



## Progress and remaining challenges for cancer control in Latin America and the Caribbean

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Cancer is one of the leading causes of mortality worldwide, and an increasing threat in low-income and middle-income countries. Our findings in the 2013 Commission in *The Lancet Oncology* showed several discrepancies between the cancer landscape in Latin America and more developed countries. We reported that funding for health care was a small percentage of national gross domestic product and the percentage of health-care funds diverted to cancer care was even lower. Funds, insurance coverage, doctors, health-care workers, resources, and equipment were also very inequitably distributed between and within countries. We reported that a scarcity of cancer registries hampered the design of credible cancer plans, including initiatives for primary prevention. When we were commissioned by *The Lancet Oncology* to write an update to our report, we were sceptical that we would uncover much change. To our surprise and gratification much progress has been made in this short time. We are pleased to highlight structural reforms in health-care systems, new programmes for disenfranchised populations, expansion of cancer registries and cancer plans, and implementation of policies to improve primary cancer prevention.

### Part 1: Introduction

Our previous 2013 Commission<sup>1</sup> on cancer care in Latin America showed the existing and increasing burden of cancer in the region and identified several obstacles to providing optimum cancer services. Although some cancer incidences are lower in developed countries than in Latin American countries, overall cancer mortality in Latin American countries is about twice that of more developed countries. Ageing of the Latin American population, which will include more than 100 million people by 2020 (roughly a sixth of the total population), will continue to increase cancer incidence. About half of all cancers in Latin America are caused by smoke and infection<sup>2,3</sup> and addressing these issues urgently is imperative. Our commission also emphasised other widespread issues in which room for improvement could have been made: fragmented health infrastructures; restricted health-care coverage; insufficient funding and human resources and heterogeneity in distribution of them; and insufficient implementation of cancer registries and national cancer plans. In this 2015 update, we assess the effect of our first Commission on evolving cancer policies in Latin America since 2013, and identify remaining challenges.

We first summarise the cancer landscape and major areas that still need to be addressed in Latin America (part 1) and developments that have taken place as a direct or indirect consequence of the first Commission, with a focus on the evolution of cancer health policy and legislation in Latin America (parts 2–8). We present numerous specific examples of new projects across Latin America aimed at improving health literacy and public awareness, availability, and quality of cancer care, and at reducing cultural, geographical, and socioeconomic disparities. We show the most important of these initiatives in panel 1 and areas in which little or no change could be identified.

A move towards universal health care should be a priority for any health system, including those in developing countries.<sup>4</sup> Many questions remain with respect to how to accomplish this overall health care. In our 2013 Commission, we recommended adoption of changes that have led towards universal health care in some Latin American countries and promotion of financial protection for health and extension of patient coverage. Although an increase in the number of individual patients with coverage would seem the appropriate metric of change, this measurement does not necessarily include comprehensive health-care packages designed for complex diseases like cancer. In part 2, we review changing health systems in the present Latin American landscape, and emphasise the ambiguity of the use of increased numbers of people covered by health-care plans as an indicator of progress.

Cancer control needs not only the integration of prevention, screening, and a high quality diagnosis and treatment machinery but also the full range of other services, including rehabilitation, survivorship, and palliative care. In 2013, our Commission noted progress in regional palliative care services. These findings were exemplified by an increase in the number of states with palliative care programmes, the incorporation of educational courses for, and specialisation into, palliative care, an increase in opioid use for pain control, and an increase in awareness of the importance of palliative care. However, our Commission reported troubling and continuing restrictions in access to pain medication and we recommended strengthening of the training of health-care providers, promotion of palliative research, and establishment of a capacity to lobby health-care administrators to ensure wide distribution of opioid analgesics. The publication of the *Atlas of Palliative Care in Latin America*<sup>5</sup> has been a major advancement in palliative care and we now show progress in palliative care

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## Panel 1: Update of actions recommended in the 2013 Commission

### Increase financial resources for cancer control

- The percentage of gross national product spent on health care has increased in several countries, but is still much lower than in developed countries
- Access to high-cost drugs and procedures has increased
- Funding of expensive cancer drugs in public health systems is still scarce, which has resulted in increasing judicialisation of medicine

### Restructure health-care systems

- The proportion of people covered by basic health insurance in Latin America increased from 46% to 60% between 2008 and 2013
- Actions to protect uninsured patients against catastrophic health expenses have been implemented (eg, in Mexico and Uruguay)
- Only Brazil, Cuba, and Costa Rica have true universal health care, while most countries still have highly fragmented health-care systems with persistent segregation of health care

### Optimise oncology workforce to meet regional needs

- Awareness of the shortage of cancer specialists and the number of oncologists in Latin America has steadily increased, most notably in Brazil and Argentina
- Several programmes (eg, in Guatemala or Mexico), make use of patient navigators to overcome cultural and logistical barriers for indigenous and rural patients with cancer
- The number of cancer cases per oncologist is still much higher than in developed countries and the number of palliative care services and physicians is still severely low
- Despite numerous initiatives to redistribute health personnel to disenfranchised areas, most cancer specialists in Latin America still practice medicine in large, tertiary cancer centres
- Innovative strategies, including use of telemedicine, retraining of specialists, and incentive systems have yet to be widely implemented

### Improve technical resources and services for cancer prevention and treatment

- Under-implementation of new technologies has not improved substantially since the past Commission in 2013

with a few exceptions, for example, the availability of PET-CT has improved in Uruguay

- Insufficient quality of histopathological assessment is still a concern, as exemplified by the poor quality of Papanicolaou smears shown in studies of cervical cancer screening
- Long waiting times are still a major issue, hampering the effectiveness of promising screening, prevention, and early detection initiatives

### Invest in research and evidence-based cancer care relevant to the region

- Important steps have been undertaken to improve registry data, resulting in an increase in cancer registries of 40% in the region between 2011 and 2014
- Population coverage of registries is often still low
- In addition to registries, many ambitious new cancer plans and policies have been signed into policy, but still await full implementation
- Community-based participatory research is a promising new area of regional research in Latin America, which addresses specific barriers and interventions to overcome them
- Long-term outcomes of new initiatives, eg, with cervical cancer screening, are not systematically being monitored
- Preclinical and clinical research in oncology originating in Latin America has not increased substantially

### Invest in education

- Many new postgraduate educational and training initiatives are available, mostly national scholarship programmes and programmes fostering international exchange
- Singular telemedicine networks have been implemented in Peru, Ecuador, and Colombia, but their effect on outcomes needs to be assessed
- Public awareness is being enhanced through networks of community-based participatory research and by integration of health services into existing platforms and infrastructure (eg, by the non-governmental organisation Pro Mujer in Argentina, Bolivia, Mexico, Nicaragua, and Peru)

by the increase in number of palliative care services, palliative physicians per inhabitant, education and training programmes in palliative care, and the availability of potent analgesics (part 3).

In our 2013 Commission, we also reported that most Latin American countries did not have adequate cancer registries and subsequently have been unable to develop forward-looking and cohesive national cancer control plans (NCCPs). According to WHO, an NCCP is defined as “a public health programme designed to reduce cancer incidence and mortality and to improve the quality of life of

cancer patients, through the systematic and equitable implementation of evidence-based strategies for prevention, early detection, diagnosis, treatment and palliation, making the best use of available resources”.<sup>6</sup> We, and others, have recommended urgent establishment of NCCPs in the Latin American region.<sup>1,6,7</sup> The development of these plans was also recommended by the World Health Assembly in its resolution 58.22 in 2005.<sup>8,9</sup> We report changes in the number of countries with an NCCP, identify new health cancer policies, and report on the proportion of countries with a population-based cancer registry in the region (part 4).

