of all neoplasm deaths.[3]

Lung cancer's unenviable distinction does not come from a particularly elevated incidence. In the study countries, breast cancer (around 132,000 new cases in 2012, according to the IARC) and prostate cancer (126,000 new cases) appear nearly twice as often as lung cancer (68,900 new cases). This is the case despite the fact that the latter strikes both sexes, while prostate cancer affects men (the equivalent for women strikes the Skene glands) and breast cancer primarily affects women (male breast cancer is rare).

Medicine, however, has to date been much less successful against lung cancer. The proportion of people who die from a disease in a given year to the number of new cases—the mortality-incidence (M:I) ratio—is a rough measure of how health systems are coping with a disease. For lung cancer, the M:I ratio was 87% in 2012, the third-highest after liver and pancreatic cancer.[4]

In global terms, these stark numbers are unremarkable: lung cancer is a common scourge. Latin America's overall incidence and mortality figures are mid-way between North America and European highs and typically African lows (see Chart 1). Whatever challenge others face, though, even this average burden from lung cancer poses a major public-health issue for the region.

This regional overview covers marked national variation. National age-standardised rates (ASR) of lung-cancer incidence and mortality differ substantially. For both, the burden of Uruguay, the most affected country, is nearly six times higher than that of Bolivia, the least affected (see Table 1). More constant is the disease's ranking as a killer: for most study countries, it is among the three cancers causing the most deaths. The only real outliers are Costa Rica and Bolivia. As Milton Soria, head of the pathology unit at Bolivia's Instituto Nacional de Laboratorios en Salud, puts it, "here, lung cancer is not as relevant as you might think" because other forms of the disease exact a higher toll. Similar M:I ratios across the region, though, indicate that no health system is detecting or treating the disease well.

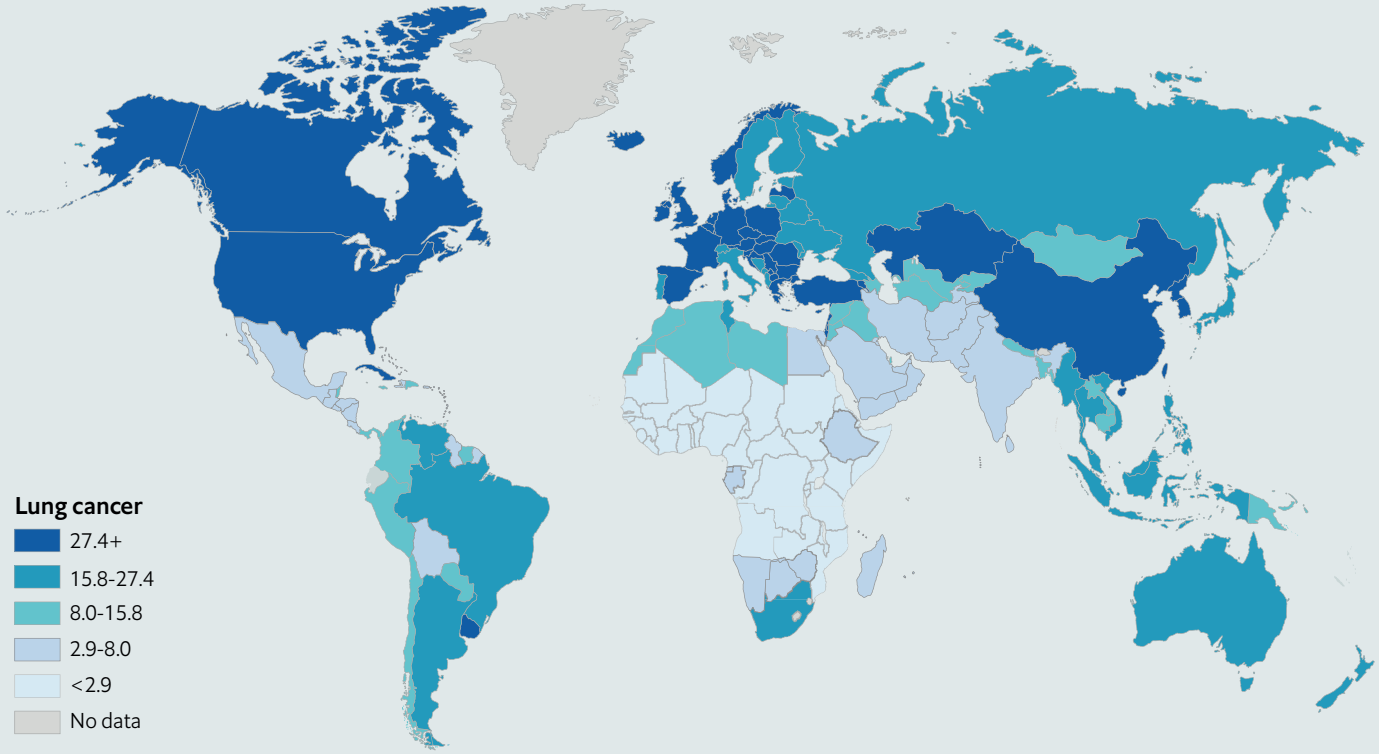
Dramatic medical advances could now ameliorate these bleak mortality figures. Oscar Arrieta, co-ordinator of the lung cancer and thoracic tumours clinic at Mexico's Instituto Nacional de Cancerología, reports that "the treatment pipeline has changed dramatically in the last five years". So much so that Mexico's extensive 2013 treatment guidelines had to be revised in 2016 and are undergoing yet another

[3] Institute for Health Metrics and Evaluation (IHME), GBD Results Tool. Available at: http://ghdx.healthdata.org/gbd-results-tool & IARC Globocan Database, Incidence/Mortality > Rates: Cancers by population. Available at: http://globocan.iarc.fr/Pages/summary_table_pop_sel.aspx

[4] IARC Globocan Database, Incidence/Mortality > Rates: Cancers by population. Available at: http://globocan.iarc.fr/Pages/summary_table_pop_sel.aspx

Chart 1

Lung cancer age-standardised incidence by country, 2012



Source: IARC Globocan Database.

Table 1: Key lung cancer data by country, 2012

	Incidence per 100,000 adults	Mortality per 100,000 adults	M:I ratio	Lung cancer rank among cancers for mortality
Uruguay	29.2	26.5	91%	1
Argentina	20.9	19.1	91%	1
Brazil	16.3	13.3	82%	1
Paraguay	14.0	12.5	89%	1
Chile	13.3	12.5	94%	2
Colombia	11.0	10.1	92%	2
Peru	10.1	8.9	88%	2
Panama	9.0	7.9	88%	3
Ecuador	7.2	7.2	100%	3
Mexico	7.5	6.7	89%	1
Costa Rica	6.9	5.8	84%	5
Bolivia	5.1	4.6	90%	6
Study country aggregate	**13.4**	**11.6**	**87%**	**1**
Study country average	**12.5**	**11.3**	**90%**	**N/A**

Notes: Mortality and incidence rates have been standardised to the global population. "Average" treats each country the same, regardless of population size. "Aggregate" treats the 12 countries as a single, aggregate population.

Source: IARC Globocan Database, Incidence/Mortality > Rates: Cancers by population. Available at: http://globocan.iarc.fr/Pages/summary_table_pop_sel.aspx

reworking. Luis E Raez, medical director of the Memorial Cancer Institute in Florida and visiting professor of medicine at Cayetano Heredia University in Peru, adds that targeted therapies and immunotherapy have grown so much in the past five years in the US that "about 20% of lung cancer patients can get oral therapy instead of chemotherapy".

The results are heartening. Two studies suggest longer lives, at least for those with appropriate biomarkers of susceptibility to given treatments. Overall, among those diagnosed at the most advanced stage (stage IV), the potential to survive five years or more has gone from 4% a few years ago to 16%.[5] "It is still a very lethal disease," Dr Raez warns, but for some lung-cancer patients greatly extended lives, even cures, are now possible.

These treatments, however, come at a cost. Ricardo Pérez Cuevas is leading a team at Mexico's Instituto Nacional de Salud Pública that is revising earlier estimates of the cost of lung-cancer treatment made

BOX: WHAT IS LUNG CANCER?

Lung cancer is a category of diseases that have in common the body organ where they strike first. Previously, key terms for describing kinds of lung cancer betrayed a focus—sometimes shielded by classical vocabulary—anchored around basic descriptions of what these cancers look like or where they occur. This reflected the limits of earlier science. The vast strides biology has made in recent decades, though, have shifted consideration to how these tumours operate, thereby opening a greater, if still limited, range of treatment options.

The main first division within the lung-cancer family is based on physical appearance:

Small-cell lung cancer (SCLC) gets its name from the size of its cells. Making anywhere from around 10-25% of lung cancers,[6] SCLC is especially aggressive and difficult to treat. In the US, even if diagnosed at stage I, the relative five-year survival rate is only 31%; for other lung cancers, depending on sub-stage, this figure ranges from 68% to 92%.[7]

Non-small-cell lung cancer (NSCLC) is again a category rather than a single disease and includes almost all remaining lung cancers. Medicine has made far more progress here than on SCLC in recent years. The main types of NSCLC are:

- *Adenocarcinoma:* this is the most common NSCLC, which occurs in the lung's mucus producing glands ("adeno" from the Greek for "gland").
- *Squamous cell carcinoma:* the next most frequent NSCLC appears in the lung lining, the so-called squamous cells (from the Latin word for "scales").
- *Large-cell carcinoma:* this third major NSCLC is much less prevalent than the others. It can appear anywhere in the lung.

These categories are neither exclusive nor exhaustive: for example, a very small number of adenosquamous cancers, with the features of both the first two listed, occur. These three, though, constitute the vast majority of NSCLCs.[8]

[5] Scott Gettinger et al, "Five-Year Follow-Up of Nivolumab in Previously Treated Advanced Non–Small-Cell Lung Cancer", *Journal of Clinical Oncology*, 2018 & Jessica J Lin, "Five-year survival in EGFR-mutant metastatic lung adenocarcinoma treated with EGFR-TKIs", *Journal of Thoracic Oncology*, 2016.

[6] See, for example, Estelamari Rodriguez and Rogerio C Lilenbaum, "Small Cell Lung Cancer: Past, Present, and Future", *Current Oncology Reports*, 2010 & Tatiana N Zamay et al, "Current and Prospective Protein Biomarkers of Lung Cancer", *Cancers*, 2017.

[7] American Cancer Society, "Small Cell Lung Cancer Survival Rates, by Stage", available at https://www.cancer.org/cancer/small-cell-lung-cancer/detection-diagnosis-staging/survival-rates.html & "Non-Small Cell Lung Cancer Survival Rates, by Stage", available at https://www.cancer.org/cancer/non-small-cell-lung-cancer/detection-diagnosis-staging/survival-rates.html#references.

[8] For a detailed description of the biology of the different types of lung cancer, see William D Travis et al, "The 2015 World Health Organization Classification of Lung Tumors", *Journal of Thoracic Oncology*, 2015.

Although all are called lung cancer, the underlying biology of these diseases has long been understood to differ. The greater aggressiveness of SCLC is one clear example. So are non-tobacco risk factors. Air pollution and wood smoke, for example, are associated with high rates of adenocarcinoma, while ingesting arsenic through drinking water increases the risk of squamous cell carcinoma.[9] Moreover, arsenic-induced squamous lung cancers have different DNA copying patterns from those where smoking is the cause.[10]

Recent bioscience advances allow far greater understanding of these biological differences, making our understanding of NSCLC yet more complex.

As with other cancers, those of the lung produce biomarkers—strands of DNA, proteins, or other molecules and attributes—which both indicate how they behave and differentiate them from cancers of the same type. Currently, dozens of identified or potential biomarkers are associated with different kinds of lung cancer.[11] Not all will necessarily have clinical value, but hopes are high: an estimated 60% of lung-cancer tumours have at least one genetic mutation that helps to initiate or drive the disease on—a higher figure than for most other cancers.[12]

To date, however, a limited number of biomarkers allow targeted clinical responses. These appear largely in adenocarcinomas. The following mutations are particularly relevant to treatment, either for their frequency or for their susceptibility to specific therapies:

- *EGFR (epidermal growth factor receptor):* more common in never-smokers, anywhere from 15% to 40% of adenocarcinomas exhibit a mutation that creates too much EGFR, a protein that encourages cell growth and division. In Latin America, the figure is 26%.[13] Several EGFR inhibitors exist.

- *ALK (anaplastic lymphoma kinase):* again more common in never-smokers, an ALK translocation is a rearrangement of an otherwise useful gene found in 4-11% of adenocarcinomas.[14] When present, it creates a protein that causes cell growth and spread. Several drugs target this protein too.

- *KRAS (Kirsten Rat Sarcoma viral oncogene):* KRAS was one of the earliest mutations found in adenocarcinomas. It affects 25-30% of such lung cancers, although in Latin America the figure appears to be 14%.[15] Its biology is complex, interacting negatively with growth factors and tumour suppressors. Despite extensive study, a therapy to inhibit KRAS's impact does not yet exist.[16] Finding one would be particularly useful: the mutation appears only where EGFR and ALK ones do not.

- *PD-1/PD-L1 (Programmed cell death 1/ Programmed cell death ligand 1):* the PD-L1 protein exists in healthy cells to protect them from autoimmunity, but cancers can hijack them to fool immune systems into not killing a tumour. This may contribute to anywhere from 24% to 60% of lung cancers. Immunotherapies—which assist the immune system—are showing great promise in cancers where abnormal PD-1 activity is found.[17]

The extent and potential treatability of EGFR- and ALK-positive tumours have made relevant molecular testing standard practice for adenocarcinomas.[18] Other biomarkers can point to specific treatment options but are less common. Biomarker testing as a part of detailed diagnosis and treatment choice is therefore only likely to increase as we understand more about the range of different diseases covered by the increasingly inexact term "lung cancer".

[9] Ole Raaschou-Nielsen, "Air pollution and lung cancer incidence in 17 European cohorts", *Lancet*, 2013 & Oscar Arrieta, et al, "Clinical and Pathological Characteristics, Outcome and Mutational Profiles Regarding Non–Small-Cell Lung Cancer Related to Wood-Smoke Exposure", *Journal of Thoracic Oncology*, 2012 & How-Ran Guo et al, "Cell Type Specificity of Lung Cancer Associated with Arsenic Ingestion", *Cancer Epidemiology, Biomarkers & Prevention*, 2004.

[10] Victor Martinez et al, "Arsenic and Lung Cancer in Never-Smokers: Lessons from Chile", *American Journal of Respiratory and Critical Care Medicine*, 2012.

[11] Tatiana N Zamay et al, "Current and Prospective Protein Biomarkers of Lung Cancer", *Cancers*, 2017.

[12] Megan Baumgart and Kishan Pandya, "The use of biomarkers in the treatment of non-small cell lung cancer", *Expert Review of Precision Medicine and Drug Development*, 2016.

[13] Data on prevalence of mutations from: Megan Baumgart and Kishan Pandya, "The use of biomarkers in the treatment of non-small cell lung cancer", *Expert Review of Precision Medicine and Drug Development*, 2016 & Oscar Arrieta et al, "Updated Frequency of EGFR and KRAS Mutations in Non Small-Cell Lung Cancer in Latin America", *Journal of Thoracic Oncology*, 2015.

[14] Ibid.

[15] Ibid.

[16] Marta Román et al, "KRAS oncogene in non-small cell lung cancer: clinical perspectives on the treatment of an old target", *Molecular Cancer*, 2018.

[17] Hui Yu et al, "PD-L1 Expression in Lung Cancer", *Journal of Thoracic Oncology*, 2016 & Xiaoling Xu et al, "The efficacy and safety of anti-PD-1/PD-L1 antibodies combined with chemotherapy or CTLA4 antibody as a first-line treatment for advanced lung cancer", *International Journal of Cancer*, 2018.

[18] William D Travis et al, "The 2015 World Health Organization Classification of Lung Tumors", *Journal of Thoracic Oncology*, 2015.

before targeted therapies became available. Although the study continues, the advent of these new drugs looks to have roughly tripled the cost of treatment per patient diagnosed at stages III and IV.

II. The high economic cost

Drug prices are not the only financial issue for lung cancer. For this research programme, The Economist Intelligence Unit modelled the economic impact of the disease in the study countries. The calculations included direct costs (those for medical interventions, such as diagnosis, treatment and palliative care) and indirect costs (arising out of lost productivity from work absence and early mortality).

In this analysis the region's poor healthcare data made it necessary to use a method called interpolation. This estimates the economic impact on countries that lack published information by making appropriate adjustments to data from a baseline country. Appendix 1 contains further details of the model's methodology, data and calculations.

Our baseline country, Brazil, shares with most of Latin America a high proportion of late lung-cancer diagnosis: in Brazil 85% are found at stages III or IV.[19] Such patients not only have a worse prognosis, they cost more to treat. The following table gives the direct costs in Brazil (per patient and total) for lung-cancer treatment, with separate calculations for the three-quarters of the population in the public health system and the remainder with private insurance. Spending on the latter, predictably, is higher per head, but to such a degree that, despite the much smaller number of patients, aggregate spending also outstrips public outlay.

Table 2: Direct lung-cancer costs in Brazil by stage, public and private sectors, 2016 (US$)

Stage of lung cancer	Patients diagnosed per stage	Cases per stage	Cost per stage per patient	Total costs per stage, all patients
Public sector				
Stage I & II	15%	3,820	5,564	21,257,654
Stage III	39%	9,933	9,587	95,224,887
Stage IV	46%	11,716	11,417	113,751,641
Total	**100%**	**25,469**	**9,825***	**250,234,182**
Private sector				
Stage I & II	15%	1,274	7,239	9,218,352
Stage III	39%	3,311	86,132	285,178,132
Stage IV	46%	3,905	71,354	278,652,826
Total	**100%**	**8,490**	**67,497***	**573,049,309**

Note: * denotes the weighted average (obtained by dividing total costs by total number of cases).
Source: The Economist Intelligence Unit

We next estimated direct costs in the other study countries by adjusting the Brazilian ones for relative differences from the baseline country in: healthcare spending per person; lung-cancer prevalence; and the split between public and private health insurance coverage.

[19] Guilherme Costa et al, "Epidemiological changes in the histological subtypes of 35,018 non-small-cell lung cancer cases in Brazil", *Lung Cancer*, 2016.

These national approximations require several grains of salt. Indeed, the per-head figures in particular say nothing specific about measured national lung-cancer treatment activities; they are simply Brazil's figure multiplied by a composite measure of how its health system differs on a grand scale from the baseline country. The figures are also implicitly based on two assumptions: first, that public-health systems in every country provide similar care levels, as do private ones, and second, that each country devotes a similar proportion of its total health spend to cancer. As discussed later in this report, the first is unlikely: unlike Brazil's public health service, Sistema Único de Saúde (SUS), for example, Mexico's Seguro Popular does not publicly fund lung cancer care. The second assumption is also improbable, given the different stages of study countries in the epidemiologic transition that accompanies economic development. Bolivia, for example, would rightly focus more on acute diseases than, for example, Uruguay would.[20] Similarly, in Peru, while further than Bolivia in this transition, "policymakers face very complicated public-health problems, such as tuberculosis as well as other communicable diseases such as malaria or hepatitis," explains Luis Mas, until recently executive director of medical oncology in Peru's Instituto Nacional de Enfermedades Neoplàsicas. Unfortunately, data to rigorously address these issues in our model do not exist.

Table 3: Direct lung-cancer costs in the 12 study countries, 2016

	Estimated direct healthcare costs for lung cancer (US$)	Prevalence	Estimated per patient direct cost for lung cancer (US$)
Argentina	207,199,992	12,626	16,411
Bolivia	6,051,264	908	6,668
Brazil	823,283,491	33,958	24,244
Chile	118,494,725	3,862	30,679
Colombia	34,138,430	5,205	6,558
Costa Rica	14,238,925	409	34,832
Ecuador	15,099,247	1,104	13,678
Mexico	76,240,001	9,676	7,879
Panama	13,104,402	415	31,599
Paraguay	7,190,620	827	8,699
Peru	15,505,888	2,576	6,019
Uruguay	32,167,918	1,645	19,559
Total	**1,351,654,887**	**73,210**	**18,462**

Note: These national figures do not reflect actual spending data and should not be used as such. They are approximations based on Brazil's figures and a step in the process of estimating the regional spending total.

Source: The Economist Intelligence Unit

Our aggregate regional figure is more robust because Brazil hews closely to the average of study countries on cancer spending and care quality. Moreover, with 46% of the lung-cancer prevalence in the study countries, its numbers would heavily influence any overall outcome.

For 2016 direct lung-cancer healthcare costs in the study countries are an estimated US$1.35bn, or 0.4% of healthcare outlay, with US$823m spent in Brazil, or 0.5% (based on health spending data from the WHO for 2015).