As we showed in our 2013 Commission, financing of cancer control by governments is crucial, but economies and circumstances, particularly in the Latin American region, vary widely. Since our first report, more evidence has emerged correlating higher health expenditure with improved survival of patients with cancer by implementation of effective primary and secondary cancer screening.<sup>10</sup> Between 2000 and 2009, life expectancy in developed countries increased by 1.7 years and innovative drugs are widely thought to be responsible for 73% of this increase,<sup>11</sup> underlining the importance of prompt approval and easy access to new drugs. In 2013, the growth in Latin American pharmaceutical markets suggested a promising picture in which the gap in market size between developed and low-income and middle-income countries would be reduced. However, present figures show that despite the rapid growth in expenditures for cancer drugs in so-called pharmerging countries such as those in Latin America, these countries will still be substantially behind the expenditures of developed countries (table 1). We previously showed that not only does overall underfunding negatively affect overall survival in Latin America, but also that inequality of funding within countries is frequently an issue because, generally, most expenditures go into the private health-care sector. Additionally, fragmented health systems (part 1) cause delays in diagnostic workup and result in advanced tumours that frequently need expensive diagnostic procedures and treatments. Indices used to measure any change in the financing of health care include the yearly expenditures for health per person and the percentage of the gross national product (GNP) invested in health. We provide evidence that despite substantial progress in access to high-cost drugs for patients with cancer, many patients still do not have access to effective treatments, such as adjuvant trastuzumab for HER2 positive breast cancer (part 5).

We previously showed the need for adequate numbers of and training of health-care personnel for prompt and satisfactory treatment of cancer and noted that Latin American countries had few oncologists, haematologists, radiotherapists, cancer surgeons, and palliative care doctors in relation to the numbers of patients with cancer.<sup>1</sup> We assess how education and training have improved since our previous Commission (part 6). Although not necessarily measures of quality of cancer care, we used several metrics to assess progress, including the number of oncologists and the annual number of cancer cases per oncologist.

In addition to a scarcity of overall funding, we have previously suggested that major health inequities lead to worse outcomes for disenfranchised groups and minorities within Latin American countries.<sup>16</sup> Despite new initiatives aiming at a more equitable distribution of resources and care in this update we consistently show that disparities persist (part 7).

	GNP spent on health in 2010 (%)	GNP spent on health in 2013 (%)	Average expenditure per person on health in 2013 (US\$)	Estimated average pharmaceutical expenditure per person in 2016 (US\$)	Estimated population for 2016 (million)	Estimated pharmaceutical expenditure in 2016 (million US\$)
<b>Developed countries</b>						
USA	17.1	17.1	8959	892	325.2	290 078
Japan	9.6	10.3	4218	644	126.7	81 595
Canada	11.1	10.9	5660	420	35.4	14 868
Europe	..	..	50	375	211.7	79 388
France	11.6	11.7	4980	..	66.6	..
Germany	11.6	11.3	5226	..	80.7	..
UK	9.4	9.1	3802	..	64.4	..
South Korea	7.3	7.2	1870	323	49.2	15 892
<b>Pharmerging countries (high-income)</b>						
Brazil	9.0	9.7	1087	180	214.5	38 610
Russia	6.9	6.5	950	179	135.3	24 219
China	5.0	5.6	381	121	1367.0	165 407
<b>Pharmerging countries (middle-income)</b>						
Argentina	6.6	7.3	1074	..	43.8	..
Egypt	4.8	5.1	169	..	90.1	..
Indonesia	2.9	3.1	108	..	258.2	..
Mexico	6.3	6.2	639	..	119.9	..
Poland	7.0	6.7	915	..	38.2	..
Thailand	3.8	4.6	266	..	68.4	..
Turkey	5.6	5.6	614	..	83.4	..
Ukraine	7.8	7.8	304	..	43.7	..
Venezuela	4.7	3.4	490	..	29.7	..
<b>Lower-middle-income group</b>						
India	..	4.0	60	33	1266.9	42 022

Countries selected on the basis of availability of data.<sup>12-15</sup> GNP=gross national product. Pharmerging=countries with an increasing pharmaceutical market.

**Table 1: Average per person health expenditures in 2016 in selected countries**

Because a large proportion of cancers are due to specific biological causes and can be prevented and cured if diagnosed early and treated adequately, and with the enormous costs and substantial inequities associated with the growing cancer burden in Latin America, cancer prevention and control need to be public health priorities. In this context, we previously discussed the high smoking rates and ineffective tobacco control policies in many countries in the Latin America region. We report new national measures for tobacco control as well as cooperation between several countries in the region to regulate cross-border advertising and illicit tobacco trade between states. Indoor air pollution, a leading environmental health threat in Latin America, is also contributing to the cancer burden.<sup>17,18</sup> We previously reported that studies have linked *EGFR*-mutated lung cancer to indoor air pollution, often from wood smoke exposure.<sup>19-21</sup> We therefore advocated for further investigation into this issue and for promotion of initiatives that might support clean-air fuel sources for

cooking and heating.<sup>1</sup> In part 8, we once again report on the problem of indoor smoke and found that there has been little change in this area.

Among preventable cancers in Latin America and the Caribbean, more than 200 000 cases are attributable to infection and account for an estimated 17% of all cancers in this region in 2015.<sup>2,22</sup> The most widely reported infections related to cancer are due to human papillomavirus (HPV), which results in high rates of cervical cancer; hepatitis B or hepatitis C virus, contributing to liver cancer; and untreated *Helicobacter pylori*, causing gastric cancer. HPV causes nearly 100% of all cervical cancers and according to GLOBOCAN,<sup>22</sup> in 2015 an estimated 74 488 women in Latin America will be diagnosed with cervical cancer and 31 303 deaths will occur. We encouraged policy makers to focus on prevention of these avoidable cancers<sup>1</sup> and we now provide an extensive update on the very substantial efforts that have been undertaken to curtail HPV, in particular, in the region (part 8).

## Part 2: Fragmented health systems

Originally, Latin American health systems sought to enrol salaried workers.<sup>23</sup> With this scenario, universal health care would hopefully be gradually achieved through economic, professional, and social development. Unfortunately, this situation has not been the case in most of Latin America, where development did not create enough employment opportunities in the formal sector.<sup>24</sup> Health system fragmentation refers to a coexistence of subsystems with different modalities of financing, affiliation, and health-care delivery, specialising in different sectors of the population and often competing with one another.<sup>25</sup>

In 2015, most Latin American countries continue to have a fragmented health-care system with many separate health coverage schemes: well-funded social security systems covering formally employed people, which include coverage of cancer treatment, and poorly financed public insurance, run by each nation's Ministry of Health for informal workers and unemployed people, including coverage of only basic cancer treatment.<sup>26</sup> This model of health-care delivery goes against the fundamental core goals of universal health care and leaves a large segment of the population exposed to out-of-pocket catastrophic expenses.