[20] The Economist Intelligence Unit, *"Cancer Control, Access and Inequality in Latin America"*

Table 4: Indirect lung-cancer costs in the 12 study countries, 2016

	Estimated indirect healthcare costs for lung cancer (US$)	Prevalence	Estimated per patient indirect cost for lung cancer (US$)
Argentina	82,413,063	12,626	6,527
Bolivia	913,617	908	1,007
Brazil	116,969,038	33,958	3,444
Chile	16,961,185	3,862	4,391
Colombia	8,059,125	5,205	1,548
Costa Rica	1,791,071	409	4,381
Ecuador	3,104,970	1,104	2,813
Mexico	36,333,140	9,676	3,755
Panama	1,749,907	415	4,220
Paraguay	1,296,821	827	1,569
Peru	7,298,856	2,576	2,833
Uruguay	8,886,882	1,645	5,403
Total	**285,777,674**	**73,210**	**3,904**

Source: The Economist Intelligence Unit

The indirect costs include the impact of absenteeism and early mortality on economic output. Finding these costs involved looking at, for each economy, GDP per worker per day; lung cancer's prevalence overall and in specific age bands; and age-specific workforce-participation rates.

This is not the whole story in Latin America. The informal economy can make up a substantial part of economic activity. The extent of informal activity is inevitably difficult to measure, but a recent IMF study used two techniques to estimate the size of national informal economies as a percentage of GDP. One relied largely on incentives to be informal, including tax levels and the size of the economy in general, while the other relied on measures of government effectiveness and the existence of corruption. The results indicate a wide variation in our study countries, with Chile, and by one of the measures Uruguay, doing as well as countries such as Denmark and Australia. In Bolivia, though, informal activity accounts for wealth equivalent to around 45% of formal GDP.[21]

Taking the national figures (and averages for the study country where these were not available) increases the total indirect cost of lung cancer by 26% or 29%, depending on the method used, to US$361m or US$369m.

The resultant figures—in aggregate about a fifth of direct costs for the formal economy and a little over a quarter including the informal economy—may seem small: they constitute barely noticeable fractions of total GDP in these countries. Their size reflects the interaction of biology and social policy. As discussed later in this report, lung cancer's average age of diagnosis is typically late, at around 70 in the US.[22] Retirement ages in Latin America come far earlier: as low as 60 years for men in Uruguay and Paraguay, and 58 in Bolivia. Accordingly, among the newly diagnosed, retirees outnumber workers. Without wages to lose, the former contribute nothing to aggregate costs and diminish per-case ones substantially.

[21] Leandro Medina and Friedrich Schneider, "Shadow Economies Around the World: What Did We Learn Over the Last 20 Years?", *IMF Working Paper*, number WP/18/17, January 2018.

[22] American Cancer Society, Key Statistics for Lung Cancer, available at: https://www.cancer.org/cancer/non-small-cell-lung-cancer/about/key-statistics.html

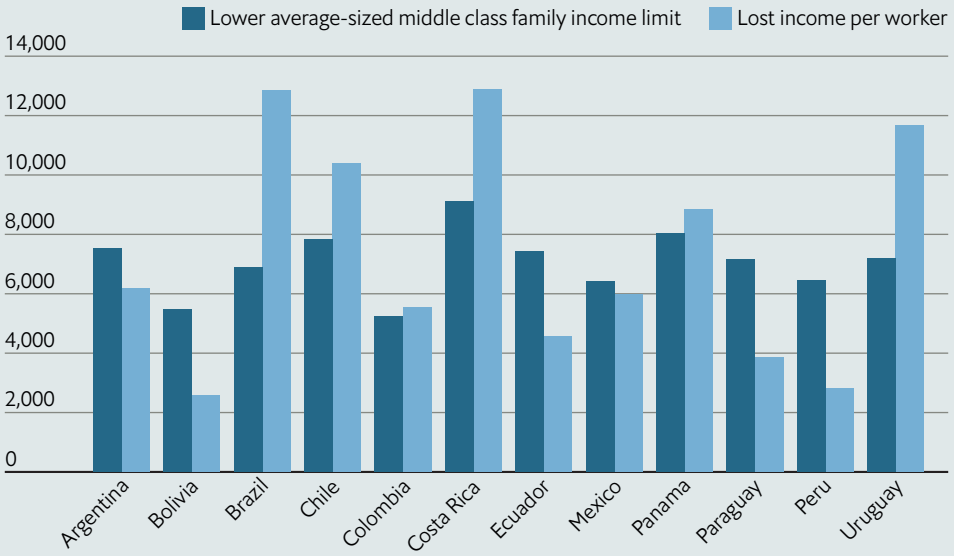
This is good news only to economists. To begin with, if nothing else changes, one unintended by-product of efforts in many study countries to extend retirement ages could be a higher economic cost for lung cancer.

More pressing at the individual level, public coverage of more than basic lung cancer care is unusual in the region (see access section below). Accordingly, many patients must pay for treatment out of retirement incomes and savings.

Those still in work also face huge challenges. The most common definition of middle class in Latin America is a household income of US$10-50 per person per day in purchasing power parity (PPP) terms,[23] and therefore less, to a varying degree by country, in nominal US dollars (in which our estimates are denominated). The accompanying graph translates the lower boundary of the middle class into nominal US dollars and multiplies it by the average number of members per household in each country. It also shows average lost wages per individual, by taking average lost GDP per worker and multiplying that by the labour share of GDP in each country.

Chart 2

The middle class and the cost of productivity lost to lung cancer, 2016
(US$)



Sources: Economist Intelligence Unit calculations; University of Groningen, Penn World Tables (for labour share of GDP data); World Bank (for PPP to US$ conversion per country).

Although relying on many assumptions, the chart's message is clear. The average wages lost if a household member in work were to develop lung cancer would devastate the finances of families that were not middle class, or at the lower-income end of that category. Even households at the upper end of the middle class would lose, on average in the 12 countries, 20% of annual household income in 2016. This, combined with direct costs of treatment in some cases, would send a large proportion of even middle-class patients into financial vulnerability.

[23] See, for example, Renos Vakis et al, "*Left Behind: Chronic Poverty in Latin America and the Caribbean*", 2015 & Luis F López-Calva and Eduardo Ortiz-Juarez, "A vulnerability approach to the definition of the middle class", *The Journal of Economic Inequality*, 2014.

Cost context and an unknown gap

Comparing lung cancer with prostate cancer provides an interesting contrast. More than twice as many people develop prostate cancer as lung cancer in Brazil, although 64% more die of the latter.[24] A recent, similar Economist Intelligence Unit cost analysis of prostate cancer in four Latin American countries provides instructive comparator figures: the study found that prostate cancer cost Brazil US$1.2bn in 2015,[25] thus slightly higher than lung cancer's total costs of US$940m in 2016, which indicates that lung cancer's higher mortality partially counteracts prostate cancer's much greater incidence.

The contributors to these costs differ more than their totals. Despite the much lower number of cases, lung-cancer treatment takes up much more money than prostate cancer: about US$823m, compared with US$620m. This is consistent with other research, including a 2016 British academic study. This study compared the total medical costs related to cancer patients during the five years after diagnosis. After removing underlying non-cancer healthcare outlay (derived from spending that occurred on appropriate control groups without cancer) lung-cancer expenses were twice as high per patient as prostate cancer ones.[26]

Indirect costs for prostate cancer, however, were markedly higher (US$580m to US$117m). Driving this are: the greater absolute number of prostate cases; lower workforce participation rates of women who, although a minority of lung-cancer cases, have no prostate gland; and lower average age of onset for prostate cancer (by four years in the US), so that fewer who develop it will have left the workforce.[27]

But is this high level of direct spending for lung cancer appropriate, especially given the frequently debated cost of many cancer treatments? Health-system resource allocation is inevitably a political decision and any specific intervention should be cost-effective. Nevertheless, in making choices, high-level comparisons provide a useful perspective.

In our study, the estimated direct costs for lung cancer paid by Brazil's public health service, SUS, is US$250m for 2016. This comes to 0.36% of government non-capital health spending (based on health spending data from the WHO for 2015). If the SUS were to spend on its three-quarters of the population at the same rate per patient as the private sector does, the equivalent figures would be US$1.7bn and 2.5%.

Lung cancer's burden depends on the measure. The disease exacted 1.2% of Brazil's 2016 disability-adjusted life years, a metric combining mortality and time spent living with a disease; it was also responsible for 2.3% of deaths that year.[28] This suggests that, while provision on the private sector's scale might be inappropriate, current state spending seems markedly low given the scale of lung cancer's current burden in Brazil.

Calling spending levels further into question, our study figures may even present too generous a picture. The process for estimating the Brazilian outlay, and therefore that for other study countries, first determines treatment costs per person at specific public and private facilities, and then multiplies the resultant numbers by national prevalence figures. This implicitly assumes that everyone who

[24] IARC Globocan, Database, Incidence/Mortality > Rates: Cancers by population. Available at: http://globocan.iarc.fr/Pages/summary_table_pop_sel.aspx

[25] The Economist Intelligence Unit, "*Tackling the burden of prostate cancer in Latin America: The prospects for patient-centred care*", 2017.

[26] Mauro Laudicella et al, "Cost of care for cancer patients in England: evidence from population-based patient-level data", *British Journal of Cancer*, 2016.

[27] American Cancer Society, Key Statistics for Lung Cancer.

[28] IHME, GBD Results Tool.

develops lung cancer gets diagnosed and treated with the degree of aggression used in either public or private hospitals.

This is unlikely for the region, or even Brazil. Dr Raez points out that, for those diagnosed, especially by non-expert clinicians unaware of recent treatment advances, "cancer nihilism" all too often skews treatment decisions. "A lot of times, general practitioners send them straight to palliative care or hospice. They don't think the fight is worth it." An additional consideration, he adds, is that palliative care is much cheaper than running a battery of genetic tests and prescribing expensive anti-cancer treatment accordingly.

Nor does everyone with the disease even get this far. In Brazil, as in study countries overall, 20% of lung-cancer cases come to the attention of registries only through death certificates. Poor health service-registry communication no doubt contributes but is not the whole problem.[29] For other cancers, where the same fragmentation would also exist, only 9% of registrations depend on death certificates.[30] Gilberto Lopes, director of global oncology at the University of Miami Miller School of Medicine, who has extensive cancer-treatment experience in Brazil, observes: "A lot of people just don't get diagnosed." For these individuals, direct care costs are nil, although the indirect ones remain.

Both missed diagnosis and undertreatment would dampen the actual spending on lung cancer in Brazil, and therefore the other countries, below the model estimates, but it is impossible to say how much. Our figures remain the most reasonable ones available if used with suitable reservation.

III. A closer look at the risks: more than just tobacco

Addressing this human and economic burden of lung cancer means understanding what it is and what drives it. Lung cancer itself is a collection of diseases rather than a monolith. Some are increasingly vulnerable to new treatments, others are not (see Box: what is lung cancer?). Its risks are also multifaceted.

Tobacco's dominant, but incomplete, responsibility

For all the diversity in lung cancer, one constant is the role tobacco plays in causing it. The link with smoking has been incontrovertible since as far back as the 1950s.[31] It requires no elucidation here. However, while the dominant cause of lung cancer in the region, it is not alone. The oft-repeated conventional wisdom that tobacco underlies 80% to 90% of incidence applies largely in wealthy countries,[32] not less developed ones.[33] For lung cancer, Latin America often falls into the latter camp: in Chile, for example, 40% of women with the disease were never-smokers. So too were, according to a recent, albeit small, study in Bolivia, 68% of those diagnosed in the past three years at the National Lung Institute.[34]

Self-evidently, tobacco's contribution to incidence varies depending on the extent of smoking and other risks. Methodologies for weighing their relative contribution all have flaws,[35] but the GBD estimates that, on aggregate in the study countries, 64% of all lung cancers are caused by tobacco.

[29] Economist Intelligence Unit calculations based on IARC, *Cancer in Five Continents*, "Indices of data quality (Volume X): All sites except non-melanoma skin (C00-96 exc. C44)" & "Indices of data quality (Volume X): Lung (C33-34)".

[30] Ibid.

[31] Otis W Brawley et al, "The First Surgeon General's Report on Smoking and Health: The 50th Anniversary", *CA: A Cancer Journal for Clinicians*, 2014.

[32] Centers for Disease Control and Prevention, *What Are the Risk Factors for Lung Cancer?*. Available at: https://www.cdc.gov/cancer/lung/basic_info/risk_factors.htm

[33] Farhad Islami et al, "Global trends of lung cancer mortality and smoking prevalence", *Translational Lung Cancer Research*, 2015.

[34] "En Bolivia, más mujeres sufren cáncer de pulmón", *Página Siete*, March 17th 2018 & "Pronóstico ytolerancia al tratamiento en cáncer de pulmón", *Revista Buena Salud*, July 30th 2014.

[35] Nabil Tachfouti et al, "Mortality attributable to tobacco: review of different methods", *Archives of Public Health*, 2014.

Inevitably, the range is wide, going from just 35% in Ecuador, with its historically low smoking rates, to 82% in Uruguay, once a regional leader in tobacco consumption.[36]

Other key lung carcinogens

These figures show both tobacco control's crucial importance for addressing Latin American lung cancer, but also the substantial burden arising from other causes. The GBD data are not outliers here. Dr Lopes reports that figures available from the region indicate that at least a quarter of those with lung cancer never smoked. Put another way, were all tobacco-attributed mortality removed, lung cancer would remain the eighth deadliest form of the disease in the study countries—roughly as deadly as cancer of the cervix.[37] Moreover, while the latter is declining, "we are seeing a rise in the number of lung cancers among those who have never smoked, though we don't quite understand why", according to Dr Lopes.

The lack of information on, and awareness of, these other risks in Latin America, however, is worrying. Various chemicals, through environmental or workplace contact, cause the vast majority of non-tobacco lung cancers.[38] Most individually have limited impact: occupational exposure to asbestos, for example, accounts for around 0.5% of incidence in Latin America's four most populous countries.[39]

Several specific lung carcinogens are nevertheless noteworthy in the region:

Radon: globally, after tobacco, the biggest cause of lung cancer is radon-222, an odourless, colourless gas. It is a product of radioactive decay by solid radon, itself usually a result of decaying uranium. Both metals occur naturally worldwide. A WHO review found that radon induces 3-14% of lung cancer, depending on the country. However, while the gas increases the risk of developing lung cancer for everyone exposed, it most often works in synergy with tobacco smoke, so that elimination of either would prevent a majority of radon-related lung cancer.[40]

Latin America's risk level is unclear. Presence of the gas varies as widely with geography as do its precursor metals. It certainly exists at unhealthy concentrations in parts of the region. Mexican data estimate that the lung-cancer effect of radon is roughly the same as in the US,[41] where it contributes 10-14% of all lung cancers and is the main cause of 3-4%.[42]

Initial surveys over a decade ago, drawing on very limited evidence and covering only seven study countries, suggested that Mexico had the highest household concentrations of radon in the region.[43] With further research, this view will probably change. Brazil, for example, possesses some of the world's largest uranium reserves, and Peru has roughly 80% as much per km^2,[44] so the preconditions for radon certainly exist. A 2015 survey in Lima, where a third of Peruvians live, found that, in 88% of districts measured, average mean concentrations exceeded WHO recommendations.[45] In Brazil, although the national picture remains unclear, studies have found worryingly high household radon concentrations in parts of Bahia, Rio Grande do Norte, Minas Gerais, São Paulo and Rio de Janeiro. An extreme case shows the danger: Caetite, a major Brazilian uranium mining centre, has radon concentrations ten times the WHO recommended maximum and lung cancer rates 19 times the national average.[46]

[36] Economist Intelligence Unit calculations based on data from IHME, GBD Results Tool, and IARC Globocan, Database Incidence/Mortality > Rates: Cancers by population.

[37] Economist Intelligence Unit calculations based on data from IHME, GBD Results Tool.

[38] For a detailed list, see R William Field and Brian L Withers, "Occupational and Environmental Causes of Lung Cancer", *Clinical Chest Medicine*, 2012.

[39] Roberto Pasetto et al, "Occupational Burden of Asbestos-related Cancer in Argentina, Brazil, Colombia, and Mexico", *Annals of Global Health*, 2014.

[40] WHO, "*WHO Handbook on Indoor Radon*", 2009.

[41] A Ángeles and G Espinosa, "Study of epidemiological risk of lung cancer in Mexico due indoor radon exposure", *AIP Conference Proceedings*, 2014.

[42] National Academy of Sciences, "Health Effects of Exposure to Radon: BEIR VI", 1999.

[43] Jan M Zielinski, "Mapping of Residential Radon in the World", presentation, 2014 & A Canoba et al, "Indoor radon measurements in six Latin American countries", *Geofísica Internacional*, 2002.

[44] Based on data from Nuclear Energy Agency and International Atomic Energy Agency, "*Uranium 2016: Resources, Production and Demand*". Available at: http://www.oecd-nea.org/ndd/pubs/2016/7301-uranium-2016.pdf & worldatlas, https://www.worldatlas.com/

[45] P Pereyra et al, "Concentration Measurements of Radon 222 Indoors in Lima–Peru", *International Journal of Physics*, 2015.

[46] "Radônio, uma ameaça", #carta, September 21st 2015.

Other countries, though, are less affected. Measurements in Argentina, for example, found that average household radon concentrations in 13 of 14 Argentinian provinces were within healthy limits and, in the exception of Santa Cruz, just 1% above.[47]

In short, radon is likely an important national, or even local, source of lung-cancer risks in several study countries, but not a region-wide issue. Lack of data, though, makes it hard for people to know if they live in a hot spot.

Air pollution: indoor and outdoor air pollution can cause lung cancer: the former is an important concern in several study countries, while the latter, to some extent, in all.

Indoor coal use, especially with poor ventilation, is a known lung carcinogen. Wood is strongly suspected.[48] A practice more associated with Africa and Asia than Latin America, more than one in five households in Bolivia (23%), Peru (34%) and Paraguay (42%) still use solid fuel indoors to heat or cook.[49] Worse still, as Dr Mas says of Peru, many such residences "have no ventilation, so cooking in the middle of the house is an issue. We don't have a high incidence of smoking, but in the High Andes a significant proportion of lung-cancer cases are related to the use of wood or biomass combustion in low ventilation environments."

The GBD estimates that indoor solid-fuel use causes 13% of lung cancer in these three countries collectively. Elsewhere in the study, where the practice is less common, the aggregate figure is below 3%.[50] It may be more widespread. Dr Arrieta explains that women's high level of wood-smoke exposure throughout the region, and differences from tobacco smoke in how this induces cancer, could help explain the high proportion of epidermal growth factor receptor (EGFR) mutations among Hispanics.

Outdoor air pollution, especially particulate matter—both PM10 and PM2.5—has recently also been acknowledged to induce lung cancer.[51] Latin America almost completely lacks specific studies on this causal link, but not the pollution itself. In the study countries, 110 cities monitor PM10 concentrations. Just 6% were below the WHO recommended average annual limit. Among the 52 that monitor PM2.5, the figure is only 8%. In both cases, about 40% of cities have levels more than double the WHO limits (see Chart 3).[52] Adding to the impact, UN data show that 83% of the aggregate study-country population live in urban areas.[53] Across these states, the GBD estimates that over 8% of lung cancer is caused by such pollution.[54]

Arsenic: arsenic in potential drinking-water sources is usually natural in Latin America. It is so pervasive in groundwater in parts of the region, including in the Andes, Amazon Basin and Paraguay Basin, that certain indigenous peoples have genetic mutations to metabolise it.[55] Mining-related pollution can also introduce, or increase, the chemical in groundwater.

In sufficient quantities in drinking water, arsenic causes lung cancer, among other diseases. The connection is particularly well-studied in Chile. The diversion of water from the Toconce and Holajar rivers into the drinking supply of Antofagasta in 1958 drove the arsenic concentration—already roughly nine times today's WHO recommended limit—to 87 times the WHO limit. Water treatment addressed

[47] The WHO recommended limit on average radon-gas concentration is 100 Bq/m3 (see WHO, "*Radon and health*". Available at: http://www.who.int/news-room/fact-sheets/detail/radon-and-health). The figures for Argentinian provinces are from J P Bonetto et al, "Radon Measurements in Argentina", presentation at Latin American Symposium on Radon—II Symposium on Radon in Brazil (Towards a National Radon Program), 2014.

[48] R William Field and Brian L Withers, "Occupational and Environmental Causes of Lung Cancer", *Clinical Chest Medicine*, 2012.

[49] Global Health Observatory data repository, "Population using solid fuels (estimates) - Data by country". Available at: http://apps.who.int/gho/data/node.main.135

[50] Economist Intelligence Unit calculations based on data from IHME, GBD Results Tool.

[51] Dana Loomis et al, "The carcinogenicity of outdoor air pollution", *Lancet*, 2013.

[52] Economist Intelligence Unit calculations based on figures in WHO Global Urban Ambient Air Pollution Database (update 2016). Available at: http://www.who.int/phe/health_topics/outdoorair/databases/cities/en/

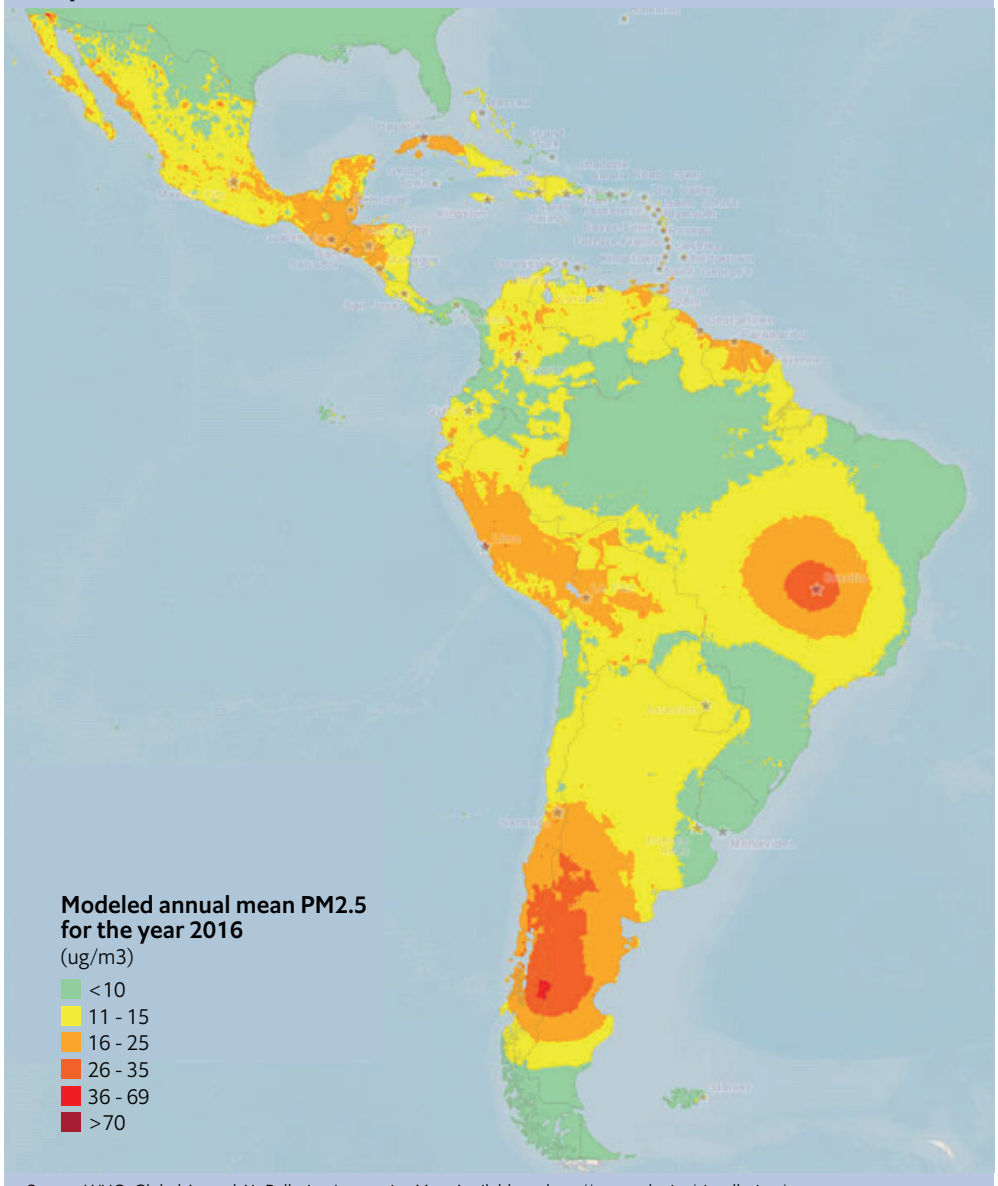
[53] Economist Intelligence Unit calculations based on figures in UN Population Division, "World Urbanization Prospects 2018", "File 1: Population of Urban and Rural Areas at Mid-Year (thousands) and Percentage Urban, 2018". Available at: https://esa.un.org/unpd/wup/dataquery/

[54] Economist Intelligence Unit calculations based on data from IHME, GBD Results Tool.

[55] Carina M Schlebusch et al, "Human Adaptation to Arsenic-Rich Environments", *Molecular Biology and Evolution*, 2015.

Chart 3

Air pollution in Latin America, 2016



Source: WHO, Global Annual Air Pollution Interactive Map. Available at: http://maps.who.int/airpollution/

the problem in the early 1970s, but the arsenic is the prime suspect for the surrounding region having a lung-cancer mortality rate more than triple that of a similar area in another part of Chile.[56]

No estimates exist for the proportion of lung cancer that arsenic causes in the region, but the issue goes far beyond Chile. Argentina and Mexico in particular have also seen substantial research into the health effects, although on other diseases than lung cancer.[57] More generally, every study country,

[56] Guillermo Marshall et al, "Fifty-Year Study of Lung and Bladder Cancer Mortality in Chile Related to Arsenic in Drinking Water", *Journal of the National Cancer Institute*, 2007.

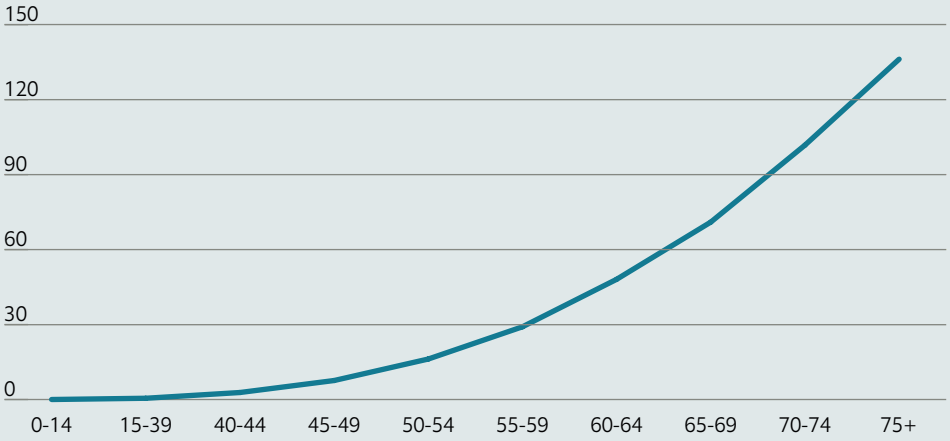
[57] Tyler R McClintock et al, "Arsenic Exposure in Latin America: Biomarkers, Risk Assessments and Related Health Effects", *Science of the Total Environment*, 2012 & Jochen Bundschuh et al., "One century of arsenic exposure in Latin America: A review of history and occurrence from 14 countries", *Science of the Total Environment*, 2012.

except Panama, has reports of at least some drinking water sources with actual or potential arsenic contamination.

Age: this correlates strongly with lung-cancer risk, with age-specific mortality growing exponentially from birth (see Chart 4). Growing older, though, is a correlate of cancer, not a cause. The reason is that major lung carcinogens have substantial latency—the time between risk exposure and disease appearance. In several populations with good data, 20-30 years have separated the statistical peaks in smoking prevalence and lung-cancer incidence.[58] Latency for arsenic exposure appears to be on the same order.[59] Studies of radon-exposed miners also indicate a mean figure of 20 years.[60] Moreover, in every case the figures making up these averages vary substantially, so that lung-cancer risk remains elevated, if slowly diminishing, for potentially decades longer.[61]

Chart 4

Lung-cancer rates per 100,000 people by age band
(Aggregate for study countries, 2012)



Source: IARC Globocan Database, Incidence/Mortality > Rates: Cancers by population.

IV. Latin America's future lung-cancer burden: countervailing winds

Given this combination of risks, where is Latin America's lung-cancer burden headed? The interplay of several underlying trends among these risks will shape incidence, and therefore the human and economic burden of the disease, in the coming years. Whether the situation will get better or worse will depend, to some extent, on the metric used.

Three forms of disease data are potentially relevant. First is the total number of cases, which has clear practical implications for healthcare systems. Population growth in Latin America is projected to continue, which will almost inevitably bring more cases in most medical conditions. So, changes in the "crude rate", or the number of cases per head, is also important to inform whether a disease needs a different relative priority within healthcare. The third, and most commonly used metric in international studies, is the age-standardised rate. Because it adjusts the crude rate for differences in population age

[58] Danny Youlden et al, "The International Epidemiology of Lung Cancer Geographical Distribution and Secular Trends", Journal of Thoracic Oncology, 2008 & Tim Adair et al, "Reconstruction of long-term tobacco consumption trends in Australia and their relationship to lung cancer mortality", Cancer Causes & Control, 2011.

[59] Guillermo Marshall et al, "Fifty-Year Study of Lung and Bladder Cancer Mortality in Chile Related to Arsenic in Drinking Water", *Journal of the National Cancer Institute*, 2007.

[60] Gonzalo Carrillo et al., "Radon and its effects on the health of uranium mine workers", *Medicina y Seguridad del Trabajo*, 2015.

[61] For example, for arsenic, Craig Steinmaus et al, "Drinking Water Arsenic in Northern Chile: High Cancer Risks 40 Years after Exposure Cessation", *Cancer Epidemiology, Biomarkers & Prevention*, 2013.

structure between countries, or the same country over time, it best measures comparative underlying risk.

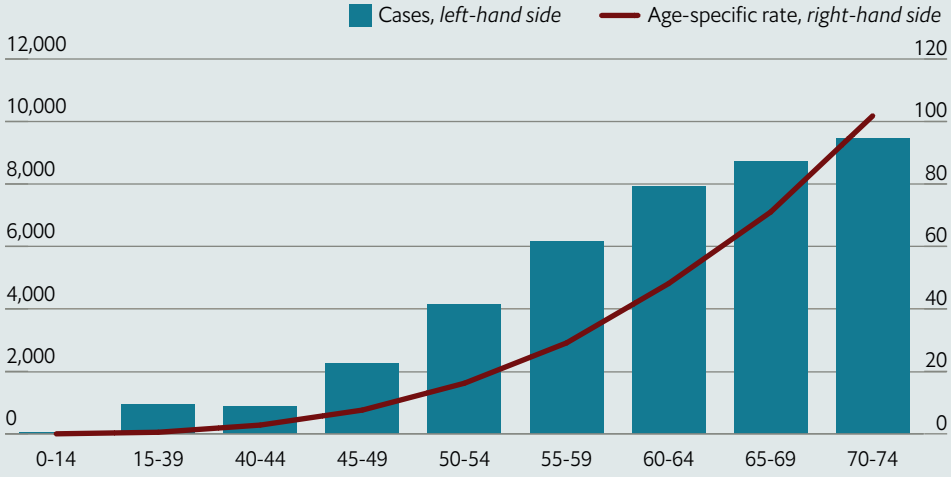
The challenge of assessing the region's future lung-cancer burden is that trends for these three metrics point in different directions.

An important reason is Latin America's rapid population ageing. Median age in the 12 study countries increased, on average, by 4.5 years from 2000-15; by 2030 it will have risen nearly five more. Increased life expectancy plays a big part in this. In all these countries, except Bolivia, it is more than 70 years; in nine it is above 75; and in Costa Rica and Chile it comes in at 80. The latter equals the North American average.[62]

The potential implications for age-correlated lung-cancer risk are stark. The chart below superimposes on the age-band risk data pictured earlier the estimated mortality figures by the same age groups. Cases grow much more slowly than the age-specific rate from around age 60 because the smaller number of people surviving to later years currently more than offsets heightened risk. As average lifespans increase, though, the greater numbers reaching their 60s, 70s and beyond threatens significantly more lung cancer.

Chart 5

Lung-cancer rates per 100,000 people and number of cases by age band
(Aggregate for study countries, 2012)



Source: IARC Globocan Database, Incidence/Mortality > Rates: Cancers by population.

The IARC estimates, based solely on demographic change, that aggregate lung-cancer deaths in the study countries will rise from around 60,000 in 2012 to just under 110,000 by 2030. Roughly a quarter of that increase comes from projected population growth, the rest from ageing.[63]

Actual case numbers, though, will almost certainly be lower because the extent of the dominant cause—tobacco smoking—has shifted substantially. Assessing the extent and timing of this behavioural

[62] UN, "*World Population Prospects: The 2017 Revision*". Available at: https://www.un.org/development/desa/publications/world-population-prospects-the-2017-revision.html

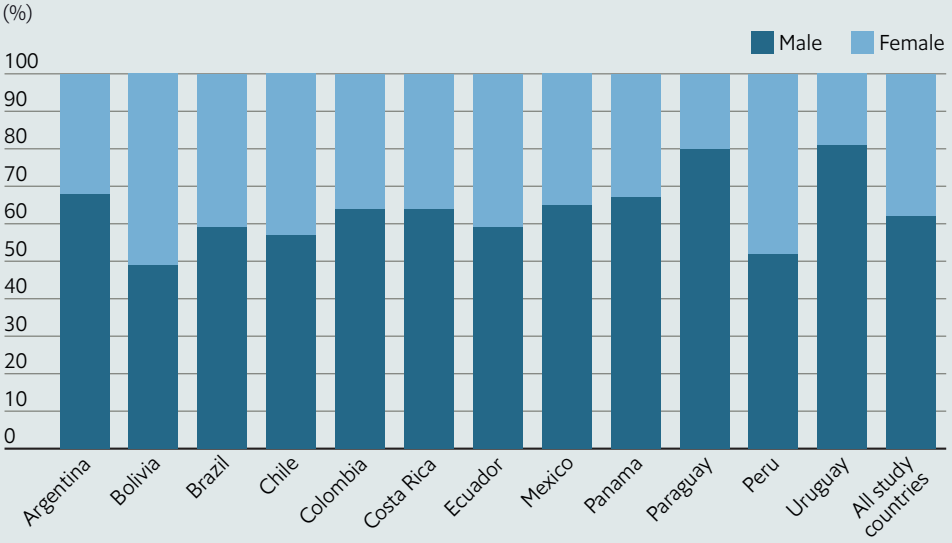
[63] Data generated at IARC Globocan Database, Online analysis > Prediction. Available at: http://globocan.iarc.fr/Pages/burden_sel.aspx

change is difficult, however, because once again data are scarce or unclear. A recent analysis of global smoking rates from 1980 to 2014 found only one relevant pre-1990 national survey from any of our study countries, and just a handful from the following decade.[64] This 1980-2014 analysis, along with a more recent WHO one covering 2000-15, report extensive decline in smoking in Latin America. The WHO report puts the drop in the percentage of smokers at between a third and 40% from 2000 to 2015, a trend expected to continue. Panama's decline of over a half during these years was the world's greatest, and even in the worst performer in our study, Chile, smoking fell by more than a fifth.[65]

Digging deeper, however, reveals complicating gender differences (see Chart 6). Everywhere, more men than women smoke, which explains higher male lung-cancer rates in all the study countries but Bolivia. Peru also has a nearly equal split in terms of incidence. In both countries this may reflect the high level of indoor solid-fuel cooking discussed before, with such work typically done by women.

Chart 6

Proportion of national lung-cancer incidence among men and women, 2012



Sources: Economist Intelligence Unit calculations, IARC Globocan Database, Incidence/Mortality > Rates: Cancers by population.

This male-female divergence has varied over time. The growth in the popularity of smoking began earlier with men, as did its decline. The drop has been noticeable for several decades among males but, as late as 2008, researchers voiced concerns about the continued growth of female smoking in the region.[66] Even now, although the WHO 2000-15 study projects a decline in female smoking prevalence, a look at the national surveys it uses suggests in half of the study countries a flat rather than dropping trend. As Mauricio Cuello, deputy director of Uruguay's Instituto Nacional del Cáncer, notes: "Unfortunately, women have been more refractory to campaigns to reduce smoking."

The decline of smoking should decrease lung-cancer incidence and mortality, first among men and later among women, but these data uncertainties, combined with only broad knowledge of latency, discussed previously, impede precise predictions.

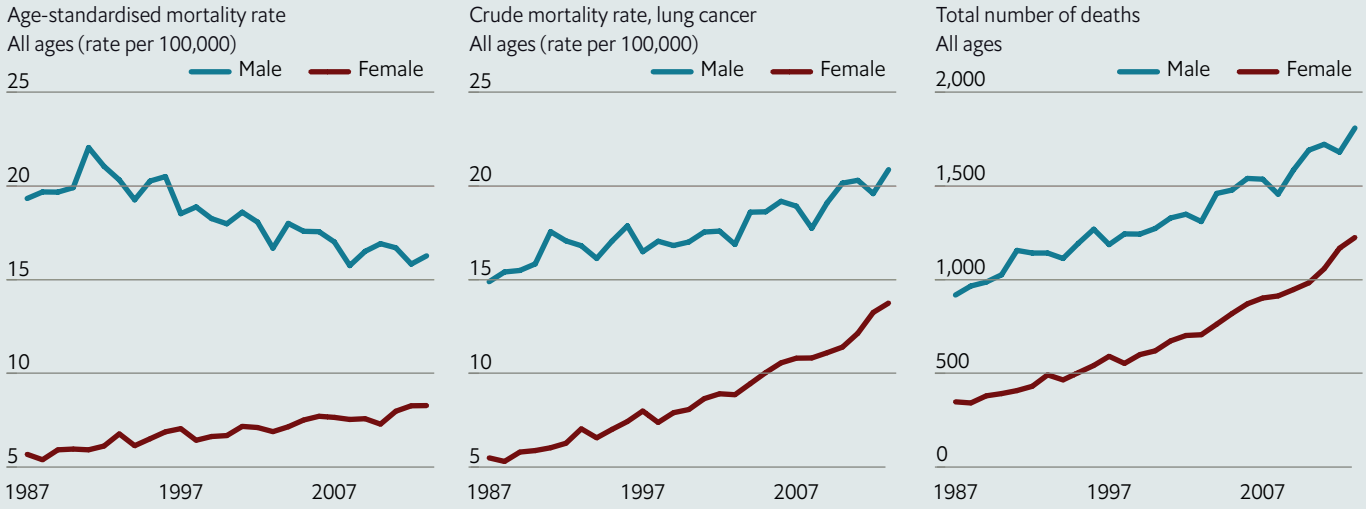
[64] Marie Ng et al, "Smoking Prevalence and Cigarette Consumption in 187 Countries, 1980-2012", *JAMA*, 2014.

[65] WHO, WHO global report on trends in prevalence of tobacco smoking, 2015.

[66] Freddie Bray and Marion Piñeros, "Cancer patterns, trends and projections in Latin America and the Caribbean", 2016 & Alberto Palloni et al, "The Enduring Effects of Smoking in Latin America", *American Journal of Public Health*, 2015 & Fernando Müller and Luis Wehbe, "Smoking and smoking cessation in Latin America: a review of the current situation and available treatments", *International Journal of COPD*, 2008.

Chart 7

Same deaths, different implications: the example of Chile



Source: IARC, Cancer Mortality Database.

Further complicating accurate prognostication is fuzziness in trends from the recent past. High-quality cancer time-series data figures are rare in the region. Within the constraints of available information, the IARC has the most authoritative estimates. Its age-standardised mortality projections for study countries evince several broad patterns that reflect the reduction in tobacco consumption.[67]

One pattern, seen in Brazil, Chile and Uruguay, is a rise in female ASR mortality in parallel with a substantial drop among men, usually starting about the mid-1990s, although sometimes earlier (see Chart 7). This combination is consistent with tobacco-use trends in all three countries, which historically had among the region's highest smoking rates, especially among males.

Panama and Ecuador evince a different experience, with male and female ASR seeing small declines, especially in more recent years, or staying largely flat. Peru is similar but has a slight rise in female ASR. All of these have historically had relatively low smoking rates and lung-cancer mortality. Presumably, even proportionally large reductions in such limited smoking would affect lung-cancer rates less.

Meanwhile, Mexico, Costa Rica and, more recently, Colombia have experienced marked drops in both male and female ASRs, although the absolute decline in Costa Rica's rate among women—never very high—was small. Other countries are outliers: Paraguay has been the only study country experiencing a rise in male ASR and Bolivia's data were insufficient for the IARC even to take an educated guess.

These clear improvements have not appeared to anything like the same extent in crude mortality rates and actual deaths. Among females, absolute case numbers have risen everywhere. The IARC estimates that the female crude rate increased in all study countries except Argentina and Mexico, where it stayed roughly flat.[68] Among men, Panama's crude rate is estimated to have flattened, with declines in Argentina and Mexico. Only Mexico has seen a drop in the actual number of male deaths—starting

[67] Based on data generated at IARC, Online analysis > Graphs: Time Trends. Available at: http://www-dep.iarc.fr/WHOdb/graph4_sel.asp. Although these data go to 2013, the trends are consistent with those projected in another study to 2017 for five study countries using death certificate-based data: G Carioli et al, "Cancer mortality predictions for 2017 in Latin America", *Annals of Oncology*, 2017.