In response to these continuing major disparities, many countries in Latin America have created special agencies that provide basic care for those who were previously uninsured. This basic universalism focuses on offering a minimal and very explicit health-care package of interventions for specific high-risk diseases.<sup>24</sup> The packages are targeted towards the poorest sectors of the population and focus mainly on preventive and primary care interventions. With increases in the number of people included in this basic coverage, the proportion of people covered by insurance systems in Latin America

grew from 46% to 60% between 2008 and 2013, according to the Pan American Health Organization (PAHO).<sup>27</sup> For example, in Peru, affiliations to health insurance programmes rose from 53% in 2008 to 65% in 2013, with high enrolment in extremely poor people.<sup>28</sup> The Mexican public insurance scheme termed Seguro Popular reported a total number of affiliated individuals of 55·6 million in 2013 (increased from 31·1 million in 2009), thus exceeding the original goal of 48·4 million people by 2013.<sup>29</sup> In Colombia, the percentage of individuals covered by the different insurance schemes went from 94% in 2010 to 96% in 2013, which represents an additional 2·5 million people.<sup>30</sup> The Argentinean Ministry of Health reported a decrease in the proportion of individuals without coverage from 48% in 2010<sup>31</sup> to 36% in 2014.<sup>32</sup> WHO, working in partnership with the World Bank, developed an agenda for 2015 to move towards universal health care worldwide in 2015, which includes cancer care in Latin America.<sup>33</sup>

In addition to these initiatives providing basic coverage, specific actions focusing on avoidance of large out-of-pocket health expenses in informally employed or unemployed patients with cancer have been undertaken. A programme in Mexico, which has been effective in providing access to standard cancer treatments, is the federal fund for protection of catastrophic health expenses as part of the Seguro Popular programme. The fund covers treatment expenses for uninsured patients with specific malignancies including: most haematological malignancies, breast, cervical, prostate, colon, testicular, and childhood cancers. This financial protection has been linked to better outcomes for children with cancer because of less treatment abandonment, which decreased from 10% a year before the programme started to 4·5% after its implementation.<sup>34</sup> For patients with breast cancer, this programme guarantees trastuzumab access to all patients with HER2 positive tumours. A follow-up study<sup>35</sup> of patients receiving neoadjuvant treatment and covered by this programme suggested that the proportion of pathological complete-response measurements achieved after treatment with trastuzumab were similar to those achieved in leading centres in the USA, despite the fact that 96% of patients included in the analysis had node-positive disease. These results show that access to treatment and comprehensive social security schemes are effective and fundamental for achievement of equitable goals in cancer care.

A similar approach to protect uninsured patients with cancer from ruinous health expenses has been introduced in other countries, such as Uruguay. Since January 2014, the administration of chemotherapy and radiation treatments is free of charge in Uruguay.<sup>36</sup> These initiatives are important because they offer people who are financially deprived access to effective cancer treatments that they would otherwise not receive.

However, although the number of people with basic coverage and protection from prohibitive expenses from



cancer care has increased, large differences remain between different types of insurance coverage, resulting in the persistence of fragmented care systems. This is particularly important for the treatment of chronic diseases such as cancer, in which complex multifaceted interventions are needed. In Latin America, only Brazil, Cuba, Costa Rica, and Uruguay can be deemed to be countries with integration of social security and public insurance, and only Brazil, Cuba, and Costa Rica can be judged to have universal health care.<sup>26,37</sup> Integration has many dimensions that need to be considered separately to adequately describe the fragmentation within a country's health system (table 2).<sup>38,39</sup> For example, within fragmented health systems, as in the case of Mexico, in which coverage is provided by six different institutions with their own independent network of hospitals, treatment centres, and unions, the availability of treatments and procedures is highly affected by the benefit packages included in each scheme, as shown in table 3. In Colombia, no fewer than 72 private insurers (known as Entidades Promotoras de Salud) in 2010 provided different packages and benefits with the support from the Colombian General System of Social Security in Health.<sup>39</sup> In 2012, in an effort to correct this, the Colombian Ministry of Health and Social Protection instituted the Plan Obligatorio de Salud (Mandatory Health Plan), which unified the existing schemes into a single benefit package for the entire population (table 3).<sup>30</sup> This package was expanded in 2013 and 2014 and now covers all types of cancer.<sup>30</sup> In an effort to reduce payment fragmentation by use of the government initiative, the number of organisations in Colombia providing health financing decreased from 72 to 48 in 4 years, and the plan is to reduce this number even further.<sup>51</sup> Likewise, in Chile, where individuals are able to enrol into the integrated public system (El Fondo Nacional de Salud) or with a private insurer (Instituciones de Salud Previsional),<sup>52</sup> the government created a Universal Access with Explicit Guarantees (Acceso Universal con Garantías Explícitas) Programme, which ensures standardised treatment for 80 conditions (including all malignancies in people younger than 15 years and 11 malignancies in adults).<sup>53</sup> The approach used in both Colombia and Chile, unifying benefits without creating a universal health system, could potentially lead to more equitable health care, but this method still has shortcomings, mainly because each insurer can independently control payment method (for example, while some health institutions in Chile, known as Las Instituciones de Salud Previsional, pay for up to 80% of inpatient expenses, others pay for only 60%),<sup>54</sup> and that the coverage does not necessarily include all malignant diseases.

Conversely, Costa Rica is one of the few countries in the region offering almost complete universal health care financially and geographically, through a single organisation, the Caja Costarricense de Seguro Social (the Costa Rican Social Security Administration).<sup>55</sup> Although

	Brazil	Chile	Colombia	Costa Rica	Mexico
Number of organisations offering coverage	Medium-high (private health insurers)	Low-medium	High	Low	Medium
Mechanisms of risk pooling to limit out-of-pocket expenditure	Low	Low-medium	Low-medium	Low	Medium
Number of eligibility categories	Low-medium	Low	Low-medium	Low	Medium
Number of different benefit packages	Low	Medium	Low	Low	Medium
Number of different premium levels	Low-medium	Medium	Low-medium	Low-medium	Medium
Number of different payers (eg, private insurance companies and different public schemes)	Medium	Low	High	Low	Medium

Fragmentation categories were defined by the Inter-American Development Bank (IADB) by use of the framework described by McIntyre and colleagues.<sup>38</sup> Ratings (low, medium, and high) for each category were established by the IADB with detailed case studies for each country.<sup>39</sup> Countries were identified and selected intentionally along a continuum of low-to-high fragmentation to represent the region's diversity.

**Table 2: Rating of the amount of fragmentation of each dimension of the health system in five Latin American countries**

the Costa Rican health-care experience has been hailed as a model for other countries, generalisation of this system to the rest of Latin America is difficult because, by contrast to its neighbours, Costa Rica has a history of political stability and social development and these factors have helped with the introduction of these reforms.

Countries with universal health care, such as Brazil, exclude numerous standard drugs in public health insurance, such as trastuzumab for breast cancer (table 3; panel 2). As a result, a private sector with much wider coverage has evolved, resulting in persistent segregation of health care. For example in Brazil, where all of the population is covered by a public, tax funded, universal health scheme called Sistema Único de Saúde (SUS), not all cancer treatments are covered. When an intravenous anticancer drug is approved by the local regulatory agency, coverage is only mandatory in the supplemental private health-care system, which covers only 25% of the population. For incorporation into the public health system, however, drugs have to be assessed by CONITEC (Comissão Nacional de Incorporação de Tecnologias no SUS), which undertakes formal health technology assessments. A similar difference between public and private insurance coverage has developed in the case of oral anticancer drugs: new legislation enforced the coverage of oral drugs in the private setting in January 2014, whereas access for publicly insured patients depends on health technology assessments by CONITEC.<sup>57</sup>

### Part 3: Palliative care

Since 2013, a major advance in the specialty of palliative care in Latin America has been the publication of the *Atlas of Palliative Care in Latin America* by the Latin American Association for Palliative Care (Asociación

Mexico		Brazil		Colombia: unified public scheme (Plan Obligatorio de Salud)	Costa Rica: unified health system (CCSS)	Chile: universal access with explicit guarantees (AUGE)
Public health system (Seguro Popular)	Social security (IMSS)	Government employees system (ISSSTE, SEDENA, PEMEX, SEMAR)	Unified public health care system (Sistema Único de Saúde)	Supplemental health system (private Insurance)		
45%	44%	7%	100%*	25%	94%	97%†
Proportion of population covered						
Covered cancers	Paediatric cancer, cervical cancer, breast cancer, germ-cell tumours, non-Hodgkin lymphoma, prostate cancer, colorectal cancer	All malignant diseases are covered	All malignant diseases are covered	All malignant diseases are covered	All malignant diseases are covered	Paediatric cancer, cervical cancer, breast cancer, germ-cell tumours, lymphoma, prostate cancer, colorectal cancer, gastric cancer, CNS tumours, leukaemia, ovarian cancer, bladder cancer, osteosarcoma
Metastatic breast cancer	Taxanes, capecitabine, platinum, vinorelbine, anthracyclines, trastuzumab, tamoxifen, aromatase inhibitors	Taxanes, capecitabine, platinum, vinorelbine, anthracyclines, trastuzumab, tamoxifen, aromatase inhibitors, bevacizumab	Taxanes, capecitabine, platinum, vinorelbine, anthracyclines, trastuzumab, pertuzumab, lapatinib, tamoxifen, aromatase inhibitors, fulvestrant, bevacizumab, everolimus	Taxanes, capecitabine, platinum, anthracyclines, trastuzumab, tamoxifen, aromatase inhibitors, fulvestrant	Taxanes, capecitabine, platinum, anthracyclines, trastuzumab, tamoxifen, aromatase inhibitors	Taxanes, capecitabine, anthracyclines, tamoxifen, aromatase inhibitors
Metastatic prostate cancer	GNRH1 analogues, antiandrogens, ketoconazole, docetaxel	GNRH1 analogues, antiandrogens, ketoconazole, estramustine, abiraterone, cabazitaxel	GNRH1 analogues, antiandrogens, ketoconazole, Docetaxel	GNRH1 analogues, antiandrogens, ketoconazole, docetaxel, abiraterone, cabazitaxel, enzalutamide‡	GNRH1 analogues, antiandrogens, ketoconazole, docetaxel	GNRH1 analogues, antiandrogens
Metastatic lung cancer	Not covered	Platinum, gemcitabine, taxanes, pemetrexed, crizotinib, erlotinib, gefitinib	Platinum, gemcitabine, taxanes, erlotinib, gefitinib§	Platinum, gemcitabine, taxanes, pemetrexed, erlotinib, gefitinib	Platinum, gemcitabine, taxanes, erlotinib, gefitinib	Not covered
Supportive care	Zoledronic acid, ondansetron, palonosetron, granisetron, tropisetron, adverse events needing admission to hospital not covered	Zoledronic acid, aprepitant, ondansetron, palonosetron, granisetron, dexrazoxane, filgrastim, pegfilgrastim, molgramostim	Zoledronic acid, ondansetron, filgrastim	Zoledronic acid, aprepitant, ondansetron, palonosetron, granisetron, dexrazoxane, filgrastim, molgramostim, pegfilgrastim	Zoledronic acid, aprepitant, granisetron, tropisetron, filgrastim	Zoledronic acid, ondansetron, filgrastim

IMSS=Instituto Mexicano del Seguro Social. ISSSTE=Instituto de Seguridad y Servicios Sociales de los Trabajadores del Estado. SEDENA=Secretaría de la Defensa Nacional. PEMEX=Secretaría de Marina. CCSS=Caja Costarricense de Seguro Social. AUGE=Acceso Universal con Garantías Explícitas. \*All citizens and foreigners in the country are covered, including undocumented non-citizens. †80% of the population is covered by the integrated public system only. 17% of the population also affiliated with a private provider can get additional drugs depending on the provider's specific scheme. ‡Enzalutamide has been approved by Agência Nacional de Vigilância Sanitária, the Brazilian regulatory agency, but it has not yet been included in the list of covered oral cancer medications established by Agência Nacional de Saúde, which regulates the supplemental (private) health system. §Erlotinib and gefitinib are covered for patients with activating EGFR mutations, but results in a loss to the health-care provider, and as such, are mostly unavailable.

Table 3: Selected cancer benefit packages according to organisation providing care in five Latin American countries<sup>20,40-49</sup>

Latinoamericana de Cuidados Paliativos).<sup>5</sup> The Atlas is the first systematic gathering of information on the status of palliative care in Latin America, and it represents cooperation between different institutions worldwide including the International Association for Hospice and Palliative Care, the European Association for Palliative Care, the Spanish Society of Palliative Care (Sociedad Española de Cuidados Paliativos), and the University of Navarra, Spain, to collect in-depth data.<sup>5</sup> Our intent is to compare data published in our previous Commission with present data to recognise any developments. However, this comparison cannot be achieved for all countries because before the publication of the Atlas, information was scarce and in some cases imprecise.

The main findings of the *Atlas of Palliative Care in Latin America* are summarised in table 4.<sup>5</sup> In 2011, 922 palliative care services existed in Latin America: 1.63 services, or units, or teams per 1 million inhabitants (range 0.24–16.6) compared with 200 services (range 33 to 13 315 services per 1 million inhabitants) reported in 2006.<sup>58</sup> An obvious increase in the number of palliative care services can be noted, including home care teams (0.4 per million inhabitants), hospital support services (0.34), and multilevel teams which include both home care and hospital support services (0.33). These findings mean restricted coverage for multilevel services in the region exists<sup>59,60</sup> and is consistent with the fact that in 2004 only 20–30%<sup>60</sup> of Latin America physicians reported to have those services available. Most of the services are located within the public health system, whereas availability in the private sector is very hampered by unclear mechanisms of insurance reimbursement structures.<sup>59,60</sup> As a result of scarce palliative care services, we and others, have advocated for ambulatory (outpatient) palliative care instead of expensive end-of-life inpatient care because this service is cost-effective and has been shown to improve quality of life for patients and their families.<sup>61</sup>

A major recommendation made by our previous Commission was related to training of palliative physicians and health-care providers. At the end of 2012, about 600 palliative care doctors (average 1.7; range 0.0–11.4 physicians per 1 million inhabitants)<sup>5</sup> were estimated to be accredited in the Latin American region. Some countries, such as Argentina, have recently integrated palliative care courses in training programmes, but many countries still have no specific training (eg, Bolivia, El Salvador, Honduras, and Nicaragua; table 4 and part 6).<sup>5</sup>