[68] The IARC data indicate a small decline for Uruguay, but the country's own registry reports a slight increase according to a comparison between Registro Nacional de Cáncer, Cáncer de Pulmón en Uruguay [2010-2014], 2016 & Registro Nacional de Cáncer, Atlas De Mortalidad Por Cáncer en el Uruguay 2004-2008, 2011. PDF available at: http://www.comisioncancer.org.uy/andocasociado.aspx?361,1046.

around 2005—while it flattened in Argentina. Otherwise, the study countries are seeing mortality figures for both sexes go up to varying degrees.

Such long-term lung cancer data, as regional cancer registries provide, are consistent with the IARC estimates. Uruguay's registry reports a steady ASR male mortality drop of 1.2% per year and rise of 3.6% among women going back to 1990. For the five-year periods 2004-08 and 2010-14, though, the crude rate and the number of cases among men grew by 3.1% and 3.4% respectively, while for women these figures were 35% and 37%.[69] The Cali registry, one of the region's oldest, tells a similar story over a still-longer period (see Table 5).

Table 5: Cali registry mortality figures

Men			
	1984-1988	**2011-15**	**Change (%)**
ASR (per 100,000)	22.6	14.3	-37%
Crude rate (per 100,000)	13.3	14.3	8%
Number	421	799	90%
Women			
	1984-1988	**2011-15**	**Change (%)**
ASR (per 100,000)	9.2	7.3	-21%
Crude rate (per 100,000)	6.1	9.9	62%
Number	216	602	179%

Sources: Registro Poblacional de Cáncer de Cali, Colombia, "Tasas de mortalidad por cáncer de pulmon, bronquios y traquea especíazficas por edad, crudas y ajustadas por edad durante el periodo 1984-2015"; Economist Intelligence Unit calculations.

In sum, reduced tobacco consumption is becoming visible in some of the region's lung-cancer data. Male ASRs have already diminished in most study countries and should continue to do so with the further declines in smoking in recent decades. Female ASRs have so far dropped in fewer countries, but this should improve in due course.

Tobacco control has also saved lives (see tobacco control section in Chapter 2). If the adjusted rate for Cali had remained the same because of no change to the underlying risk, the rise in the number of male deaths between the two periods would have been nearly 300% rather than 90%.[70]

Nevertheless, reduced tobacco consumption has yet to stem the increase of lung-cancer mortality brought on by demographic change. Looking ahead to the near future, the most likely scenario is further growth in lung-cancer cases even as ASRs, and in due course crude rates, moderate. The exact numbers, however, are impossible to estimate.

V. The wider context

Before turning to how study countries are addressing lung cancer, a brief discussion of context is necessary.

[69] Economist Intelligence Unit calculations based on Registro Nacional de Cáncer, Cáncer de Pulmón en Uruguay [2010-2014], 2016 & Registro Nacional de Cáncer, Atlas De Mortalidad Por Cáncer en el Uruguay 2004-2008, 2011.

[70] Economist Intelligence Unit calculations based on Cali registry data.

Cancer control in Latin America

Lung cancer prevention and treatment are inevitably part of a wider effort. In *Cancer Control, Access and Inequality in Latin America: A tale of light and shadow*, The Economist Intelligence Unit examined this in extensive detail.[71] Its findings of most relevance here are:

- **Resources are limited for any cancer:** Latin American government health budgets are small in absolute and relative terms compared with those in developed countries. Moreover, cancer is often a low priority for fund allocation. Most countries have insufficient cancer control resources, including trained personnel and equipment, much of which is over-concentrated in large cities. This impedes treatment access.

- **Awareness and early detection often fall short:** aside from increasingly strong understanding of tobacco's dangers, in study countries general awareness of most cancer risks and symptoms remains inadequate, especially beyond better-educated demographic groups. Moreover, cancer screening has a mixed record in the region. Where used, notably for cervical and breast cancer, flaws in programme structure, service quality, infrastructure, follow-up and integration with other health services often greatly impede effectiveness.

- **Inefficient care and unequal access are common:** health-system fragmentation pervades and undermines Latin American cancer control. Many study countries have several parallel health systems. Pervasive poor communication, let alone interaction, between systems restricts the kind of cancer treatment available to that which an individual's provider happens to deliver. Those without private or social security-based insurance face the biggest challenges. Public health systems underperform private ones in most study countries. Moreover, while some government programmes to absorb the high costs of cancer care usually exist, many do not cover all cancers.

- **Palliative care is usually lacking:** in most study countries, palliative care services, if they exist, are insufficient with poor integration into mainstream healthcare systems.

The fight against tobacco: a civil war

Progress that study countries have made in tobacco control has occurred in the face of strong domestic and international opponents. Tobacco production is, notes Dr Cuello, "a very important industry in Latin American countries". Brazil and Argentina are the world's second- and tenth-largest tobacco growers, respectively, and the top and ninth-biggest exporters of unmanufactured leaf, respectively. For Brazil, foreign earnings were just shy of US$2bn in 2016, or over 1% of national exports.[72] Moreover, in Latin America in total, tobacco production and processing provide 650,000 jobs.[73]

Nor has industry activity declined because of anti-tobacco efforts. According to UN Food and Agriculture Organisation (FAO) data, the aggregate volume of tobacco leaf grown in the study countries stayed largely constant between 2008 and 2015, as did the resultant income denominated in PPP dollars.[74] As Diego Paonessa, executive director of the Liga Argentina de Lucha contra el Cáncer, a network of volunteers whose aim is to eradicate cancer through prevention and early detection, explains of his country: "Politicians think it is nice to talk about tobacco control but, in the north-west,

[71] The Economist Intelligence Unit, "*Cancer Control, Access and Inequality in Latin America*".

[72] Data from FAOSTAT database, UN Comtrade database. Available at: http://www.fao.org/faostat/en/#data/QC

[73] Jorge Tovar, "Tobacco Cultivation in Latin America", Centro de Estudios sobre Desarrollo Económico Working Papers #2014-12, 2014.

[74] Data from FAOSTAT database

we have a lot of tobacco production [that] earns a lot of money and has a lot of employees. We don't really talk about that much."

Nor has the tobacco industry taken increasing government tobacco control with equanimity. Every study country except Chile has seen a prominent legal challenge of some kind, with plaintiffs including the region's two major international firms (Philip Morris and BAT), leading domestic companies and, in Costa Rica, even members of parliament who publicly supported the industry.[75]

Complainants have tried various grounds, from grand constitutional claims about the separation of powers and freedom of expression to precise objections about which agency can issue a rule on flavouring in cigarettes. Venues have also been diverse, from domestic courts to a range of international tribunals and arbitration facilities, including the Andean Court of Justice, the World Trade Organisation's dispute settlement mechanism and the International Centre for Settlement of Investment Disputes.[76]

The last of these saw the highest-profile action, in which Philip Morris sought damages arising from Uruguay's stringent packaging legislation. The tribunal ruled for Uruguay in 2016,[77] and governments have typically won these cases, but the industry has scored some successes. Notably, in two cases launched in 2009 and 2010 by local Paraguayan firms, the country's supreme court ruled that ministerial decrees implementing the Framework Convention on Tobacco Control (FCTC), an international treaty aimed at the global tobacco epidemic, were unconstitutional; instead, legislation was needed.[78] The latter finally appeared, but only at the end of 2015.

Some producers are apparently seeking to undermine tobacco control through extrajudicial means. Tobacco smuggling in the region is a substantial problem: in Brazil, between 2008 and 2013, even while the total amount smoked declined, the proportion of illicit tobacco used rose from 16.6% to 31.1%; analyses usually point to Paraguay as the main source of the problem, including allegedly 73% of illegal tobacco sold in Latin America.[79]

Overall, as Dr Cuello warns, while tobacco "has been dealt a heavy blow in Uruguay, and in Latin America overall, anti-smoking measures have been constant and growing, this is not a tamed industry."

Stigma: collateral damage in the war against tobacco?

However essential, awareness-raising around tobacco risks can produce unintended negative effects. Recent doctoral research in Mexico and Uruguay indicates that exposure to tobacco-control messaging correlates with higher levels of stigma towards smoking.[80] This may encourage individuals to try to quit, but it has downsides even for tobacco control. Dr Cuevas notes that Mexico has strong tobacco-control measures, "but things are different if somebody seeks assistance from healthcare to stop smoking. There is a limited supply of help because people don't understand that [it] is an addiction."

Worse still, hostility towards smoking all too easily transfers to those who develop lung cancer. Dr Raez puts it bluntly: "Stigma is a major problem. In Latin America—as in other places in the world—the way we see lung cancer is that 'these guys are guilty. They did it to themselves.' There is no compassion."

[75] For details of court cases, see Tobacco Control Laws, Tobacco Litigation, website by Campaign for Tobacco-Free Kids. Available at: https://www.tobaccocontrollaws.org/litigation

[76] Sergio Puig, "Tobacco Litigation in International Courts", *Harvard International Law Journal*, 2016.

[77] Philip Morris and Abal Hermanos SA vs Uruguay, ICSID Case ARB/10/7, July 8th 2016.

[78] Tabacalera del Este SA et al. vs Paraguay, Sentencia No 754, Corte Suprema de Justicia October 18th 2010.

[79] Roberto Iglesias et al, "Estimating the size of illicit tobacco consumption in Brazil" *Tobacco Control*, 2017 & Benoît Gomis and Natalia Botero, "Sneaking a Smoke: Paraguay's Tobacco Business Fuels Latin America's Black Market", *Foreign Affairs*, 2016.

[80] Paula Lozano, "Smoking-related Stigma: A Public Health Tool Or A Damaging Force?", doctoral thesis, University of South Carolina Scholar Commons, 2016.

Survey data illustrate the problem's extent. In 2014 Harris Poll found that large majorities in Colombia (75%), Argentina (73%) and Mexico (68%) believe that those with lung cancer brought it on themselves through smoking. Majorities also agree in Colombia (70%), Argentina (62%) and Mexico (58%) that those with the disease in their countries receive little compassion. In this respect, regional respondents are far harsher than those elsewhere: the worldwide average was just 40%.[81]

More recently, Global Lung Cancer Coalition surveys found that, after counting out the many uncertain respondents, substantial proportions of people in Brazil (44%), Argentina (34%) and Mexico (31%) agree that, because of the link with smoking, "I have less sympathy for people with lung cancer than for people with other types of cancer". In the first two countries, levels of sympathy had even dropped in the preceding seven years.[82]

Stigma of this kind harms in multiple ways. Less money tends to be available for lung cancers than for others because of societal opprobrium, believes Dr Lopes. Stigma also makes some symptomatic individuals delay seeking medical help, increasing the problem of late diagnosis.[83] The effects carry over into the patient experience. Luciana Holtz, CEO of the Oncoguia Institute, a cancer education and patient advocacy group, explains that social isolation can result: "Patients really want to talk with others living with lung cancer, but it is difficult." Worse still, she adds, stigma impedes change. "As representative of a patient group, I know that when we have the patient voice, the patient experience with us, it makes the case stronger. But the stigma makes patients go silent because they sometimes are still smoking or don't know why they have this type of cancer. There is a sort of taboo."

[81] Encuesta Podría ser tu pulmón, Harris Poll, 2014.

[82] Global Lung Cancer Coalition, "Argentina: symptom awareness and attitudes to lung cancer: Findings from a global study", press release, January 2018 & "Brazil: symptom awareness and attitudes to lung cancer: Findings from a global study", press release, January 2018 & "Mexico: symptom awareness and attitudes to lung cancer: Findings from a global study", press release, January 2018.

[83] Lisa Carter-Harris, "Lung Cancer Stigma as a Barrier to Medical Help-Seeking Behavior: Practice Implications", *Journal of the American Association of Nurse Practitioners*, 2015.

CHAPTER 2: ASSESSING THE POLICY RESPONSE TO LUNG CANCER IN LATIN AMERICA

I. Introducing The Economist Intelligence Unit's Latin America Lung Cancer Traffic Lights

A quick overview

Like the risks and burden of lung cancers, health-system responses vary across Latin America, sometimes starkly. Eduardo Cazap, founder and first president of the Latin American and Caribbean Society of Medical Oncology, for example, says of lung-cancer treatment that "overall, Argentina is in relatively good shape" with appropriate guidelines and reasonably accessible care. In neighbouring Paraguay, by contrast, Miguel Agüero, a clinical oncologist at the country's Instituto Nacional del Cáncer, reports that "lung cancer is a disaster. We don't have regulations. We don't have guidelines. A few people are trying hard, but we have only one public hospital for cancer. We can't do much beyond basic chemotherapy."

Treatment is not the only element of lung-cancer control, but variations also pervade other key areas, such as awareness, advocacy, prevention, diagnosis, access, palliative care and data quality. To assess study countries across this range of fields, The Economist Intelligence Unit has created a traffic-light system. In general, for each area covered (called domains), a green light indicates that countries are doing well by relevant global or regional standards; amber denotes an area of concern; and red a need for substantial attention.[84]

The domains and the measures used within them (indicators) have been assessed using distinct criteria. They should not, therefore, be aggregated into a single traffic-light score. (For more details see Appendix II).

The traffic lights cover the most important regional lung-cancer issues. There are two sets: the first, called Priority Lights, are, according to this study's expert advisory board, the most immediately pressing. The second set, Important Lights, are also still essential for success but less likely to provide rapid benefit without progress on the priorities.

As with any simple scheme that models complex reality, caveats are essential. The indicators underlying the domain traffic lights are a mix of policy and outcomes data, so results may reflect hopes of how policy implementation might shape the environment as much as current conditions. The reality of information gaps also constrain the choice of indicators. Finally, while always seeking the best available information from international, national and academic sources, on occasion we have had to fall back on expert judgement.

[84] The full traffic-light results are available for download alongside this report: http://www.eiuperspectives.economist.com/LungCancerLatAm

Accordingly, rather than assigning precise scores, the traffic lights are offered as rough approximations. Our hope is not that they become a medal table, but spark discussion on how Latin American countries might better address the region's deadliest cancer.

BOX: HOW TO READ THE TRAFFIC LIGHTS

This study considers a range of areas (called domains) essential to lung-cancer control in Latin America. Each domain is made up of two or more distinct data points (called indicators). For each of the latter, every country received a light of red, amber or green. Domain scores were then assigned based on an average of the indicator lights.

What does this mean in practice? The scoring is designed so that a green light indicates that a country is doing well either by relevant global or regional international standards. An amber light means that the area is one of concern, and red that it requires substantial attention.

Because the indicators differ from domain to domain, the specific criteria on which the judgement is made inevitably vary. The example of Brazil's scores in three illustrative domains should illustrate the kind of data used and the likely meaning of a given score.

Brazil scores green on tobacco control. It has ratified the Framework Convention on Tobacco Control and, according to the World Health Organisation (WHO), has high compliance with this treaty on smoke-free public place and marketing legislation. It also has a low age-standardised smoking rate compared with the rest of the region. All is not perfect: its decline in smoking over the past 15 years has only been moderate compared with that in other study countries, and the level of tax as a percentage of the cost of a pack of cigarettes falls just shy of the WHO's recommendation of 70%. Nevertheless, these shortcomings are sufficiently small that the country still merits a green overall.

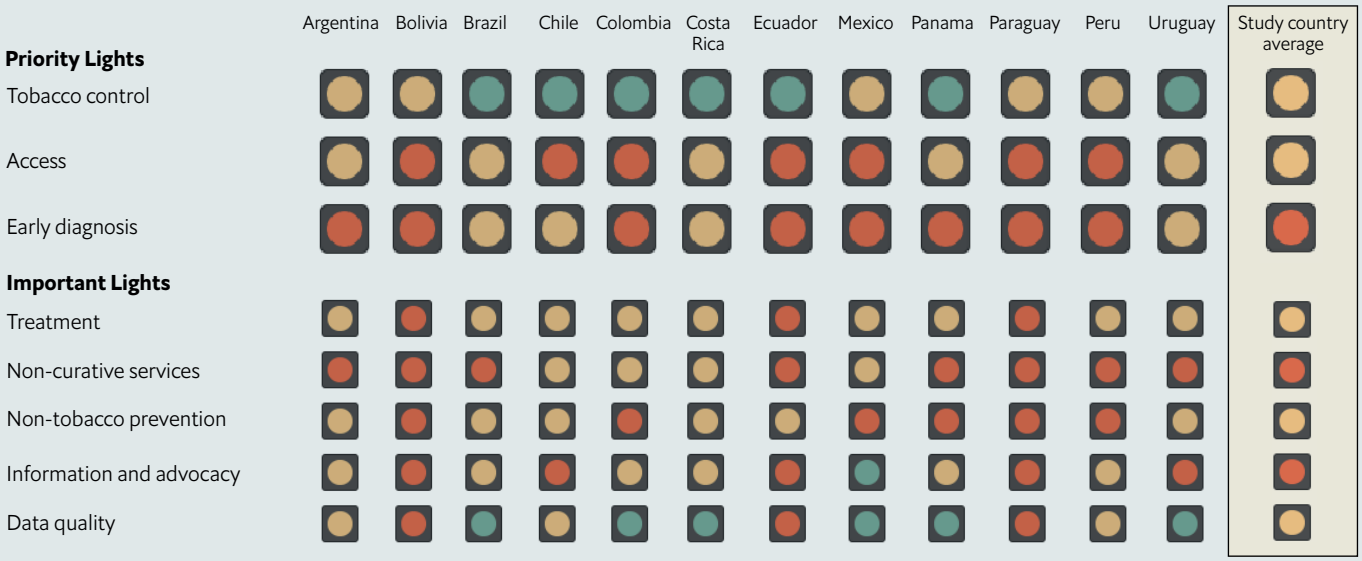
On non-tobacco prevention, however, Brazil's combination of strengths and weaknesses point to an amber rating. The country's regulations around the level of arsenic in drinking water meet WHO global guidelines, and the percentage of people using indoor solid fuel for heating and cooking is low by regional standards. By contrast, a lack of attention even to the measurement of household radon levels, combined with air-pollution levels well above WHO recommendations, indicate that more attention is needed on specific indicators within the domain.

Finally, Brazil gets a red light for non-curative services. There, low levels of palliative care by global standards and no indication of any attention to the incipient need for lung-cancer survivor services suggest that this area will need substantial work to meet the needs of those with lung cancer.

The traffic-light results are as follows:

Chart 8

Latin America Lung Cancer Traffic Lights: summary of results



Source: The Economist Intelligence Unit.

Before discussing the individual domains in detail, the lights collectively give two striking findings.

1) Disappointing results may reflect a low priority

The most immediate impression from the traffic lights is, despite some variation, how poorly the region is doing overall. No country is doing extremely well: just 14 greens appear amid far more ambers (42) and reds (40), in nearly equal numbers.

General cancer-control weaknesses, discussed in The Economist Intelligence Unit's report on cancer control in the region,[85] certainly contribute to this result. For example, indicators for oncologist numbers and equipment supply could apply to any cancer. Too often, though, the problem is worse for lung cancer. As discussed below, efforts to improve access to other cancers frequently leave out those in the lung. Dr Raez reports that Peru's much-praised cancer-control plan, Plan Esperanza, initially did so because health authorities did not see any interventions sufficiently cost-effective to justify government funding.

Limited research attention also indicates a poor-cousin status. Dr Lopes explains that lung cancer "gets a lot less funding per death than any of the next four or five deadliest forms of the disease". This global phenomenon is certainly present in Latin America.[86] In Chile, only 2% of oncology research funding goes to lung cancer, roughly consistent with the proportion of scientists working on it there. Similarly, between 2004 and 2013 only 2.5% of Brazilian oncology papers dealt with lung cancer, and just 2% in Mexico between 1989 and 2012.[87]

[85] The Economist Intelligence Unit, "*Cancer Control, Access and Inequality in Latin America*".

[86] Ajay Aggarwal et al, "The State of Lung Cancer Research: A Global Analysis", *Journal of Thoracic Oncology*, 2016.

[87] Jorge Jimenez de la Jara et al, "A snapshot of cancer in Chile: analytical frameworks for developing a cancer policy", *BioMed Central*, 2015 & Ajay Aggarwal et al, "The State of Lung Cancer Research: A Global Analysis" & Ajay Aggarwal et al, "The challenge of cancer in middle-income countries with an ageing population: Mexico as a case study", *ecancermedicalscience*, 2015.

More generally, the region's poor showing reflects a lack of official attention. Dr Mas notes that "lung cancer is a big problem in my country but seen as secondary by the government compared to other cancers". Dr Agüero goes further, putting responsibility for deficiencies in his country with "the government. I don't think they care about lung cancer." More generally, says Mr Paonessa, "the disease is not on political agendas in Latin America".

2) Progress must move beyond tobacco control and data quality

As Dr Cuello puts it, in Latin America, "without any doubt the biggest issue in addressing lung cancer is control of smoking". Dr Raez agrees that this is a fundamental first step, adding that it is "more cost-effective than to fight cancer with expensive medications that prolong survival but don't cure patients".