We previously recognised a need to increase regional research in palliative care to overcome country-specific barriers. In 2008, only 10% of specialised physicians in the region participated in research activities in palliative care. This national research was largely prompted by the integration of national and international research groups in the region.<sup>62</sup> In 2015, we identify 11 Latin American

#### Panel 2: A Brazilian example of disparities in funding between the private and the public sector with respect to EGFR tyrosine kinase inhibitors for lung cancer

An important example showing the difficulties associated with the assessment of cancer drugs in Brazil is that of the incorporation of EGFR tyrosine kinase inhibitors into the treatment of patients with lung cancer and activating mutations in the *EGFR* gene. Comissão Nacional de Incorporação de Tecnologias no SUS (CONITEC) initially denied the inclusion of gefitinib and erlotinib into the Brazilian market and public system, on the basis of the organisation's assessment of the scientific literature and conclusion that the drugs did not improve overall survival. After this decision, a mandated period of public consultation followed, in which groups of oncology professionals, patient advocacy organisations, and industry argued that clinical experience and population-based studies have clearly shown improvements in overall survival. In addition to this success, progression-free survival and quality of life improved in the clinical trials, which might not have shown an overall survival benefit because of substantial crossover of patients to the active arm of the study during the clinical trial. This evidence was then accepted and gefitinib and erlotinib were added into the Brazilian health system. In practice however, these drugs are still not available for most patients, as testing for *EGFR* mutations and the respective tyrosine kinase inhibitors (TKIs) are still not separately refunded. Public providers are expected to do the test within their budgets and to pay for the drugs with the chemotherapy coding, which creates a financial loss for individual hospitals, due to the higher cost of *EGFR* TKIs when compared with more traditionally used drugs. A survey<sup>66</sup> of 1792 patients with adenocarcinoma of the lung treated in Brazil in 2014 showed that only 33% of patients in the public system, compared with 62% in the private setting, were tested for *EGFR* mutations.

countries with at least one palliative care association and nine countries with active research groups (35 groups for the whole Latin American region). Additionally, 64 international collaborative initiatives are focused on training and research in palliative care.<sup>5,59</sup>

The scarcity of legislation for end-of-life care, poor rates of signing advance directives, and little availability of potent analgesics are further obstacles leading to disparities in palliation. However, some countries in the region have passed laws aimed to increase the availability of advance directives. In 2008, Mexico City instituted the Ley de Voluntad Anticipada (Advance Directives Act),<sup>63</sup> which was later followed by other states in the country and was included in the Ley General de Salud (National Health Act) in 2013.<sup>64</sup> The adoption of such laws into practice has been slow and only about 3000 advance directives have been signed in Mexico City since 2008, with 840 documents signed in 2013, and 1633 in 2014.<sup>65</sup> Of note, of all the advance directives signed in Mexico City, 48% were in private hospitals, 31% were in specialised National Institutes, and only 21% were in public hospitals.<sup>66</sup>

Inadequate availability of opioids in the region is well known. In 2002, Latin America accounted for less than 1% of the world's opioid consumption, but for 7% of the world's population.<sup>67</sup> In response to the urgent need to implement regional and national guidelines, ten countries in Latin America have published at least one guideline or standard of care for palliative care, three have a national palliative care law, seven have a national palliative care

	Total palliative services* (per million)	Physicians with palliative care accreditation	Medical schools teaching palliative care (%)	Palliative care research groups	Consumption of strong opioids† (mg per capita)	ALCP Index‡
Argentina	151 (3·8)	100	6 (22)	5	12·88	4·39
Bolivia	6 (0·6)	..	0 (0)	0	0·16	-5·42
Brazil	93 (0·5)	..	3 (2)	1	11·16	2·94
Chile	277 (16·1)	70	12 (57)	27	10·97	6·25
Colombia	23 (0·5)	43	3 (5)	4	6·59	-0·12
Costa Rica	63 (14·7)	49	2 (29)	0	9·63	8·10
Cuba	51 (4·5)	37	22 (100)	4	2·16	3·03
Dominican Republic	8 (0·8)	..	1 (10)	1	0·99	-4·58
Ecuador	12 (0·8)	..	3 (25)	0	1·51	-3·84
El Salvador	4 (0·6)	..	1 (17)	0	3·05	-3·74
Guatemala	7 (0·5)	..	1 (11)	0	0·92	-4·46
Honduras	2 (0·2)	..	0 (0)	0	0·63	-5·21
Mexico	119 (1·1)	250	5 (9)	4	8·76	6·00
Nicaragua	13 (2·1)	..	0 (0)	0	1·18	-4·30
Panama	9 (2·6)	2	2 (50)	2	3·03	0·22
Paraguay	4 (0·6)	..	2 (21)	0	..	..
Peru	12 (0·4)	..	0 (0)	3	1·64	-2·33
Uruguay	23 (7·0)	20	2 (100)	0	5·86	3·63
Venezuela	45 (1·6)	4	1 (13)	0	2·88	-0·58
Total	922 (1·6)	575	66 (14)	51	..	..

Selected countries on the basis of the survey by ALCP.<sup>2</sup> Countries represented by individuals with previously published studies on the status of palliative care in their own country; or by individuals whom the ALCP Steering Committee or working group members have made reference to as palliative care professionals. ALCP=Latin American Association for Palliative Care (Asociación Latinoamericana de Cuidados Paliativos). \*Palliative services include home-care teams, hospital support services, and multilevel teams consisting of a combination of these. †For example, morphine, hydromorphone, fentanyl, and pethidine (strong agonists of the morphine receptor). ‡ALCP index=an index showing development of palliative care at the national level; high development (rank at the 75th percentile) of palliative care is described as a score of 3·80 or more and low development (rank at the 25th percentile) is a score of less than -4·30.

**Table 4: Indicators of quality in palliative care in Latin America**

plan or programme, and five have included palliative care in their cancer control plan. One example of progress in the region is Uruguay, which in 2013 launched the National Palliative Care Plan to increase training for physicians in palliative care, increase the number of people with access to palliative care, and enhance access to analgesic drugs, particularly opioids.<sup>68</sup> This plan has led to the integration of new opioids into regulatory initiatives. However, consumption of strong opioids is low throughout Latin American countries, with no country exceeding 15 mg per capita (table 4). By comparison, consumption in developed countries is usually between at least 50–400 mg per capita.<sup>5,69</sup>

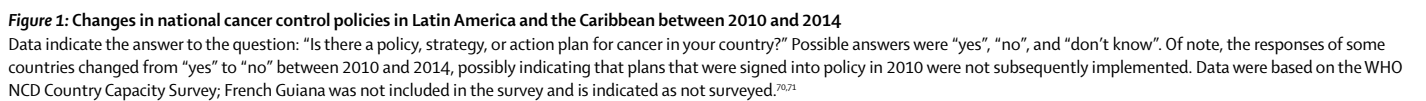
In an effort to measure progress in palliative care, the Latin American Association for Palliative Care developed an index that provides a general representation at the national level. This report<sup>59</sup> showed that Costa Rica, Chile, Mexico, and Argentina were high-ranking in their level of palliative care with a high Asociación Latinoamericana de Cuidados Paliativos index, whereas Bolivia, Honduras, Dominican Republic, and Guatemala ranked low (table 4).