Most Latin American countries have made substantial progress in this area since the FCTC entered into force in 2005. Seven achieve green lights in this domain and a further five amber. As discussed below, the work is by no means perfect nor complete, but it is a strong start. Similarly, data quality, with six green lights, reflects marked advances over even five or ten years ago, which are discussed further in the relevant section.

Far more worrying are the other traffic lights. Tobacco control accounts for half of all green lights in the study; data quality for all but one of the rest. As Dr Lopes notes, though, "while it is extremely important that countries work against tobacco, it is extremely short-sighted [to rely on that alone]. If everyone stops smoking today, it will take two to three decades for incidence to go down, and tens of millions of people will still develop lung cancer." Moreover, notes Dr Arrieta, whatever the future holds will not change "the tangible problem of addressing patients already with the disease." Other elements of cancer control need attention now.

II. Prevention (tobacco control and non-tobacco prevention)

Chart 9

Tobacco control and non-tobacco prevention domains

Source: The Economist Intelligence Unit.

Dr Raez explains that, even with recent medical advances, lung cancer's poor survival and expensive treatment mean that "the primary focus has to be prevention. It makes more sense." The two prevention-related traffic lights are discussed together here.

Good on tobacco

As already noted, tobacco control is an area of relative strength. All study countries have ratified the FCTC except Argentina, and its health authorities and non-governmental organisations (NGOs) are pushing for the country to do so this year. Implementation has also been active. The WHO reports that domestic legislation in eight study countries complies highly with treaty provisions on smoke-free public places and marketing. Rules in two more countries do so moderately well.

The record on tobacco pricing is more ambiguous. Only three study countries impose taxes to the WHO's recommend degree (70% of the price of a cigarette pack), and in nine the overall price of tobacco relative to GDP is less than the average in their World Bank income groups. Affordability, though, has decreased in seven study countries and risen nowhere.

One of the key findings of our study on cancer control in Latin America was the lack of spending on healthcare in general—and cancer in particular. As we wrote in that report, "the result of these budgetary choices is that most countries have insufficient resources for current cancer needs, let alone likely future ones…Access to medication…is the area where study countries on average do worst."[88] Little has changed since.

However, tobacco taxes have become increasingly widespread. Their main aim is to reduce smoking, where they are of varying but usually measurable effectiveness, with particular impact among those less financially well-off and young people.[89] These taxes also, though, do raise money: in the seven study countries for which data are available, taxes on tobacco and cigarettes make up on average 1.1% of state revenue.[90]

The best available evidence is that active enactment of tobacco-control laws and policies should reduce future smoking, and therefore, eventually, lung-cancer levels.[91] The resultant green lights, however, should not breed complacency for two reasons.

First, the battle against tobacco is far from won. Indeed, it is easy to forget how recently the battle was joined. Dr Arrieta reminds that, in most countries, anti-smoking measures "have only begun to be implemented in the past ten years, and their success will rely on their ability to profoundly impact lifestyle over the long term". Moreover, in three study countries, age-standardised smoking prevalence still stands above 20%.

The other issue is that the green lights result, to a great extent, from the existence of legislation and policies. However, Ignacio Zervino, co-ordinator of programmes at the Argentine advocacy group Fundación Pacientes con Cáncer de Pulmón, explains that "poor implementation of law is a big challenge". Dr Cazap agrees: "Latin America has many policies. We need to make them operative. That is the issue."

Inevitably, implementation varies. On smoke-free places, for example, an academic study found good compliance in Colombia, and Uruguay has a simple web page where individuals can report violations.[92] By contrast, most bars and restaurants in Mexico City and in Morelos just to the south do not follow

[88] The Economist Intelligence Unit, "*Cancer Control, Access and Inequality in Latin America*".

[89] IARC, "Effectiveness of Tax and Price Policies for Tobacco Control", 2011.

[90] Economist Intelligence Unit calculations based on data in OECD, "*Revenue Statistics in Latin America and the Caribbean 1990-2016*", 2018.

[91] Anh Ngo et al, "The effect of MPOWER scores on cigarette smoking prevalence and consumption", *Preventative Medicine*, 2017 & David Levy et al, "Smoking-related deaths averted due to three years of policy progress", *Bulletin of the World Health Organisation*, 2013.

[92] Randy Uang et al, "Implementación de espacios libres de humo de tabaco en Colombia: monitoreo, financiamiento externo y apoyo empresarial", *Salud Pública de México*, 2017 & Uruguayan Ministry of Public Health, "Denuncia por incumplimiento de tabaco".

the law. Moreover, Panama is considering changes to its legislation because of frequent complaints of non-compliance.[93] Finally, Osvaldo Aren, an oncologist and executive director of the Centro de Investigación Clínica Bradford Hill in Chile, believes that, whatever the legislation, in practice in his country "no effective government policies are in place to persuade people not to smoke". That government's health ministry admits that it does not know how well the rules are followed because local—rather than national—authorities deal with complaints.[94]

On the positive side, widespread anti-tobacco efforts appear capable of exerting a cross-border effect independent of specific enforcement. The clearest example is Paraguay. It did not pass an anti-tobacco law until December 2015, and the necessary implementing regulations appeared only in August 2017.[95] Even their impact appears muted: Dr Agüero reports that, in practice, "right now we don't have tobacco control. There are so many places where you are free to smoke and no real regulation". Oncologists are lobbying for change. Yet, even in this environment, the WHO estimates that unstandardised smoking prevalence fell from 30% to 18% between 2000 and 2015.[96]

A welcome, region-wide cultural shift, driven by heightened anti-tobacco awareness, is the likely explanation. Dr Lopes explains that "you don't see ads in Formula 1 races, which are big in Latin America, or smoking in American movies or telenovelas from the region. In Brazil, you barely see people smoking in public places. Smoking is not culturally desirable. That is a huge difference from two generations ago."

Less progress on everything beyond tobacco

If study countries have largely grasped the nettle of tobacco-related prevention, action related to other risks—notably radon, air pollution and arsenic—lags behind, with no green lights and half of countries showing a red light in our traffic-light assessment. Take Panama, for example, which was only slightly below average in this domain. Juan-Pablo Barés, president of FUNDACANCER, a Panamanian NGO, and former director-general of Panama's Instituto Oncologico Nacional, notes of his country that knowledge of these risks "is very low. We don't have any kind of programme that systematically evaluates" them.

On household radon, little evidence exists for any attention. Only four countries have seen substantial efforts to measure the problem, let alone determine potential necessary remediation policies.

Arsenic in drinking water has seen more regulation. Most countries have adopted the WHO's recommended 10 microgram/litre limit. But rules do not necessarily equate to action. Although Chile and Argentina have invested substantially in systems to remove arsenic from drinking water,[97] elsewhere regulations are often more aspiration than reality.

Recently, for example, high water arsenic levels in Costa Rica's Guancaste province turned into a political issue after an ombudsman's report claimed the Ministry of Health and others kept relevant information hidden.[98] High levels appeared in the first large Peruvian survey of the risk in 2014: of over 100 drinking-water sources across 12 districts, arsenic in over half were greater than five times

[93] "Morelos sin avances en cumplimiento a Ley de establecimientos 100% libres de humo de tabaco", *Codice*, July 12th 2017 & "Incumplen Ley Antitabaco 60% de bares y restaurantes en CDMX", *VertigoPolitico*, May 3rd 2017 & "Autoridades reforzarán el cumplimiento de la Ley Antitabaco", *La Prensa*, April 5th 2016.

[94] "A tres años de la ley antitabaco, Salud desconoce las sanciones aplicadas", *La Tercera*, April 24th 2016.

[95] Gaceta Oficial de la República del Paraguay, Ley N° 5538, December 30th 2015 & Presidencia de la República del Paraguay / Ministerio de Salud Publica y Bienestar Social, Decreto N° 7605/2017, August 14th 2017.

[96] WHO, WHO global report on trends in prevalence of tobacco smoking.

[97] José Luis Cortina et al, "Latin American experiences in arsenic removal from drinking water and mining effluents", chapter 22 in Marek Bryjak et al eds, *Innovative Materials and Methods for Water Treatment: Solutions for Arsenic and Chromium Removal*, 2018.

[98] "AyA, Salud e ICE 'ocultaron' contaminación de agua con arsénico", *Semanario Universidad*, November 22nd 2017.

WHO recommendations.[99] Elevated concentrations regularly appear in drinking water in various parts of Mexico,[100] and a 2017 study found levels eight times the safe limit just south of Buenos Aires.[101] Meanwhile, this year a study of some 200 wells in Brazilian Amazonia also reported too much arsenic.[102]

New reports keep appearing because, in general, the problem's scope is little understood. As Dr Cazap notes, "there is practically no, or very, very limited information about radon or other pollutants, such as arsenic. Governments are extremely reluctant to face the situation, in part because it is expensive to control these contaminants." This is dangerous. Dr Aren explains that the measurement of arsenic levels was the first step towards addressing the issue in northern Chile.

Data on air pollution, by contrast, are readily available, but the message is worrying. As noted earlier, outdoor air pollution is pervasive. As a result, ten study countries achieve the lowest result on this indicator. Worse still, policy falls behind global recommendations, with national PM10 and PM2.5 limits exceeding WHO recommendations in all study countries, except for PM2.5 in Bolivia.[103] Uruguay's clean urban air measurements—and therefore in part contributing to its amber light on this domain—may reflect Montevideo's sea breezes more than policy. The country lacked formal air-quality standards as late as 2015, although it was working on them.[104] Meanwhile, in countries with high use of indoor solid fuel, people are unaware of the health danger, warns Dr Mas: "We need to educate them on ventilation and simple things, such as installations of chimneys." He adds, however, that in Peru campaigns are occurring.

Prevention, like general lung-cancer control, must go beyond tobacco control.

[99] Christine Marie George et al, "Arsenic exposure in drinking water: an unrecognized health threat in Peru", *Bulletin of the World Health Organisation*, 2014.

[100] Andrew T Fisher et al, "Standards for arsenic in drinking water: Implications for policy in Mexico", *Journal of Public Health Policy*, 2017.

[101] R S Barranquero et al, "Arsenic, fluoride and other trace elements in the Argentina Pampean plain", *Geologica Acta*, 2017.

[102] "Arsenic and manganese contamination in Amazonia groundwater", press release, Swiss Federal Institute of Aquatic Science and Technology, April 10th 2018.

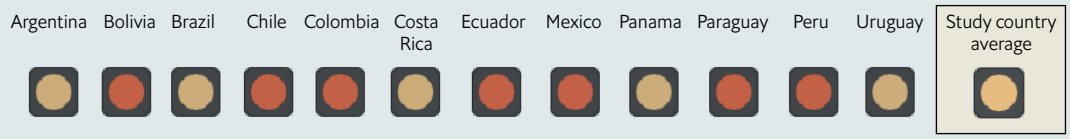
[103] Horacio Riojas-Rodríguez et al, "Air pollution management and control in Latin America and the Caribbean: implications for climate change", *Revista Panamericana de Salud Pública*, 2016.

[104] "Dirección de Medio Ambiente impulsa normas de calidad de aire, agua y gestión de residuos", press release, September 9th 2015, Uruguayan President's Office.

III. Access

Chart 10

Access domain



Source: The Economist Intelligence Unit.

Cost

In Latin America those with private insurance or very deep pockets can get excellent care in sometimes world-class facilities. This traffic light, though, focuses on access to diagnosis and treatment for those with restricted means or living outside of major population centres. No country does this very well: five score amber, seven red. The access barriers presented by the general issues of healthcare fragmentation and inadequate resourcing, discussed in The Economist Intelligence Unit's report on cancer control in the region,[105] are probably exacerbated by lung-cancer stigma.

The problems begin with the differences in care quality between private and public providers. Given the diversity of healthcare systems, no single country's experience is representative, but variations between Brazil's SUS and private providers are instructive.

[105] The Economist Intelligence Unit, "Cancer Control, *Access and Inequality in Latin America*".

Research and interviews for our economic model determined elements of lung-cancer treatment in two SUS facilities—one specialist cancer and one general hospital—along with a typical private facility. Rates of surgery and use of adjuvant chemotherapy were similar, but marked differences appeared elsewhere. For example, the private facility's diagnosis process involved a computed tomography (CT) scan and biopsy for every patient, but just 40% in public facilities had the first and 5% the second. Similarly, half of private patients had pre-surgery chemotherapy, but no SUS patients did. The quality and content of specific medical interventions also differed widely: stage III and IV chemotherapy costs per treated patient, for example, were 25-35 times higher in the private sector. The net result is the private facility's around seven times greater per-head patient spending, as noted in Chapter 1.

Such figures, especially on chemotherapy, do not surprise Dr Lopes. "In Brazil, patients in private healthcare get coverage for all approved drugs," he explains. "In the public sector, most have access only to generic chemotherapy, except in some centres of excellence with supplemental funding." Ms Holtz agrees: "In the private system, you have a list of procedures and drugs that your doctor can prescribe. In the public one, the list is not the same."

Brazil is no exception. Across the region, another sign of the lack of access to better therapies is the pattern of testing for genetic mutation of cancers. One survey found, for example, that testing for tumour susceptibility to immunotherapy is almost entirely "limited to the patients with private insurance".[106] Dr Aren adds that, in Chile, because pharmaceutical companies cover the cost "EGFR and ALK [anaplastic lymphoma kinase] testing is available for all. The dilemma in public health-system patients is whether or not to test, knowing that targeted therapy will not be available because it has limited financial coverage."

Nor is Brazil Latin America's worst case. In some countries, a simple lack of drugs or equipment impedes access to treatment. For example, in April 2018 in La Paz, Bolivia, all public-sector radiotherapy ground to a halt for over two weeks when the only available machine stopped working.[107] Meanwhile, in Ecuador, failure of the state system to pay outstanding debts to hospitals has impeded the purchase of necessary cancer drugs.[108] Finally, in Paraguay's sole public-sector cancer provider, Dr Agüero reports "no money for drugs" beyond basic chemotherapy.

Such access problems are common to treatment for all cancers in less economically advanced Latin American countries. Wealthier states usually have a government fund that pays for patient treatment for high-cost diseases, including cancers, either for everyone or for the uninsured. Some of these schemes, though, omit lung cancer, notably Mexico's Seguro Popular, which covers the more than 40% of the population without some private or social security-based insurance, and Chile's GES, which offers explicit coverage guarantees for all, including the 81% enrolled in public insurance. In 2018 Dr Aren reports, another Chilean government fund, the Programa de Prestaciones Valoradas, began to provide limited payments for certain targeted therapies, but these still fall well short of the full cost. Similarly, notes Dr Mas, despite improved access to treatment for other types of cancer under Peru's Plan Esperanza, for lung cancer "in general, patients receive attention, but it is limited, with access to new medicines very limited". For example, ALK-related medications are not covered.

[106] Juliano Cé Coelho, "Molecular Testing for Non-Small Cell Lung Cancer in Latin America", *Journal of Thoracic Oncology*, 2017.

[107] "Pacientes con cáncer de la CNS están 13 días sin radioterapia; se alista compra de servicios", *Le Razon*, April 30th 2018.

[108] "El cáncer en Ecuador: ¿y los pacientes qué?", *PlanV*, March 15th 2016 & "José Jouvín: 'Solca espera un plan de pagos para el 24 de abril'", expreso.ec, April 7th 2018.

As a result, in such countries, lung cancer is both a financial and health catastrophe. Dr Aren notes that in Chile, "access to therapy as recommended by international guidelines is a true challenge for most patients with lung cancer". Dr Arrieta goes further: in Mexico lung-cancer treatment for the uninsured "is completely unaffordable. Therapy costs have increased significantly since the introduction of targeted therapies, and people within our country's socioeconomic landscape cannot afford this."

Government reluctance to cover lung-cancer costs results partly from a depressing, but understandable, calculation when resources are limited. The treatment is expensive compared with some other cancers and, even with recent advances, frequently does little more than extend life briefly, and then only for those in specific sub-groups. As Dr Lopes notes, "we are still in the early stages of the treatment revolution, and this affects policymakers". Dr Mas adds that "access to targeted therapies and immunotherapy in general at current prices is threatening to any economy in the world". Cost is an especially acute problem in the region where, despite lower GDP, comparative studies have found health systems needing to pay more for specific high-cost drugs, including those for lung cancer, than in Spain or the UK.[109] Dr Mas believes that agreements between the state and pharmaceutical companies will be needed to improve access.

Attitudes toward lung cancer may also play a role in the lack of coverage. Dr Arrieta believes that Seguro Popular's lack of coverage results in part from the "huge stigma" those with the disease face. Dr Raez suspects stigma may also have contributed, along with limited funding, to Plan Esperanza policymakers' original reluctance to address lung cancer and give priority to other neoplasms.

Some study countries have shown, though, that it is possible to meet the cost of lung-cancer care. Our traffic-light system shows that Argentina in theory covers a wide range of drug treatments, including immunotherapy, although, as discussed below, obtaining these can be complex. In the country there is also good access to other elements of care such as surgery and radiotherapy. Dr Cazap reports that, in Argentina, these elements are of reasonable quality, although waiting times could be improved. Similarly, in Panama, for the small number not covered by Social Security, the Instituto Oncológico does an economic assessment of ability to pay based on which it frequently waives all charges. Dr Barés says that one of the things international colleagues most likely do not know about is Panama's degree of drug availability for patients and free treatment.

Other countries may be driven to this even against their will. Patients, in their quest to gain access to high-cost medications, have been pursuing litigation based on the constitutional or general rights to health that are common in the region. In Brazil, for example, in the second half of 2014, 4.8% of cancer patients used the courts to get access to their drugs.[110] The practice goes further, with numerous examples from Argentina, Costa Rica, Colombia, Uruguay and recently also Ecuador. Lung-cancer drugs, in particular, have seen rulings in Costa Rica and Ecuador, as well as being one of the most common type of medications sued for in Brazil.[111]

[109] Federico Tobar and José Charreau, "Comparación internacional del precio de los medicamentos de alto costo: Argentina, Países del Cono sur, España e Italia", Instituto de Estudios Sobre Políticas de Salud, 2011.

[110] Gilberto Lopes, "Suing the state for access to cancer medications: The Brazilian experience", *Journal of Clinical Oncology*, 2015.

[112] Ole Norheim and Bruce Wilson, "Health Rights Litigation and Access to Medicines: Priority Classification of Successful Cases from Costa Rica's Constitutional Chamber of the Supreme Court", *Health and Human Rights Journal*, 2014 & Roberto Iunes et al, "Universal Health Coverage and Litigation in Latin America", *World Bank en breve notes*, number 178, 2012 & "Pacientes con cáncer acuden a los jueces para tener fármacos", *El Comercio*, September 6th 2017.

In Argentina, meanwhile, Mr Paonessa reports that "the books say we have universal assistance, but in the real world this does not always happen", with legal action sometimes needed to obtain genetic therapy or immunotherapy. Dr Cazap adds that because patients exercise their rights in this way, some insurers cover lung-cancer treatment fully, but others argue that they lack resources and insist that patients access government programmes. "It is frequent to have litigation," he adds. "At the end of the day, most patients receive medication either through their own coverage or through the government with delays. The system is a bit chaotic."

The drawbacks of having, in Mr Paonessa's words "a judge take the decision, not the doctors" are clear, but patients across Latin America are unlikely to go quietly into the night.

Location

Even free healthcare is little good if one cannot afford the time and money needed to reach it. The frequent concentration of medical equipment and personnel in cities, especially capitals, in Latin America makes the geography of care a particularly difficult issue for those living outside of these cores. As a proxy for their access challenges, the traffic lights measure the proportion of radiation therapy equipment concentrated in each country's capital or major cities and the percentage of the population that lives there. In most, the differences between the concentration of linear accelerators in major cities and the concentration of the population there were high (over 20 percentage points). In Argentina and Brazil, they are small, but further research shows that rural access remains challenging in both.[112]

The results do not surprise Dr Raez: "Most healthcare technology is concentrated in the major cities in Latin America, so we have similar problems with access in most countries." In practice, in larger countries especially, this problem can make access to diagnostic or treatment services extremely difficult or practically impossible for those in rural areas and small cities. Even in geographically compact countries, the challenge is significant. Panama's high-quality, financially accessible public lung-cancer care is available only in the country's single public-sector cancer hospital, in Panama City. Only 43% of the population live in the capital, although most can reach it after a few hours' journey. However, 10% of the population lives in far western Chiriquí province. For them, a car or public bus journey to Panama City takes 7-8 hours with clear traffic, turning a weekly chemotherapy treatment from a matter of hours into a three-day round trip for the patient and any accompanying carer.

Easy solutions do not exist: cancer centres often require complex equipment, making concentration of facilities natural amid limited resources. Nevertheless, even where other elements of access are good, the urban-rural divide remains a substantial challenge in much of Latin America.

[112] For example, see Paul Goss et al, "The Challenges of Cancer Control Facing Argentina", New York Presbyterian Cancer Care website, 2014 & Carolina Gonzaga, "Temporal trends in female breast cancer mortality in Brazil and correlations with social inequalities", *BMC Public Health*, 2015.

IV. Early diagnosis

Chart 11

Early diagnosis domain

Source: The Economist Intelligence Unit.

Widespread late diagnosis

Finding lung cancer early is, literally, a matter of life and death. Current US relative five-year survival figures show 55% for localised lung cancer but just 4% of those found with a distant spread.[113] Japan's divide is even starker, with stage I relative five-year survival at 80%, but stage IV just 4%.[114]

Comparable figures are lacking for Latin America, although overall lung-cancer survival rates in the study countries typically lag markedly behind the US and Japan.[115] What stage-specific studies do exist in Latin America, though, also indicate a similar rapid decline of survivability with later diagnoses. One Buenos Aires clinic had stage I five-year survival as high as 75%. Meanwhile, Cali cancer registry data indicate a survival drop from 15% at early stage III to 4% at stage IV.[116]

Despite its importance for outcomes, early diagnosis is one of the two domains in which study countries as a group do worst, with eight red and four amber lights, all of which are only slightly above our scoring barrier for red. Although data are lacking—itself a sign of problems—the traffic-light research found that in most of these countries around 85% or more are diagnosed at late stages (III or IV), with the majority at stage IV. In Mexico, the figures are particularly stark, with a study of all patients at the country's Instituto Nacional de Cancerología between 2007 and 2010 finding that 98.6% of diagnoses occurred in late stages, including 75% or all cases arriving at stage IV.[117] Dr Arrieta explains that "stage I-II lung cancer is practically anecdotal in our country".

Admittedly, catching the disease early is challenging, as symptoms do not appear until later stages. Nevertheless, some other countries do better. In the US, only 66% of lung cancer is caught at late stages, while in Japan the figure is just 58%.[118] While far from ideal results, as Dr Lopes notes, reaching them in Latin American ones "would mean helping a lot of people".

Unfortunately, explains Dr Arrieta, the region faces a large "challenge in referring patients to facilities with the necessary infrastructure and personnel to make an accurate diagnosis".

Is screening the answer?

This leads to the biggest current debate around lung cancer in the region: the potential utility of low-dose screening with CT machines.[119] Dr Raez and Dr Lopes favour its introduction to the greatest extent possible. The strongest evidence for this approach comes from the US National Lung Screening

[113] Kimberly D Miller et al, "Cancer Treatment and Survivorship Statistics, 2016", *CA*, 2016.

[114] Japan National Cancer Centre et al, "2008生存率集計報告書" [in Japanese], 2017.

[115] Claudia Allemani et al, "Global surveillance of trends in cancer survival 2000–14 (CONCORD-3)", *Lancet*, 2018.

[116] Gustavo Lyons et al, "Tamaño del tumor y supervivencia en carcinoma de pulmón, estadio IA," *Medicina (Buenos Aires)*, 2008 & Carolina Chavarriaga Florez and Jennifer Paola Bonilla Rojas, "Supervivencia de cáncer de pulmón. Manizales 2003-2007", Master of Public Health thesis, University of Manizales, 2013.

[117] Oscar Arrieta et al, "Clinical and Pathological Characteristics, Outcome and Mutational Profiles Regarding Non–Small-Cell Lung Cancer Related to Wood-Smoke Exposure", Journal of Thoracic Oncology, 2012.

[118] Japan National Cancer Centre et al, "2008生存率集計報告書".

[119] For a fuller discussion, see Luis Raez et al, "Challenges in Lung Cancer Screening in Latin America", *Journal of Global Oncology*, 2018.

Trial (NLST). It found that screening decreased lung-cancer mortality by 21%, largely through earlier case identification (63% were stage I and 7% stage II).[120] US health authorities now recommend annual screening for those aged 55-80 years with a 30 pack-year smoking history and who either currently smoke or gave up in the past 15 years.[121]

In Japan, meanwhile, although not formally recommended, screening even among non-smokers has become popular in several prefectures. In the city of Hitachi, where 40% of residents had undergone CTs for lung cancer, in 2009 mortality from the disease was 24% lower than in the country overall.[122] Widespread screening may also explain why 35% of lung cancer in Japan is found at stage I.[123]

In Latin America, however, screening generates muted enthusiasm at best. A Brazilian trial (BRELT1), supported by the SUS, screened nearly 800 patients, but this is by far the largest completed pilot in any study country to date.[124] Mexico, meanwhile, is engaged in a 3,000-patient trial that targets a risk profile of greater relevance to its own population than that in the NLST, in particular including those with high levels of exposure to wood smoke.[125] By contrast, Argentina's consensus statement and Colombia's national clinical guidelines consider screening, but say it needs further study.[126]

Several reasons underlay such reservations. First are concerns about effectiveness in Latin America given high rates of lung disease such as tuberculosis; however, the BRELT1 results suggests that, while this may lead to more false positives, further imaging can dismiss almost all of these.[127] The more pressing concern is health-system capacity. Screening requires CT scanners, which are expensive and, as the traffic-light data indicate, already in short supply in several study countries. Even in Europe, which is better supplied, such equipment is insufficient for this task.[128] Dr Raez explains that, in practice, "We can't put pressure on governments when screening is still expensive and the availability of the needed CT scanners limited."

Even with the equipment, though, screening might do little good. Such programmes in the region have a very poor record of overcoming health-system fragmentation, so that those with positive results too often are not assessed further, let alone referred for treatment.[129] Both steps would be essential for lung-cancer screening, as it throws up many false positives, even in the best circumstances. Mauricio Burotto, until recently an oncologist at Clinica Alemana de Santiago in Chile, notes that "we don't have the medical infrastructure currently to support screening". Dr Cuello agrees: "Addressing fragmentation of the care process is the priority."

Dr Arrieta is a proponent of screening and considers it necessary to reduce late diagnoses. However, he acknowledges that implementation of this "in a very economically strained health system is very hard" and does not, on its own, overcome organisational barriers within health systems to early diagnosis. "In all honesty," he adds, "the early diagnosis of lung cancer in the region will likely be a medium-term goal; it requires a large amount of government input and therefore it will not depend solely on the will of physicians."

[120] National Lung Screening Trial Research Team, "Reduced lung-cancer mortality with low-dose computed tomographic screening", *NEJM*, 2011.

[121] GuidelineCentral, Lung Cancer: Screening—Adults Ages 55-80 who have a 30 pack-year smoking history and currently smoke or have quit within the past 15 years

[122] Takeshi Nawa, "Low-dose Computed Tomography Screening in Japan", *Journal of Thoracic Imagining*, 2015.

[123] Japan National Cancer Centre et al, "2008生存率集計報告書".

[124] Ricardo Sales dos Santos et al, "Low-dose CT screening for lung cancer in Brazil: a study protocol", *Jornal Brasileiro de Pneumologia*, 2014.

[125] Abelardo García ed, *Cáncer De Pulmón De Células No Pequeñas*, 2016.

[126] For example, "Consenso Nacional Intersociedades sobre Carcinoma de Pulmón No Células Pequeñas" (Argentina), 2012 & "Guia de Practica Clinica...cáncer de pulmón" (Colombia), 2014.

[127] Ricardo Sales dos Santos et al, "Do Current Lung Cancer Screening Guidelines Apply for Populations With High Prevalence of Granulomatous Disease? Results From the First Brazilian Lung Cancer Screening Trial (BRELT1)", *Annals of Thoracic Surgery*, 2015.

[128] Raez et al, "Challenges", 2018.

[129] The Economist Intelligence Unit, "*Cancer Control, Access and Inequality in Latin America*".

Ms Holtz puts the dilemma succinctly and echoes our thinking: given the balance of arguments on both sides "we don't know whether to fight for screening or not."

If not screening, then what?

Without screening, though, how should health systems diagnose lung cancer earlier?

One clear need is better health-system responsiveness. This will not downstage every diagnosis but should lead to finding some cases more quickly. Currently, though, the diagnosis process is often hit and miss. In a survey of Brazilian lung-cancer patients for Instituto Oncoguia, 39% reported having to see three or more clinicians before a diagnosis, and 35% complained of having to go "from doctor to doctor" to find someone who could accurately identify the disease.[130] In Paraguay, meanwhile, 70% of lung-cancer diagnoses take place at the National Institute of Respiratory Diseases because people are referred there rather than to an oncologist.[131]

Such difficulty in diagnosis is understandable. Patricia Mondragón—chair of the Mexican patient advocacy group Respirando con Valor—explains that lung cancer "can easily be confused with other respiratory conditions, such as pneumonia," making insufficient training among general practitioners a bigger problem.

Ms Holtz adds that, as a result, "different kinds of doctors—lung doctors, cardiologists, gynaecologists, general practitioners—need to be more aware of the symptoms." More than that, says Dr Lopes, physicians need a "cultural change, so that they have a low threshold for imaging for any smokers who complain of new symptoms." The training must also involve unlearning unhelpful legacy knowledge among those who know at least something. Dr Raez notes, "you still see a nihilistic approach from some primary care physicians [who] are not very familiar with the advances in lung cancer care over the last five years."

No single solution exists that will alleviate fragmentation and improve clinician knowledge of lung cancer. Accordingly, the traffic lights reward any substantial effort to enable earlier diagnosis, including Brazil's trial of screening but also guidelines on lung cancer for primary physicians in Mexico, and measurement and targets for speed of diagnosis in Colombia. Costa Rica got full marks for an integrated system to fast-track suspected lung-cancer cases.[132] Unfortunately, in most study countries, no substantial effort could be found.

A final blockage to diagnosis is patient fear of being stigmatised. We found, however, no evidence of any study country with a formal effort, either self-standing or as part of the national cancer control plan, to address lung-cancer stigma. This was the only indicator on which every country scored red.

Health-system reluctance on lung-cancer screening is understandable but it makes the general lack of effort to speed up screening all the more worrying.

[130] Instituto Oncoguia, "Pesquisa sobre Câncer de Pulmão", slide presentation, December 19th 2016.

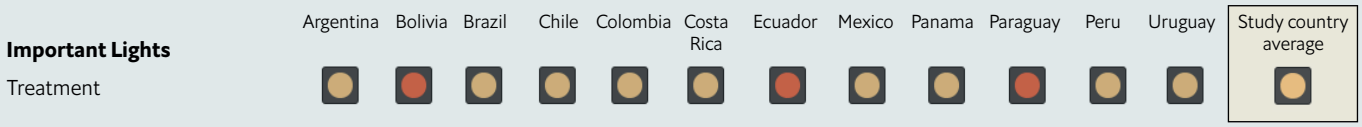
[131] "Cáncer pulmonar deja dos muertos por día", ABC Color, November 21st 2017.

[132] "CCSS diseña vía rápida para atención de enfermos con sospecha de cáncer de pulmón", *Primero en Noticias*, February 19th 2014.

V. Treatment

Chart 12

Treatment domain



Source: The Economist Intelligence Unit.

After tobacco control and data quality, treatment is the area where the region does best. Although no country gets green, Uruguay falls just short, and overall, nine countries reach amber. This may even be slightly harsh. This domain includes an outcomes indicator, the M:I ratios based on 2012 data. No study country does very well here, but any improvement since that year will not appear in the data. Had this been excluded, Argentina and Uruguay would have scored green, suggesting reasonably strong treatment efforts. That said, neither is perfect by any means. Dr Cuello says of Uruguay that, while its strengths in treatment include "equity and resource availability, care processes are very fragmented".

Guidelines and their implementation

Good treatment requires coherence and conformity with best practice, an important step towards which is publication of authoritative treatment guidelines. These can come from ministries of health, individual medical societies, or groups of such associations issuing "consensus documents". The type of source does not inevitably guarantee acceptance: for example, before the recent appearance of guidelines from the Sociedade Brasileira de Oncologia Clínica, Brazilian private hospitals routinely used international guidelines rather than those from its health ministry because they found the latter unhelpful.[133] Accordingly, our study looked for the existence of a document that commands general respect.

These exist in eight study countries. Seven documents are reasonably comprehensive (our proxy for assessing them was an emphasis on multidisciplinary care and recommendations of genetic testing of relevant tumours). Costa Rica falls short on the latter, but Gonzalo Vargas Chacón, co-ordinator of the country's Consenso Nacional de Especialistas en Cáncer, reports that he chairs a group led by the college of physicians and surgeons and partnering with the health ministry to draw up more advanced ones. Four countries are without guidelines: Bolivia, Paraguay, Ecuador and Chile. The latter is particularly surprising, given its generally higher level of health-system resources, although Dr Aren reports that guidelines are currently being developed. This deficiency has clinical consequences. Dr Aren explains that, in Chile for example, the resultant lack of "alignment in criteria across the country currently poses difficulties for lung-cancer diagnosis and treatment". Dr Lopes adds that use of international guidance is only a partial solution. "Having national guidelines is important because they take into consideration the resources which specific healthcare systems have."

[133] Vanessa Karen de Sá et al, "Lung cancer in Brazil: epidemiology and treatment challenges", *Lung Cancer: Targets and Therapy*, 2016.

The existence of guidelines does not guarantee their application. For example, despite their frequent emphasis on medical personnel working together, Dr Raez reports that multidisciplinary clinics are rare in the region "because they cost money and time" for health systems with limited resources. Dr Barés adds that even something as specific as EGFR mutation testing is "a complex process, which requires a complete team, technology and resources". Panama's solution is to concentrate public oncology care in a single facility. Meanwhile, Uruguay, says Dr Cuello, is turning to legislation, with a proposed law that would create multidisciplinary referral centres for cancer and other diseases to improve case management.

A fully multidisciplinary clinic or clinics may not be possible in every situation, but it need not be a case of all or nothing. In 2011 Hospital San Juan de Dios, one of Costa Rica's three adult general hospitals, instituted a weekly, multi-disciplinary, lung-cancer meeting for relevant clinicians. This helped improve average patient survival time from 5.4 to 7.6 months at little extra cost.[134]

Health-system resources for treatment

The difficulties of multidisciplinary care point to a broader issue. Dr Cuello calls "a lack of human resources in oncology" one of the biggest lung-cancer challenges in the region. To this he could easily add the dearth of specialised equipment. The Economist Intelligence Unit's 2017 Latin American Cancer Control Scorecard (LACCS) identified the same issue.[135] The traffic lights developed for this report a different mix of data to illustrate the same problem. Only Uruguay has levels of cases per clinical oncologist and of CT scanners per million comparable to those found in North America and Europe.[136] Similarly, on an indicator also used in the LACCS, just Uruguay and Chile have sufficient radiotherapy capacity for all their needs. Otherwise, the results of these indicators mostly reflect economic status, with wealthier countries generally getting medium scores and those less well-off, notably Bolivia, Paraguay and Peru, doing poorly. The biggest exception is Mexico, which has human-resource and equipment challenges greater than is consistent with its level of economic development.

The Economist Intelligence Unit's report on cancer control in Latin America contains a detailed discussion of the resourcing problem, which we will not repeat here.[137] Worth noting, though, is that the lack of capacity to treat can undermine other aspects of lung-cancer control. On efforts to improve early diagnosis, for example, Dr Cazap explains that "if people are better informed about lung cancer and ask for a consultation, I am not sure our healthcare system is ready to face the situation in an efficient way". He adds that this is one consideration that has delayed the introduction of colorectal screening in Argentina, which has middling results on resources. Peru does worse. There, reports Dr Mas, aspirations of widespread healthcare coverage and efforts to open cancer centres in various parts of the country still leave "few centres that have radiotherapy and generally limited access to treatment".

Speed of treatment

Resource challenges, along with fragmentation, help explain another important problem with lung-cancer treatment in parts of Latin America: getting started in the first place.[138] In the US, in the median

[134] Mónica Araya et al, "Follow-Up on Results of a Multidisciplinary Team in the Management of Non-Small Cell Lung Cancer in a Developing Country", *Journal of Thoracic Oncology*, 2016.

[135] The Economist Intelligence Unit, *"Cancer Control, Access and Inequality in Latin America"*.

[136] CT scanners per million formally falls into our early diagnosis domain because of their utility in this field, but their numbers are discussed here.

[137] The Economist Intelligence Unit, *"Cancer Control, Access and Inequality in Latin America"*.

[138] The Economist Intelligence Unit initially wanted to include the speed of treatment as an indicator in the traffic-light system, but lack of data across the 12 study countries led to its exclusion.

case, lung-cancer therapy begins 16 days after diagnosis; in Finland 15 days and South Korea, for surgery, 20; other European studies are closer to 35 days.[139] Uruguay's well-resourced public system does reasonably well, with a one-facility public-sector study hitting an average of 28 days.[140] In Colombia, the figure was 48 days,[141] which is consistent with the lower availability of oncologists and equipment found in research for the traffic lights. In Mexico, though, Dr Arrieta reports from his own research that the median time reaches four and a half months, which he calls, with understatement, "far from ideal".

In our study, the treatment domain, in principle, seeks to separate general health-system treatment capacity from questions of access addressed in an earlier section. Ultimately, this is not completely possible. One area is equipment. Private hospitals in Brazil, for example, have six times more CT scanners per 1m population than do public ones,[142] which may explain why our economic burden research found that such scans are far more expensive (on a per-scan basis) in public than private hospitals (see Chapter 1). Similarly, treatment delays are much longer in the public sector: in a comparative Argentine study, the time from diagnosis to first therapy in public hospitals was 71 days, compared with 33 in private ones.[143]

VI. Non-curative services

Chart 13

Non-curative services domain

Source: The Economist Intelligence Unit.

Those with lung cancer need medical services beyond diagnosis and curative treatment. This traffic light looks at two key additional areas: palliative care and rehabilitation. This turns out to be one of the study countries' weakest areas.

Palliative care

Lung cancer's high mortality adds to the potential demand for end-of-life care in Latin America by tens of thousands. Palliative care offers comfort, dignity and support for patients and families as death approaches, but for lung cancer—as increasingly with other cancers—it offers far more. An influential US study found that beginning palliative care at the time of diagnosis to control symptoms extended average patient life expectancy by 2.7 months (30%), increased quality of life and more than halved the number of patients suffering from depression.[144]

Other cancers have seen similar findings,[145] making greater integration of palliative services across cancer care best practice. Terminology may also be shifting. "Supportive care" is sometimes used to describe symptom relief during treatment, with "palliative care" reserved for the same activity once

[139] Regina M Vidaver et al, "Typical Time to Treatment of Patients With Lung Cancer in a Multisite, US-Based Study", *Journal of Oncology Practice*, 2016 & Fernando Abrao et al, "Impact of the delay to start treatment in patients with lung cancer treated in a densely populated area of Brazil", Clinics, 2017 & JK Olsson et al, "Timeliness of care in patients with lung cancer: a systematic review", *Thorax*, 2009.

[140] Maria Palleiro et al, "Lung cancer quality of care in Uruguay: First experience in a public hospital", *Journal of Clinical Oncology*, 2017.

[141] Cuenta de Alto Costo, *Indicadores de gestión del riesgo en pacientes con cáncer de pulmón en Colombia*, 2018.

[142] Luiz Araujo et al, "Lung cancer in Brazil", *Jornal Brasileiro de Pneumologia*, 2018.

[143] Gonzalo Recondo et al, "Access to oncological care in patients with breast and lung cancer treated at public and private hospitals in Buenos Aires, Argentina", *Journal of Clinical Oncology*, 2018.

[144] Jennifer Temel et al, "Early Palliative Care for Patients with Metastatic Non–Small-Cell Lung Cancer", *NEJM*, 2010.

[145] David Hui and Eduardo Bruera, "Integrating palliative care into the trajectory of cancer care", *National Review of Clinical Oncology*, 2016.

curative interventions have ceased. In practice, though, the two terms are blurred, even though, while palliative care remains more commonly used, both clinicians and patients respond better when such services are labelled "supportive".[146] As Dr Cazap notes, "'palliative' care is sometimes seen incorrectly as being about morphine access and end-of-life; calling it 'supportive' makes a statement that it is not just that".

Whatever the term—and this study retains the traditional wording—examples of palliative care integrated into cancer treatment do exist in Latin America. Dr Barés, for example, reports that at Panama's Instituto Oncologico Nacional "each patient with lung cancer is referred to the palliative team as a part of continuous patient care". Dr Cazap adds that the practice is well understood in Argentina, and the clinical guidelines for lung-cancer treatment in Mexico and Colombia both say that palliative care should begin from diagnosis.[147]

The problem is often finding providers of such patient support. Dr Raez explains that "in a lot of Latin America, proper palliative care is pretty much not existent: it's confused with lack of treatment". Only four study countries—Argentina, Chile, Costa Rica and Uruguay—have widespread services, according to a 2014 World Palliative Care Association report, and since then Panama has taken extensive steps to improve.[148] Elsewhere, though, provision tends to be spotty at best or, as Dr Agüero says of Paraguay, in practice "it is not really available for us". Moreover, notes Dr Lopes, where services are basic they can focus on pain relief but overlook other needs of lung-cancer patients, such as oxygen availability.