## Part 4: National cancer plans and cancer registries

In the 2011 country profiles for non-communicable diseases, WHO reported that 52% of Latin American and Caribbean countries had an integrated policy, or programme, or action plan for cancer.<sup>70</sup> For 2014, WHO reported an 8% increase in the number of countries (60% of the whole region) with an NCCP,<sup>71</sup> with these countries having newly adopted plans: Suriname, Ecuador, Dominican Republic, Trinidad and Tobago, Puerto Rico, Peru, El Salvador, and Colombia (figure 1). Belize has established the plan of action for the prevention and control of non-communicable disease, however, this plan, in itself, is not a specific NCCP. Peru's Plan Esperanza is an example of a successful NCCP implemented in Latin America in which a multidisciplinary team including policy makers joined efforts to obtain and develop cancer control policies.<sup>72</sup> In the specific cancer primary prevention policies that were operational at a national level in 2011 and 2014, an increase in the number of healthy lifestyle policies was reported, including those directed against obesity, tobacco use, and harmful alcohol use (figures 2–5).<sup>70,71</sup> According to the 2014 WHO cancer country profiles,<sup>71</sup> nationwide immunisation had been officially introduced against HPV in 51% of Latin America countries and against hepatitis B virus in 100% of Latin American states. Measures related to cancer screening and early detection were also reported, with 54% of countries reporting a national mammography policy, 90% a cervical cytology policy, and 57% some form of colorectal cancer screening policy (either with faecal occult blood test or colonoscopy). Overall, the proportion of operational cancer control policies in the region has increased between 5–10% over the past 3 years.<sup>70,71</sup> Figures 1–5 describe differences in cancer plans, policies, and cancer registries between 2011 and 2014 in Latin America.

Several national policies related to cancer control have been introduced since the publication of our first Commission, for example, the Belize National Plan of Action for the Prevention and Control of Non-Communicable Diseases (2013–23).<sup>73</sup> The objectives are: 30% reduction in tobacco use; 10% reduction of sedentary lifestyle, and 10% reduction of harmful alcohol use. In addition, the Puerto Rico Chronic Disease Action Plan (2014–20) has also been introduced.<sup>74</sup> The objectives were: implementation of electronic health records; adoption and implementation of an expanded chronic care model; and policies on nutritional standards and physical activity. A further policy which has been introduced is the Suriname National Action Plan for the Prevention and Control of Non-Communicable Diseases (2012–16).<sup>75</sup> The objectives of this plan are: development of a national cancer plan; increased access to generic drugs; 50% reduction in tobacco use; 40% reduction in alcohol misuse in young people; and implementation of protocols for screening and prevention of chronic diseases in 80% of the population. These ambitious plans, although signed into policy, are not fully





In this context, Peru is one of the few countries in the region that has not only created and adopted, but, as of 2013, already implemented an NCCP, the Plan

Esperanza, including assessment and quantitative reporting of its subsequent changes.<sup>76</sup> As of December, 2014, more than 106 000 patients with cancer were included in the Plan Esperanza, of whom 88 000 were treated at the National Cancer Institute of Neoplastic



**Figure 2: Changes in national obesity control policies in Latin America and the Caribbean between 2010 and 2014**

Data indicate the answer to the question: "Is there a policy, strategy, or action plan for reducing overweight or obesity in your country?" Possible answers were "yes", "no", and "don't know". Of note, the responses of some countries changed from "yes" to "no" between 2010 and 2014, possibly indicating that plans that were signed into policy in 2010 were not subsequently implemented. Data were based on the WHO NCD Country Capacity Survey; French Guiana was not included in the survey and is indicated as not surveyed.<sup>70,71</sup>

Diseases (Instituto Nacional de Enfermedades Neoplásicas) in Lima. As a result, the proportion of patients who paid out-of-pocket cancer expenses for cancer treatment decreased from 58% in 2009 to 7% in 2014.<sup>76</sup> At the same time, the proportion of patients

included in the universal health care system and provided with cancer coverage by the public health insurance system (El Seguro Integral de Salud) increased from 17% to 64%. In 2013, ten neoplastic diseases were included in the Plan Esperanza and



**Figure 3: Changes in national tobacco control policies in Latin America and the Caribbean between 2010 and 2014**

Data indicate the answer to the question: "Is there a policy, strategy, or action plan to decrease tobacco use in your country?" Possible answers were "yes", "no", and "don't know". Of note, the responses of some countries changed from "yes" to "no" between 2010 and 2014, possibly indicating that plans that were signed into policy in 2010 were not subsequently implemented. Data were based on the WHO NCD Country Capacity Survey; French Guiana was not included in the survey and is indicated as not surveyed.<sup>70,71</sup>

overall, 16 million people have received preventive interventions consisting of educational sessions and counselling and 2·5 million have been screened for cervical, breast, gastric, colon, or prostate cancer, or for a combination of these diseases.<sup>76</sup>

Apart from national cancer plans, Latin American countries are also included in and targeted by international policies aimed at cancer control and prevention. Such international efforts that were prompted since our 2013 Commission include The



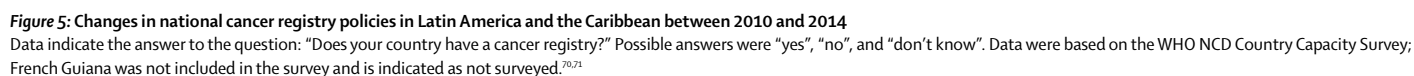
**Figure 4: Changes in national alcohol control policies in Latin America and the Caribbean between 2010 and 2014**

Data indicate the answer to the question: "Is there a policy, strategy, or action plan for reducing the harmful use of alcohol in your country?" Possible answers were "yes", "no", and "don't know". Of note, the responses of some countries changed from "yes" to "no" between 2010 and 2014, possibly indicating that plans that were signed into policy in 2010 were not subsequently implemented. Data were based on the WHO NCD Country Capacity Survey; French Guiana was not included in the survey and is indicated as not surveyed.<sup>70,71</sup>

Global Action Plan for the Prevention and Control of Non-Communicable Diseases 2013–2020, endorsed by WHO, which aims to achieve a 25% reduction in premature mortality from Non-Communicable Diseases by 2025.<sup>77</sup> The objectives of this programme

include: prevention of liver cancer through hepatitis B immunisation; prevention of cervical cancer through screening linked with timely treatment; and vaccination against HPV. Other objectives include: breast cancer screening linked with timely treatment and oral cancer





objectives of this initiative are: enhancement of advocacy and communication; building of health-care capacity for screening, diagnosis, treatment, and palliative care; and quantification of access to HPV vaccination and strengthening of research in breast and cervical cancer.<sup>78</sup>

A third example of an international effort for cancer control since the 2013 Commission is the International Cancer Control Planning Partnership (ICCP), which was launched by the Center for Global Health and the National Institutes of Health in the USA with The Latin America and Caribbean Society of Medical Oncology (Sociedad Latinoamericana y del Caribe de Oncología Médica) and PAHO as founding members along with the Union for International Cancer Control and International Atomic Energy Agency's Programme of Action for Cancer Therapy.<sup>79</sup> This partnership was set up to implement and assess NCCPs with a worldwide framework and international support. The main initiatives include: the establishment of the National Cancer Control Planning Web Portal, several educational training initiatives, fellowships, workshops, and leadership forums.