Survivorship

To date, very high lung-cancer mortality means that issues of survivorship—an increasingly important field for other cancers—"are not on most of the agendas in Latin America", says Dr Cazap. This will probably change. Ms Holtz notes that typical survivor issues, such as difficulties in returning to work, soon will be "important to lung-cancer patients too, as we are starting to talk about stabilisation of the disease".

Given lung-cancer survivorship's to date limited relevance, including a traffic light focusing on specialist programmes would have been unfair. Instead, we look at pulmonary rehabilitation, which addresses several survivor challenges, including shortness of breath and fatigue.[149]

Even by this restricted measure, study countries fall short. In ten of 12 study countries care guidelines contain no reference to pulmonary rehabilitation. Colombia's Ministry of Social Protection has guidelines for dealing with lung-cancer patients, including rehabilitation, although this document specifically focuses on those whose disease has an occupational cause.[150] Only Mexico's medical guidelines have an extensive discussion of pulmonary rehabilitation which, like palliative care, it recommends should be integrated into treatment from the beginning.[151]

This is not cutting-edge science: Colombia's guidelines are a decade old. Nevertheless, notes Dr Raez, pulmonary rehabilitation for lung-cancer patients "doesn't really happen yet in Latin America". Dr Arrieta agrees: "Most health systems in the region do not have adequate space and qualified personnel

[146] Nada Fadul et al, "Supportive Versus Palliative Care: What's in a Name?", *Cancer*, 2009 & R Maciasz et al, "Does it Matter What You Call It? A Randomized Trial of Language Used to Describe Palliative Care Services", *Support Care Cancer*, 2013.

[147] Abelardo García ed, *Cáncer De Pulmón De Células No Pequeñas* & Ministerio de Salud y Protección Social, *Guía de Práctica Clínica para la detección temprana, diagnóstico, estadificación y tratamiento del cáncer de pulmón*, 2014.

[148] The Economist Intelligence Unit, "*The 2015 Quality of Death Index: Ranking palliative care across the world*", 2015.

[149] Marc Feinstein et al, "Current Dyspnea Among Long-Term Survivors of Early-Stage Non-small Cell Lung Cancer", *Journal of Thoracic Oncology*, 2010 & Christie Pratt Pozo et al, "Survivorship Issues for Patients With Lung Cancer", *Cancer Control*, 2014.

[150] Ministerio de la Protección Social, *Guía de Atención Integral de Salud Ocupacional Basada en la Evidencia para Cáncer de Pulmón relacionado con el Trabajo*, 2008.

[151] Abelardo García ed, *Cáncer De Pulmón De Células No Pequeñas.*

to offer this service. It is important that clinicians and hospital administrative personnel are aware of its importance."

In short, when looking beyond curative interventions, few study countries help lung-cancer patients with additional needs as they seek to die, or live, with dignity.

VII. Information and advocacy

Chart 14

Information and advocacy domain

Source: The Economist Intelligence Unit.

Awareness-raising

Cancer awareness and survival are linked.[152] Unfortunately, notes Ms Holtz, in Latin America "most people don't even know the symptoms". Polling data back her up. In a recent Brazilian survey, half of people could not name a single symptom of lung cancer, while in Argentina the figure was 40%, but an additional 14% gave an incorrect symptom. In both, on average, respondents could name just one correct symptom, usually a non-specific one such as shortness of breath or a cough.[153]

Given constrained budgets, Dr Cazap believes that the most realistic approach "to earlier diagnosis and better outcomes would be related to awareness and education". Dr Agüero adds that sometimes even the basics in this area are still necessary: "We need to teach people to go to the doctor when they feel something is wrong. People in Paraguay don't want to."

Our traffic lights, though, show only mixed lung-cancer awareness efforts.

Tobacco control education, as distinct from regulation, is central here. Surprisingly, given the tobacco-control traffic-light results, only seven study countries conducted anti-smoking campaigns in either 2014 or 2016 (as recorded by the Tobacco Atlas). Moreover, of these campaigns, Argentina's and Brazil's efforts did not use the key mass media of TV or radio. For Chile and Bolivia, with their large numbers of smokers, the lack of such a campaign is worrying.

Beyond anti-smoking education, lung-cancer awareness efforts must encompass, at the very least, education on the symptoms of the condition. Here, little is taking place. The study gave a green light for at least one substantial campaign in recent years to spread knowledge about the disease, and an amber one for any sign at all of activity to do so. These activities might include standalone efforts or ones taking advantage of international focal periods, including Lung Cancer Awareness Month in November, Lung Cancer Awareness Day (November 17th) or World Lung Cancer Day (August 1st).

[152] Maja Niksic et al, "Is cancer survival associated with cancer symptom awareness and barriers to seeking medical help in England? An ecological study", *British Journal of Cancer*, 2016.

[153] Global Lung Cancer Coalition, "Argentina: symptom awareness and attitudes to lung cancer: Findings from a global study" & "Brazil: symptom awareness and attitudes to lung cancer".

Only four countries had substantial campaigns. Mexico saw the most consistent activity, and in 2018 the country declared a National Lung Cancer Day (April 5th). Argentina, Brazil and Colombia have also seen large-scale activity in recent years. Otherwise, awareness-raising seems to have been limited to occasional press releases, media interviews with lung-cancer experts or one-off events. On two occasions the last of these involved purchasing 50 seats at international football matches and covering them in black cloth to illustrate lung cancer's death toll.[154] In most study countries, awareness-raising went no further, if it occurred at all.

Patient advocacy

Outside of Colombia, where healthcare companies and organisations such as medical group Protorax have promoted awareness campaigns,[155] they were the work of patient advocacy groups. Some of these organisations specialise in lung cancer, such as Mexico's Respirando con Valor, or are more general cancer societies with a substantial lung-cancer programme, such as Brazil's Instituto Oncoguia. Argentina benefits from both, Liga Argentina de Lucha Contra el Cáncer and Fundación Pacientes de Cáncer de Pulmón, each of which has engaged in lung-cancer awareness work in recent years.

The problem for advancing awareness further, notes Dr Raez, is that beyond these groups "in Latin America lung-cancer advocacy is close to zero". Although stigma partly explains this absence, the main issue is that the disease is so lethal that few survivors remain to engage in such activity. Therefore, the existence of lung-cancer advocacy groups, says Mr Zervino, tends to be "almost random and they are often initiated not by patients but by their relatives or friends."

The value of such campaigning is nonetheless difficult to overestimate. Although no specific lung-cancer patient association exists in Chile, the country's Recarte Soto Law, which provides coverage for high-cost diseases, is named for the lung-cancer patient who led the campaign for its adoption—an irony given lung cancer's current lack of coverage. Ms Mondragón adds that, by providing a forum for patients to talk about their experiences, these associations "can sensitise and inform decision-makers with real information", with substantial attendant political impact.

Although she believes that awareness of the disease is still lacking in Mexico, it is noteworthy that the country—the only one that we awarded a green light in this domain—outperformed Brazil and Argentina significantly in awareness in the survey described previously. Only 21% of Mexican respondents were at a loss to name a single symptom and, on average, they could list twice as many as their peers from the other countries.[156] Unfortunately, this has yet to translate into earlier diagnoses.

[154] "La explicación de los 50 espacios negros en el Estadio Nacional", September 6th 2017, *CRHoy.com* & "50 panameños mueren cada 2 meses por Cáncer de Pulmón", www.saludpanama.com.

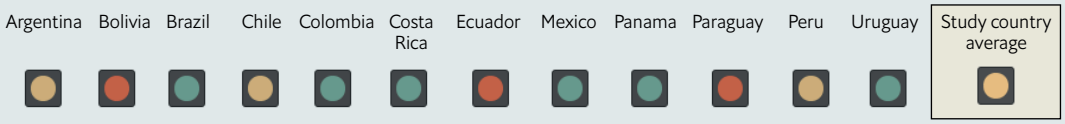
[155] Protorax, "Campaña de concientización sobre el cáncer de pulmón", http://www.cirujanosdetorax.com/campana-de-concientizacion-sobre-el-cancer-de-pulmon/.

[156] Global Lung Cancer Coalition, "Mexico: symptom awareness and attitudes to lung cancer".

VIII. Data quality

Chart 15

Data quality domain



Source: The Economist Intelligence Unit.

Registration and vital statistics

Just as for individuals, information and awareness at the national level save lives. Good cancer data are essential. As Mr Paonessa notes, "it is difficult to make [good] decisions without the real numbers".

The caveats throughout this paper are proof enough of the frequent lacunae in detailed lung-cancer information. Even some traffic-light data rely on interviewee estimates from their own institutions. Other potentially useful information—such as the proportion of adenocarcinomas tested for EGFR mutation or the average time between diagnosis and the beginning of treatment—are unobtainable in broadly comparable international figures.

This traffic light focuses on more basic lung-cancer information. Even for such fundamental data, though, the results are mixed.

Effective population-based cancer registries are the foundation of understanding a national or regional cancer burden. Indeed, Dr Cuello believes that Uruguay's high-quality national registry may be its biggest advantage in lung-cancer control because it gives a more complete vision of the issues.

Last year's Economist Intelligence Unit report on Latin American cancer control noted progress but also remaining weakness in this area.[157] Signs of improvement continue to appear. Neither Mexico nor Peru had registries of sufficient quality in 2013 for inclusion in the IARC's latest edition of *Cancer in Five Continents*, but both had one each in last year's *International Incidence of Childhood Cancers*.[158] Panama has been improving its registry since 2012, which probably explains its near-doubling in reported lung-cancer incidence even as mortality has remained stable.[159] Nor are the leaders standing still. Colombia is moving towards a national registry based on payments made for cancer from its high-cost account, and Uruguay is integrating its electronic patient records with its registry, a process Dr Cuello says should be complete by 2020.

Nevertheless, the need for further progress in Latin America remains "urgent", to quote a recent IARC analysis.[160] Very few countries have widespread population-registry coverage. In Paraguay, for example, although a nominal registry may exist, Dr Agüero reports that "we don't have data for lung cancer or any kind of cancer. We don't even know how many patients we have, which makes it difficult to plan." Even where some good regional registries exist, as in Chile and Argentina, the gaps are problematic. Dr Burotto says of the former "we don't know the true numbers for lung-cancer incidence and mortality".

[157] The Economist Intelligence Unit, "*Cancer Control, Access and Inequality in Latin America*".

[158] IARC, *Cancer in Five Continents*, "Cancer registry list"; 2012; [IICC-3] "Contributing cancer registries", 2017.

[159] Panamá Ministerio de Salud, "Registro Nacional del Cáncer de Panamá Boletín Estadístico Año: 2013 - 2015", 2018.

[160] David Forman and Monica Sierra, "Cancer in Central and South America: Introduction", *Cancer Epidemiology*, 2016.

As for Argentina, Mr Paonessa notes that at the national level the country "does not have good information; however, we are working on this issue as a priority".

Worse still, within existing cancer registries, information quality on lung cancer falls behind that of other forms of the disease. Data from 21 population-based registries from seven study countries met the quality requirements to contribute to the latest IARC Cancer in Five Continents. If those same requirements were applied solely to lung-cancer data, however, only six registries, from four countries, would have passed muster.[161]

As noted earlier, these registries rely heavily on death certificates for lung-cancer data. This makes the weakness of mortality data in the region an additional concern. Traffic-light research indicates that only Mexico, Chile and Costa Rica have high-quality information, with Argentina, Bolivia, Ecuador, Paraguay and Peru all needing marked improvement.

Lung cancer-specific data

Registries and national mortality statistics provide only a very general view. To dig deeper, a natural step is a cancer-specific registry. Although many exist for other forms of the disease, lung cancer ones are still novel. The oldest are in Japan, which takes in new information only every few years, and Denmark, which has been functioning since 2003.[162] Several in Europe, including Norway and Spain, and in the US began only in the past five years. None exist in Latin America, although the Latin American Clinical Oncology Group is looking to establish one.

To fill the gap, the Latin-American Consortium for the Investigation of Lung Cancer (CLIPaP) has taken a different approach. Dr Arrieta explains that the consortium allows the sharing, between centres in various countries, of information from individual databases created by different CLIPaP members. Some of these, on their own, include over a thousand subjects. This has allowed large-scale regional studies, such as one with more than 5,000 patients on EGFR inhibitors, and niche research that would otherwise not be possible, including one of several hundred from across the region on lung cancer in those under 40 years old.[163] Dr Arrieta believes that, for the region, "this might be the best way to have a rather robust data repository".

Accordingly, the traffic-light assessment measures the degree of participation in CLIPaP. Seven countries get a green light for this sub-domain, either through participation of their national cancer centres or other participants who provide a substantial amount of patient data. The better relative performance here compared with that for cancer registries and death data probably indicates that researchers understand the value of good data better than those responsible for funding other statistics gathering.

[161] Economist Intelligence Unit calculations based on data in IARC, *Cancer in Five Continents*, "Indices of data quality (Volume X): All sites except non-melanoma skin (C00-96 exc. C44)" & "Indices of data quality (Volume X): Lung (C33-34)".

[162] Noriyoshi Sawabata et al, "The Japanese Lung Cancer Registry Conducted by the Japanese Joint Committee for Lung Cancer Registration", *Japanese Journal of Lung Cancer*, 2012 & Erik Jakobsen and Torben Rasmussen, "The Danish Lung Cancer Registry", *Clinical Epidemiology*, 2016.

[163] Oscar Arrieta et al, "Updated Frequency of EGFR and KRAS Mutations in NonSmall-Cell Lung Cancer in Latin America" & Luis Corrales-Rodríguez, "An international epidemiological analysis of young patients with non-small cell lung cancer," *Lung Cancer*, 2017.

CONCLUSION: TIME TO PAY ATTENTION

Lung cancer is Latin America's deadliest neoplasm. From the study countries specifically, it takes over 60,000 lives and costs over US$1.5bn annually. While eventually reduced smoking should bring down incidence, that will take years, maybe decades, and even without tobacco the region's level of lung cancer would make it a major killer. As our traffic-light assessment shows, though, this is a disease that not only receives insufficient attention, but stigma also impedes efforts to do so.

Some weapons in the fight against lung cancer are obvious, such as improved treatments and tobacco control, but there is no single silver bullet. In Dr Raez's words, "it is like going to war, we need to improve everything". Each study country has different strengths and weaknesses, but policymakers and health-system authorities in most could benefit from considering the following, first in the priority areas:

- **Tobacco control:** efforts here have generally been positive, but countries may need to overcome domestic resistance to stay the course. Moreover, success in this area should not breed complacency in others. Tobacco control is not enough.
- **Access:** beyond the region's general access challenges, at the very least where catastrophic health cost funds exist, inclusion of lung-cancer treatment should be reconsidered if it is not covered.
- **Early diagnosis:** Brazil's and Mexico's trials will show if screening is a viable option in the region. While awaiting results, though, countries should consider ways to improve knowledge of lung cancer among primary-care physicians and general health-system efficiency to promote downstaging.

Other important areas are:

- **Treatment:** where they do not exist, national lung-cancer treatment guidelines are needed in order to better focus limited resources on treatment and promote multidisciplinary care.
- **Non-curative services:** the needs of patients after treatment need more attention, whether improved support in a dignified death or meeting the needs of living as a lung-cancer survivor.
- **Non-tobacco prevention:** scattered efforts at addressing lung-cancer risks also require ramping up, especially as clean air and drinking water have much broader health and quality of life benefits than reduction of lung-cancer incidence.
- **Information and advocacy:** the message that smoking causes lung cancer has reached the public in the region, but further awareness is insufficient. Advocacy groups are well-placed to meet this need but require support to take root.
- **Data quality:** as with tobacco control, improvements have occurred but need to continue. In particular, registries should consider why lung-cancer data quality is lower than for other forms of the disease.

Underlying much of this agenda is a necessary cultural change. Lung cancer is not nature's punishment for smoking. It deserves the attention and access to resources of every cancer.

APPENDIX I: METHODOLOGY OF THE ECONOMIC MODEL

The Economist Intelligence Unit developed a model to provide insight into the economic impact of lung cancer in the 12 study countries in Latin America.[164] The key model parameters where data were needed included:

- Population parameters (size and growth) for each country;
- healthcare spending per head for each country;
- prevalence of lung cancer for each country;
- split of patients between public and private healthcare coverage;
- breakdown of patients by stage of lung cancer for Brazil;
- details of the diagnostic and treatment pathway for lung cancer in Brazil; and
- costs of diagnosis and treatment in the public and private sector for Brazil.

Consistent sources were used for individual parameters across countries where possible. For example, Economist Intelligence Unit data and data from reputable global sources, such as the World Bank, were used for key population and economic parameters in the model. A literature review was conducted to gather additional data inputs for the model and to understand previous approaches to assessing the impact of cancer on a country's economy.

Searches were performed using the following sources:

- Embase.com (which covers Embase and Medline);
- PubMed;
- Google Scholar; and
- Google.

Where published sources of data were not identified, estimated inputs were obtained through interviews with experts in the field. Using existing methodology from the literature,[165] we developed a method of assessing the economic impact of lung cancer, incorporating both direct and indirect costs.

1. Direct costs

Direct costs are the costs associated with diagnosis and medical treatment for each patient with lung cancer. This section describes the input parameters for the direct cost model built for Brazil. These broadly included:

- Epidemiological and population inputs;
- stage of lung cancer;
- treatment pathways and healthcare coverage (public or private); and
- diagnosis and treatment costs.

[164] The full economic model is available for download alongside this report: http://www.eiuperspectives.economist.com/LungCancerLatAm

[165] W Max et al, "The economic burden of prostate cancer, California, 1998", *Cancer*, 2002 & C Cook et al, "The annual global economic burden of heart failure", International Journal of Cardiology, 2014.

Epidemiological and population inputs

In order to obtain the numbers of people affected by lung cancer in each country we obtained data on the incidence and prevalence of the disease, as well as the total population. Table 6 summarises the sources used for epidemiological and population data in the model.

Table 6: Sources of epidemiological data

Model parameter	Source	Year of data used
Incidence	Global Health Data Exchange[166]	2016
Prevalence	Global Health Data Exchange[167]	2016
Split of patients by stage	Costa et al 2016[168]	2016
Population: ● Total population in each Latin American country	World Bank[169]	2016-22

Incidence and prevalence estimates were obtained from the Global Health Data Exchange for 2016.[170] This source provided the most recent prevalence estimates (2016) across all of the selected Latin American countries (see Table 7).

Table 7: Incidence and prevalence data for selected countries

Country	Incidence	Prevalence
Argentina	11,008	12,626
Bolivia	821	908
Brazil	29,880	33,958
Chile	3,307	3,862
Colombia	4,714	5,205
Costa Rica	366	409
Cuba	5,679	6,668
Ecuador	990	1,104
Mexico	8,468	9,676
Panama	352	415
Paraguay	764	827
Peru	2,268	2,576
Uruguay	1,449	1,645

Source: Global Health Data Exchange, Global Burden of Disease Results Tool

Charts 16 and 17 show the incidence and prevalence of the condition in the selected countries for 2016. The highest incidence and prevalence rates are reported in the southern regions of Latin America, such as Uruguay, Argentina and Chile, reflecting the high tobacco consumption in these countries.[171]

[166] Global Health Data Exchange, Global Burden of Disease Results Tool. Available at: http://ghdx.healthdata.org/gbd-results-tool

[167] Ibid.

[168] G Costa et al, "Epidemiological changes in the histological subtypes of 35,018 non-small-cell lung cancer cases in Brazil", *Lung Cancer*, 2016.

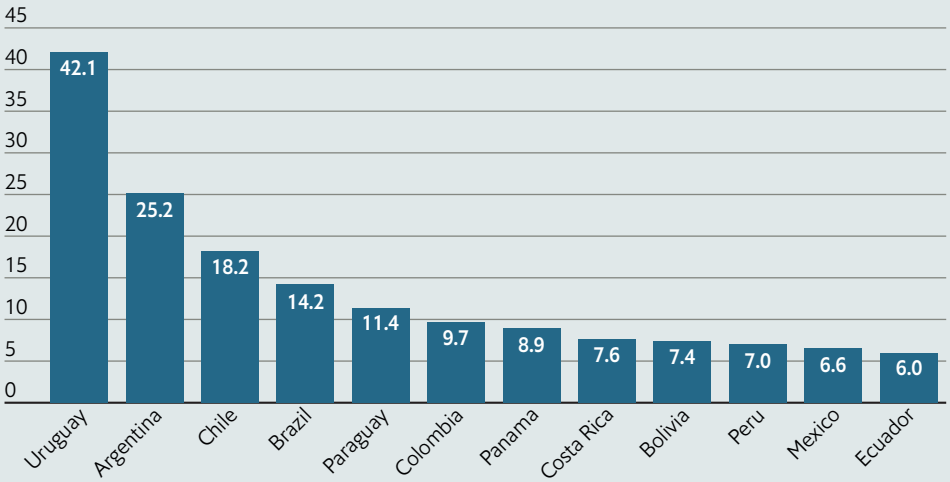
[169] The World Bank. Population data. Available at: http://data.worldbank.org/country/

[170] Global Health Data Exchange, Global Burden of Disease Results Tool

[171] M Pineros et al, "Descriptive epidemiology of lung cancer and current status of tobacco control measures in Central and South America", *Cancer Epidemiology*, 2016.