High quality epidemiological data should be the basis of cancer control plans and comprehensive cancer registries should be a fundamental requirement for successful implementation of NCCPs. In 2011, only 21% of Latin American and Caribbean countries reported having a population-based cancer registry, compared with 67% in 2014 (figure 1). Of the registries in 2014, more than 60% are national, 45% are population-based (covering all new cases in a well-defined population) and 36% are subnational (covering all new cases within a specified geographical area).<sup>70,71</sup> However, the proportion of the population covered by these cancer registries is still very low compared with developed nations, such as the North America (83% population coverage) or Europe (32% population coverage).<sup>80,81</sup>

One of the most successful examples of a high quality epidemiological registry is the Cali Cancer Registry in Colombia, which started in 1962 as an academic initiative. The Cali Registry has been recognised as one of the most trustworthy and reliable sources of epidemiological cancer data in Latin America. The information is collected by actively searching hospital and other medical facility files periodically. This registry has led health authorities to establish specific public health strategies in the region.<sup>82</sup>

To aid in the creation of population-based cancer registries in Latin America and worldwide, the International Agency for Research on Cancer has created the Global Initiative for Cancer Registry Development<sup>83</sup> to empower countries to develop national cancer registries by providing support and sharing knowledge. Key activities in each region include provision of localised training and tailored support, promotion of research, and assistance with advocacy and the development of networks. In 2014, the regional hub in Latin America has been established in Buenos Aires at the National Cancer Institute of Argentina (Instituto Nacional del Cáncer de Argentina) to develop and promote the initiative's activities in the region.<sup>83</sup>

## Part 5: Financing of cancer care

The IMS Institute for Healthcare and Informatics forecasts that for 2016, worldwide expenditure for medicines will be US\$1.2 trillion (\$615–645 billion spent on branded drugs and \$400–430 billion spent on generics); 30% of this expenditure will be from pharmerging markets (in 2012 this amount was 20%).<sup>12</sup> Thus, although the USA is expected to increase its spending on drugs by 1–4%, pharmerging countries are expected to increase their expenditures by 12–15%, primarily on cancer care.<sup>12</sup>

Between 2003 and 2008, growth of the cancer therapeutics industry was consistently more than 15% per year, after the approval of bevacizumab and the inclusion of trastuzumab into adjuvant breast cancer treatment guidelines.<sup>84</sup> In 2012, the US Food and Drug Administration approved a record number of drugs, especially in oncology.<sup>84</sup> However, although the pharmaceutical market and research environment in emerging economies such as Brazil, China, and India is growing rapidly (eg, by 17% in Brazil and 14% in China in 2013), this growth does not benefit many publicly insured patients in Latin America (parts 2, 5).<sup>85</sup> Average expenditures on health care per person, in addition to total health-care spending as a percentage of GNP, are still much lower in pharmerging countries than in developed countries (table 1).<sup>12–15</sup> In some pharmerging countries, the percentage of GNP spent on health care has increased between 2010 and 2013 (eg, in Brazil from 9.0% to 9.7% and in Argentina from 6.6% to 7.3%), but this expenditure is still much lower than it is in developed countries (eg, Canada spent about 11% in 2013).<sup>13</sup>

Poor access to high-cost drugs and the under-implementation of new technologies have not improved greatly since 2013, although some important progress has been made. This advancement includes substantial efforts in several countries to offer HPV vaccination (part 7). Additionally, PET-CT is now available in the private and (in special situations) the public sector in Brazil and nationwide in Uruguay. In Uruguay, funding of PET-CT and other highly specialised medical procedures and expensive drugs are provided for all residents by the National Resources Fund (Fondo Nacional de Recursos).<sup>86</sup> Panel 3 summarises reports from CONITEC and incorporations of several new technologies or drugs into the public health-care system in Brazil.<sup>87–105</sup> Available drugs in the public and private health systems for several Latin American countries are shown in table 3.

Despite all of these efforts, funding of expensive cancer medicines in Latin America is still insufficient, particularly in the public health systems. This situation has resulted in the judicialisation of medicine: increasingly, drug claims are presented to the legal systems on the grounds of protecting right to health policies. These claims have varying grades of severity, scope, and differential effects in the countries of Latin

America.<sup>106</sup> In Brazil, for example, the constitutional right to health care leads many citizens to sue the State for access to cancer drugs that are not officially included in SUS. In most of the cases, patients win these trials,<sup>107</sup> but many such claims clog the judicial system and result in inefficient and erratic availability of drugs for patients with cancer. Roughly 240 000 health-related lawsuits at several levels are estimated to be in the Brazilian judiciary at present. A study<sup>107</sup> of 80 462 cases available from a commercial database showed that, overall, 2862 patients (3·6%) obtained their cancer drugs through the legal system.<sup>107</sup> This number increased by 65·5% over 2 years—from 426 in the first half of 2012 (3·3% of all patients) to 705 in the second half of 2014 (4·8% of all patients). 1483 (3·9%) of 38 326 patients in the private sector took legal recourse to access drugs compared with 1379 (3·3%) of 42 136 patients in the public system. Likewise, in Uruguay, the number of disputes has grown steadily, especially in the past 4 years.<sup>106</sup> The increase in legal claims is partly due to the success of previous legal claims and their publicity in the media.<sup>106,108</sup>

Drugs most often obtained through court orders from 2012 to 2014 were: trastuzumab, sunitinib, erlotinib, capecitabine, and abiraterone. The process is very dynamic and court orders for trastuzumab decreased from 109 in the first half of 2012 to 29 in the second half of the year, probably because of the incorporation of this drug into the public health-care system. As coverage for oral drugs approved by regulatory agencies has become mandatory in the private setting, a future decrease in the number of court orders is plausible. For example, the number of patients in Brazil who have had access to sunitinib through the legal system decreased from 153 in 2012 to 104 in 2014 because access to sunitinib for insured patients with cancer improved.<sup>107</sup>

Enrolment in clinical trials sponsored by the pharmaceutical industry is sometimes an option for patients in Latin America, providing access to high-cost drugs that are otherwise unavailable. In several Latin American countries, for example Brazil, clinical research is facing difficulties because of ineffective regulatory processes, so therefore the migration of clinical trials from developed countries to low-income and middle-income countries noted in the past decade has come to a halt.<sup>109,110</sup> Additionally, clinical trial participation is only an option for a few patients with cancer and cannot substitute for approval and funding of these drugs once they have been shown to be effective. Patients participating in these trials sometimes cannot complete treatment once off a trial and these studies usually do not lead to approval in Latin America, so that ultimately, pharmaceutical trials are not helpful to most patients in this region.