Chart 16

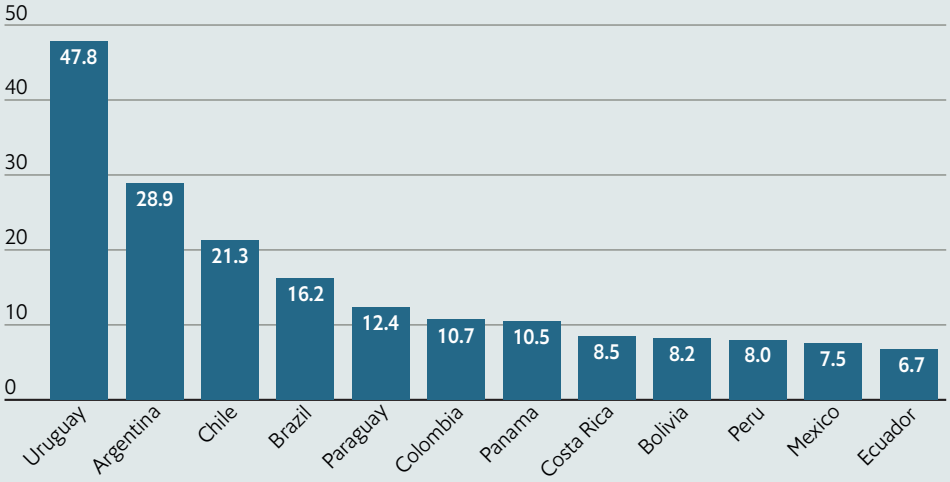
Incidence of lung cancer in 12 Latin American countries
(rate per 100,000)



Source: Global Health Data Exchange, Global Burden of Disease Results Tool.

Chart 17

Prevalence of lung cancer in 12 Latin American countries
(rate per 100,000)



Source: Global Health Data Exchange, Global Burden of Disease Results Tool.

Our model used prevalence figures for the selected countries for 2016 as its basis. Prevalent cases will incur costs as well as incident cases, although we would expect the costs to be highest in the first year after diagnosis, which was our reason for using prevalent cases in the model.

Stage of lung cancer

Lung cancer is divided into stages according to how large the tumour is, whether and to what extent it has spread to adjacent tissue, lymph nodes and the rest of the body. The stages of lung cancer are described in the table below.

Table 8: Staging of lung cancer

Stage I: the cancer is small and located only in the lung and has not spread to any lymph nodes.
Stage II: the cancer is slightly larger and may have spread to nearby lymph nodes.
Stage III: there is a second tumour in the same lung or the cancer has spread to nearby tissue, such as the chest wall or to more distant lymph nodes in the middle of the chest or at the top of the lung or near the collarbone. Also described as locally advanced disease.
Stage IV: the cancer has spread to both lungs, the covering of the lung or heart or the fluid surrounding them, or to another part of the body, such as the liver or other organs. This is the most advanced stage of lung cancer and is also described as advanced disease, or terminal.

Source: Cancer Care, "Types and staging of lung cancer". Available at: https://www.lungcancer.org/find_information/publications/163-lung_cancer_101/268-types_and_staging

Treatments vary according to the stage of lung cancer. There is a correlation between stage at diagnosis and treatment costs, with the early stages of lung cancer (stages I-II) associated with lower treatment costs, and later stages (stages III-IV) associated with higher treatment costs.[172] In Brazil, lung cancer is predominantly diagnosed in the later stages, when prognosis is poor.[173] Only 15% of patients are diagnosed in the early stages, with 85% of patients diagnosed in stages III-IV.[174]

No single source or equivalent literature describing the proportion of patients diagnosed at each stage of lung cancer in all 12 study countries was identified, therefore we applied the same split of patients diagnosed at each stage of lung cancer to all 12 Latin American countries of interest.[175] We think it is reasonable to assume that staging will be relatively similar in all 12 study countries, as even in developed countries such as the UK, a large proportion of people are diagnosed in the later stages.[176]

Table 9: Split of patients by stage at diagnosis with lung cancer in Brazil compared with the UK

	Brazil		UK	
Lung cancer stage	Proportion of people per stage	Prevalence	Proportion of people per stage	Prevalence
Stage I and II	15%	5,094	22%	17,334
Stage III	39%	13,244	19%	14,970
Stage IV	46%	15,621	48%	37,820

Sources: Global Health Data Exchange, Global Burden of Disease Results Tool & G Costa et al, "Epidemiological changes in the histological subtypes of 35,018 non-small-cell lung cancer cases in Brazil"

The treatment pathway and healthcare coverage

The model considered the costs for diagnosis and treatments received in each stage of lung cancer. It used a simplified treatment pathway based on the approaches used in Brazil. These were identified through published Brazilian lung-cancer management guidelines and related literature.

[172] V de Sa et al, "Lung Cancer in Brazil: epidemiology and treatment challenges", *Lung Cancer: Targets and Therapy*, 2016.

[173] E Raez et al, "Challenges in Facing the Lung Cancer Epidemic and Treating Advanced Disease in Latin America", *Clinical Lung Cancer*, 2017.

[174] G Costa et al, "Epidemiological changes in the histological subtypes of 35,018 non-small-cell lung cancer cases in Brazil".

[175] Ibid.

[176] Cancer Research UK, Lung Cancer: Stages, types and grades. Available at: http://www.cancerresearchuk.org/about-cancer/lung-cancer/stages-types-grades/types

The aspects of the treatment pathway included in the model were:

- Diagnosis, including computed tomography (CT) and positron-emission tomography (PET) scans;
- surgery;
- radiotherapy;
- chemotherapy and other medicinal therapies;
- outpatient treatment and visits; and
- hospitalisation (including for palliative care and surgery).

Outpatient costs refer to the cost of visiting a doctor or specialist for scans, diagnostic procedures, chemotherapy and radiotherapy. The figures for outpatient and hospital costs also include costs accrued from medical equipment used during these appointments. Hospitalisation for lung-cancer treatment is only required for surgery and palliative care/treatment, for which we estimate costs separately.

The treatments patients can access depend on their health insurance. For example, for patients in the terminal stages of lung cancer in the private sector, if the initial chemotherapy drug regimen is unsuccessful (first-line treatment), it can be switched to a second-line treatment and so on if these sequential treatments are also unsuccessful. In the public sector, patients are only likely to receive first-line and occasionally second-line treatment, very rarely third-line and never fourth-line treatment. In addition, the time spent in hospital for palliative treatment can be up to two weeks in the private

Table 10: Coverage of population with public and private health insurance

Country	Health coverage split (% of population covered)	
	Public	Private
Brazil	75	25
Argentina	92	8
Bolivia	66	34
Chile	77	23
Colombia	97	3
Costa Rica	100	0
Ecuador	80	20
Mexico	94	5
Panama	78	22
Paraguay	93	7
Peru	94	6
Uruguay	98	2

Note: For all countries public and private coverage add up to 100% in our model, even if there may be uninsured people in a country. This is a simplification, as complete data for some countries were not available. Where available figures did not add up to 100%, for example in the case of Colombia, we had to make reasonable assumptions based on the literature.

Sources: The World Bank. Population data, The Economist Intelligence Unit; R Atun et al, "Health-system reform and universal health coverage in Latin America", Lancet, 2014; R Diaz, "PARAGUAY: Public health Care Free of Charge", 2010; Oxford Business Group, "The Report: Panama 2015", 2015; C V Fuertes, "Universal Health Coverage Assessment: Bolivia", Global Network for Health Equity, 2016.

sector, but in the public setting the patient is often expected to spend their last days at home, which also has an influence on costs.

Our model therefore also took into account the proportion of people with public and private healthcare coverage (summarised in the table below), and difference in the treatments they are likely to receive. Where we could not find this information in the literature and treatment guidelines we interviewed lung-cancer oncologists working in Brazil. For all of the 12 study countries, apart from Brazil, Costa Rica and Colombia, we struggled to find information on the health insurance coverage for the whole population. For the proportion of people where data were unknown or not available, we assumed that they accessed public health insurance; this was to ensure that our model accounted for 100% of the population for each country.

Cost of treatments

To estimate the costs and frequency of use of the components of the diagnosis and treatment pathway in the public sector we were able to use a real-world data sample from the Brazilian Lymphoma and Leukaemia Association (Abrale).[177] This included admissions data from two public hospitals in Brazil for conditions including lung cancer. One hospital was a university hospital (Cancer Institute of the State of São Paulo), which is considered to have some of the best treatments for lung cancer available in the public sector (hospital 1). The second hospital was a general public hospital (Hospital Regina New Hamburg) not connected with a university (hospital 2). The use of data from both a specialised public hospital and a general one enabled us to capture the diversity of treatments available in the public sector.

The sample provided de-identified, routinely collected health data on the following data fields for all patients admitted to either hospital for lung-cancer treatment between April 2008 and September 2017:

- Date of procedure;
- name of procedure;
- procedure type (eg, surgery, diagnostic, treatment);
- outpatient/inpatient status of the procedure;
- price of procedure;
- number of procedures received; and
- treatment type (eg, adjuvant chemotherapy, palliative chemotherapy, radiotherapy).

For the public sector we assigned a cost extracted from the hospital data to each item in the treatment pathway. The items in the treatment pathway and associated costs were reviewed by five different lung-cancer oncologists working in Brazil. To determine the frequencies of each procedure, we used information extracted from local treatment guidelines in Brazil, as well as consulting our lung-cancer oncologists.

[177] Brazilian Lymphoma and Leukaemia Association, https://www.uicc.org/membership/abrale-brazilian-lymphoma-and-leukaemia-association

To gather data inputs for the private healthcare sector in Brazil, we used information from interviews with oncologists for the frequency of treatments and data on costs from the Hierarchical Brazilian Classification of Medical Procedures,[178] the Brazilian Clinical Oncology Manual[179] and IQVIA.[180]

We calculated average direct cost per patient per year in each stage of lung cancer in both the public and private sectors. This average was multiplied by the number of people in each stage covered in each sector, and these values summed up, to get the total cost for each stage of lung cancer. Total cost for patients in each stage was summed up to obtain overall lung-cancer costs for one year. Cost estimates were in Brazilian Real and converted to US dollars using the exchange rate for 2016, applied to 2016 cost and prevalence data.

2. Indirect costs

From the perspective of employers, costs associated with lost productivity due to employee disability and absence from work due to ill-health and the need for treatment among people with lung cancer are likely to be substantial.[181]

In order to calculate the indirect costs of lung cancer we considered the impact in terms of loss of GDP due to work absence and early mortality for patients who were part of the workforce.

Estimation of impact of lung cancer on the workforce

First, we used the prevalence of lung cancer per age band and applied the labour force participation rate for each age band to these numbers in order to calculate how many individuals with lung cancer would have been part of the working population.[182] For those not in employment we assumed that there was no associated loss of productivity due to lung cancer.

Using the literature, we then used the proportions of people diagnosed in each stage of lung cancer to calculate how many working individuals with lung cancer would be in the different lung-cancer stages.

Work absence

We made the following assumptions about those able to work with a diagnosis of lung cancer:[183]

- Only people with early-stage lung cancer (stages I and II) are likely to be able to carry on working. We assumed that everyone in stages I and II would still be contributing to the workforce. We assumed that patients in stages I and II would be absent from 14 days of work in a year.[184]

- People diagnosed with stage III will be working but most working days will be lost due to sickness and need for treatment. We assumed that 90% of working days would be lost based on estimates from oncologists we interviewed for the economic model.

- Individuals in stage IV would be unable to work as they are expected to die within a year of diagnosis.[185] They were therefore considered in terms of early mortality rather than work absence.

[178] Medical Association of the Samaritano Hospital (AMHS), The Hierarchical Brazilian Classification Medical Procedures (CBHPM), AMB-CID-CBHPM Tables. Available at: http://amhs.com.br/english/tabelas-amb-cid-cbhpm.asp

[179] Brazilian Manual of Medical Oncology

[180] IQVIA, IQVIA Core

[181] K R Yabroff et al, "Economic burden of cancer in the United States: estimates, projections, and future research", *Cancer Epidemiology, Biomarkers & Prevention*, 2011.

[182] International Labour Organisation, Labour force by sex and age (ILO estimates and projections).

[183] Instituto Brasileiro de Geographia e Estatistica, Escassez e fatura: distribuição da oferta de equipamentos de diagnóstico por imagem no Brasil. Available at: https://www.ibge.gov.br/

[184] Lixens France SA, Non-confidential summary of socio-economic analysis. Available at: https://echa.europa.eu/documents/10162/94b1e2f4-e719-4976-b36c-ead11cc70618

[185] R N Younes et al, "Chemotherapy beyond first-line in stage IV metastatic non-small cell lung cancer", *Revista da Associação Médica Brasileira*, 2011.

To work out the costs associated with work absences we considered the working population living with lung cancer per age band and per stage, and the associated number of days missed from work. By multiplying the days lost by the number of working individuals in each age band and stage we got a total number of days lost from work. We multiplied the days lost by the daily GDP per member of the workforce for Brazil to obtain an estimate of the total impact of work absence.

Early mortality

Only individuals in stage IV were considered to die in the same year of diagnosis, and therefore contribute to indirect costs due to early mortality. By multiplying the number of stage IV individuals who had been working by the annual GDP per member of the workforce, we obtained total indirect costs due to early mortality.

3. Interpolation of results to other Latin American countries

After running the model for Brazil, we established the economic impact of lung cancer in the other 11 study countries, using a method known as interpolation. Due to the low data availability in Latin America, this method is useful for making economic estimates where no (or limited) published data exist, based on a baseline country with the most complete data.[186] In this study the baseline country we selected was Brazil. It has similarities with most of Latin America in that lung cancer is predominantly diagnosed in the later stages, when prognosis is poor.[187]

Adjustments were made for the variables for which data were available. In our model these were:

- Healthcare spending per head 2016-22;
- prevalence of lung cancer in 2016; and
- split of public and private healthcare coverage.

Direct costs

To obtain the direct costs per patient, the per-patient costs for each stage of lung cancer for the public and private sectors in Brazil were multiplied by the ratio of healthcare spend per head in each study country by the healthcare spend per head in Brazil. This gave the average direct per-patient costs for each stage of lung cancer in both healthcare settings for each country.

The number of patients in each stage of lung cancer in each country was then calculated based on the prevalence data for that country and the proportion of people diagnosed per stage in Brazil. These figures were then split into those receiving public and private healthcare for each country.

Finally, the number of patients in each stage in public and private healthcare was multiplied by the interpolated average cost per patient per stage in each setting for that country.

[186] C Cook et al, "The annual global economic burden of heart failure".

[187] E Raez et al, "Challenges in Facing the Lung Cancer Epidemic and Treating Advanced Disease in Latin America".

Indirect costs

For indirect costs, basic assumptions on days lost due to work absences and early deaths were the same across all countries. Specific data were used for each country on:

- Prevalence of lung cancer by age band;
- labour force participation rate by age band; and
- GDP per member of the workforce.

The same methods were then used to calculate indirect costs as for Brazil.

APPENDIX II: METHODOLOGY OF THE TRAFFIC-LIGHT ASSESSMENT

The aim of the traffic-light assessment is to provide a broad assessment of how well 12 Latin American countries are doing in various aspects of lung-cancer control. For each area covered (called a domain), a green light indicates that countries are doing well either by global or regional international standards (what this means in practice is explained for the specific domains below). An amber light means that the area is one of concern, and a red that it requires substantial attention. Each of the domains has been assessed using distinct criteria and it is not intended that they be aggregated into a single traffic-light score.

Selection of the domains, and the measures used within them (called indicators) involved a process that included: a literature review by The Economist Intelligence Unit Healthcare team to identify priority areas; discussion during an advisory board meeting with regional experts on the most important issues to include; and further refinement by The Economist Intelligence Unit in light of insights gained into what data were available.

The domains and indicators are designed to cover the most important issues relating to lung cancer in the region. They are divided into two sets. The first are the so-called Priority Lights, which advisory board members indicated were the most crucial areas in addressing lung cancer. The second set are the so-called Important Lights that, while not as immediately pressing as the priority ones, are still essential for success in this field.

Each domain is made up of one or more indicators. For each, every country was assigned a light of red, amber or green. Domain scores were then assigned based on an average of those lights. This involved a simple mathematical process of assigning a score of 0 points for red, 1 for amber and 2 for green, and then taking the average of these. In most cases, if that average was above 1.5 for the domain, the country was assigned an overall domain light of green; if between 1 and 1.5, amber; and, if lower, then red. In certain cases, these boundaries were varied based on specific circumstances of the domain. These are explained in detail in the traffic-light workbook that accompanies this report.

The three priority traffic-light domains are:

1. Tobacco control

Given the high percentage of lung-cancer cases that arise from smoking, attempts to reduce the practice are essential to prevention.

The indicators within this domain assessed:

a. whether the country is a party to the Framework Convention on Tobacco Control;

b. the coverage of legislation on smoke-free places;

c. the proportion of the price of a pack of cigarettes made up of taxes and the cost of cigarettes relative to GDP per head;

d. the extent of legislation banning marketing of tobacco products; and

e. the current age-standardised smoking rate and progress on reducing rates over the past 15 years.

2. Access to care

Lung cancer is a catastrophic disease, medical care for which would be very difficult for most individuals or families to afford on their own. This domain combines an assessment of the likely out-of-pocket cost for those of limited means along with a proxy for the level of access in rural areas.

The indicators within this domain assessed:

a. whether the least well-off economically in the country can receive affordable diagnosis and treatment for lung cancer; and

b. the degree of over-concentration of radiotherapy equipment in capitals or major cities (as this is a proxy of rural access, where this statistic indicated an appropriate concentration, scholarly and journal articles were consulted to consider the extent of rural access).

3. Early diagnosis

As with other cancers, a steep inverse relationship exists between the lateness of diagnosis and the likelihood of long-term survival. Accordingly, early diagnosis is crucial. This requires not just equipment, but efforts to improve the rate of diagnosis and to reduce stigma, so that more potential patients are willing to seek medical advice.

The indicators within this domain assessed:

a. the existence of efforts to address the problem of late diagnosis;

b. the combined percentage of new patients diagnosed at stages III and IV;

c. the availability of CT scanners per head (scoring based on regional averages); and

d. whether any efforts exist to reduce stigma towards those with lung cancer.

The five important traffic-light domains are:

1. Treatment

When prevention fails, effective, multi-disciplinary treatment is necessary. It is not always possible to assess the extent to which this occurs in practice, but if there is an absence even of policy to mandate such care, it is much less likely to occur.

The indicators within this domain assessed:

a. whether authoritative national guidelines for lung-cancer treatment exist and, if so, whether they stress the need for multi-disciplinary care and for testing appropriate tumours for relevant mutations;

b. the size of the cancer workforce, with the number of new cases per year per clinical oncologists used as a proxy;

c. the extent of equipment, with the proportion of patients needing radiotherapy able to access it used as a proxy;

d. the availability of key drugs independent of market price and state subsidy (as these issues are addressed as part of the access indicators); and

e. the mortality/incidence ratio for lung cancer.

2. Non-curative services

The large proportion of people with lung cancer for which treatment fails means that palliative care is essential for properly addressing the challenge of the disease. Meanwhile, the small number of survivors is expected to increase, so some understanding of their needs is also important.

The indicators within this domain assessed:

a. the degree of availability of high-quality palliative care that includes consideration of the specific needs of those with lung cancer; and

b. the presence in authoritative national guidelines of recommendations on pulmonary rehabilitation.

3. Non-tobacco prevention

Smoking is likely to be the cause of two-thirds of lung cancer in the study countries in aggregate. This domain looks at efforts to prevent the disease when caused by other leading major risks.

The indicators within this domain assessed:

a. progress towards measuring, or regulating, household radon levels;

b. average outdoor air pollution in urban areas;

c. the proportion of the population who use solid fuel indoors for cooking or heating; and

d. regulation of arsenic concentrations in drinking water.

4. Information and advocacy

Awareness and advocacy are key elements of successful cancer control. This domain looks at the extent to which lung-cancer related awareness programmes and advocacy groups exist. Because of the basic nature of what was measured, an overall green light requires green lights for all three indicators.

The indicators within this domain assessed:

a. whether a national-anti-smoking campaign had taken place in recent years and the range of media used to promote this campaign;

b. whether any sorts of campaigns, awareness-raising around given national or international lung cancer days, or any other efforts existed to improve awareness of lung cancer as distinct from purely anti-smoking activities; and

c. whether a group in the country exists that is associated with the Global Lung Cancer Coalition.

5. Data quality

Good data are essential for understanding and addressing the specific lung-cancer challenges of individual countries.

The indicators within this domain assessed:

a. the quality and extent of population-based cancer registration;

b. the quality of mortality data; and

c. the extent to which national organisations participate in the Latin American Consortium for the Investigation of Lung Cancer.

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