To assess the cost-effective benefits of new cancer treatments in Latin America, local pharmacoeconomic studies are essential. In 2014, a global systematic review,<sup>110</sup>

### Panel 3: CONITEC resolutions by intervention or technology for various cancers

#### CA125

Use for follow-up of patients with ovarian cancer<sup>87</sup>

#### Trastuzumab

For adjuvant and neoadjuvant treatment only; rejects treatment of advanced breast cancer with trastuzumab<sup>88,89</sup>

#### α interferon

For adjuvant treatment of stage III melanoma<sup>90</sup>

#### Rituximab

Not offered for follicular lymphoma; as first and second line treatment for CD20+ non-Hodgkin lymphoma<sup>91,92</sup>

#### Erlotinib

For treatment of advanced lung cancer with *EGFR* mutation, but no additional funds for *EGFR* testing or the drug, which hinders the delivery of the drug to patients in most public hospitals<sup>93</sup>

#### Gefitinib

For treatment of advanced lung cancer with *EGFR* mutation, but no additional funds for *EGFR* testing or the medication, which hinders the delivery of the medication to patients in most public hospitals<sup>94</sup>

#### HPV vaccine

Tetravalent vaccine against HPV in the public health system<sup>95</sup>

#### Cetuximab

Rejects treatment of patients with colorectal carcinoma with liver metastases and patients with head and neck cancer<sup>96,97</sup>

#### Everolimus

Rejects treatment of postmenopausal patients with advanced breast cancer<sup>98</sup>

#### PET-CT

PET-CT for staging of non-small-cell lung cancer, of potentially resectable liver metastases, and for staging and assessment of treatment response in Hodgkin's and non-Hodgkin lymphomas<sup>99–101</sup>

#### Radioactive iodine

For thyroid carcinoma<sup>102</sup>

#### Hormonal treatment

Neoadjuvant hormonal treatment for breast cancer<sup>103</sup>

#### Imatinib

Adjuvant imatinib to treat gastrointestinal stromal tumours<sup>104</sup>

#### Temozolamide

Rejects postsurgery treatment of high grade gliomas with temozolamide<sup>105</sup>

CONITEC=Brazilian National Commission of Incorporating Technologies in the Public Health System.

about the effect of non-communicable diseases and the impoverishment they cause, identified 28 studies of which only one was carried out in Latin America.<sup>111</sup> Of 153 studies included in another global systematic review<sup>112</sup> about the effect of non-communicable disease on health-care spending and national income, only five were carried out in low-income and middle-income countries. To address the scarcity of local pharmacoeconomic data,

	Number of clinical oncologists	Cancer incidence* per year	New cancer cases per year per oncologist	Annual cancer mortality*
Brazil	2577	576 000	224	224 700
Germany	2899	528 000	182	217 600
Mexico	352	148 000	420	78 700
Panama†	10	5400	540	2900
UK	476	331 000	695	157 800
Uruguay	120	13 300	111	8700
USA	13409	1 600 000	119	617 000

\*Numbers have been rounded. †Lopez RI, Instituto Oncologico Nacional de Panama, Panama, personal communication; and Touya D, unpublished.

**Table 5: Number of clinical oncologists, cancer incidence, number of new cases per year per oncologist, and cancer mortality in selected countries**<sup>121,124,127-129</sup>

Latin American countries have begun to establish specialised centres or agencies for health technology assessments, which are intended to guide decisions on public policy and interventions, such as the adoption of drugs and medical devices. For example, in Brazil the Institute of Technology Assessment in Health (Instituto de Avaliação de Tecnologia em Saúde)<sup>113</sup> is increasingly producing local evidence to support decisions for incorporation of novel health-care technologies. The National Cancer Institute of Argentina is also undertaking local cost-effectiveness studies.<sup>114</sup> Other specialised organisations for health technology assessment in Latin America, many of them newly founded, include: the Institute of Technology Assessment in Health (Instituto de Evaluación Tecnológica en Salud) in Colombia;<sup>115</sup> the National Centre for Health Technology Excellence in Health (Centro Nacional de Excelencia Tecnológica en Salud) in Mexico;<sup>116</sup> Institute for Clinical Effectiveness and Health Policy (the Instituto de Efectividad Clínica y Sanitaria) in Argentina;<sup>117</sup> and CONITEC in the Unified Health System (SUS) in Brazil.<sup>118</sup> Evidence on the cost-effectiveness of interventions in Latin American countries will hopefully accelerate approval of cost-effective drugs (even if the drugs are expensive in absolute terms), and help to differentiate these from interventions that are not cost effective (even if inexpensive), in relation to a nation's GNP.

Where available, biosimilars (and generics) have the potential to offer cost-saving alternatives with similar efficacy and safety to original products.<sup>119</sup> The advantages of biosimilars are based on their lower development and manufacturing costs, with equal efficacy and safety compared with the reference biological drug.<sup>119</sup> Biosimilars are expected to have a substantial role in the health-care systems of low-income and middle-income countries and 60% or more are already available in specific therapeutic areas. By 2020, the role of biosimilars in oncology is expected to be of even higher importance than it is at present.<sup>84</sup>

## Part 6: Training in oncology and palliative care

Since our previous Commission, awareness about the shortage of cancer specialists has increased in Latin American countries, driven partly by meetings such as the PAHO-initiated conference entitled “Innovative cervical and breast cancer control strategies”, in which increases in oncological training for medical and non-medical personnel in both screening and diagnostic testing was strongly recommended.<sup>120</sup>

Subsequently, the number of oncologists across Latin America has steadily increased, most notably in Brazil and Argentina, the two most populous Latin American states. The 2015 medical census<sup>121,122</sup> in Brazil has shown an increase of 77% in the number of oncologists since 2011 (from 1457 to 2577). Concurrently, the number of haematologists has also increased by 40% (from 1420 in 2011 to 1985 in 2015) and radiotherapists by 12% (from 444 in 2011 to 497 in 2015).<sup>120,122</sup> These rises are in the context of an 11% increase in cancer cases in Brazil (from 518 000 new cases in 2012 to 576 000 in 2014).<sup>123,124</sup> Thus, despite these encouraging trends, the present number of 220 new patients with cancer per year per oncologist is still high. Similar to improving trends in specialised health-care workers in Brazil, Mexico has had a 55% increase in the number of clinical oncologists (227 in 2012 compared with 352 in 2014), 42% increase in surgical oncologists (582 in 2012 compared with 828 in 2014), 46% increase in paediatric oncologists (138 in 2012 compared with 202 in 2014), and 167% increase in gynaecological oncologists (39 in 2011 compared with 104 in 2014).<sup>125,126</sup> Overall, these increases have resulted in 420 new patients with cancer per year per oncologist in Mexico (table 5).

Apart from increases in the number of oncologists, another suggestion to improve education and the quality of cancer care by our previous Commission was to stimulate international exchange programmes. One identifiable effort is the implementation of the Red de Institutos Nacionales de Cancer in 2011, a network of National Cancer Institutes of member states of the Union of South American Nations (União de Nações Sul-Americanas) and partner countries. Specific initiatives introduced by this network are exemplified by educational exchange and training of health personnel in cervical cancer screening.<sup>130</sup> An emphasis has been on training in the use of acetic acid for cervical inspection with the objective of prompt treatment of any abnormal finding. This approach is based on promising data from India where application of this technique has been estimated to potentially save 22 000 lives per year from cervical cancer.<sup>131</sup> Another international educational initiative in Latin America has been the establishment of an international biobank<sup>130</sup> that is also used to train pathologists, nurses, and technicians. New pathological reference training centres in Bogotá (Colombia) and Mexico City (Mexico) have also been established.<sup>130</sup>



Another international exchange programme is that sponsored by the US Global Cancer Institute, that enables Latin American oncologists who are early in their career to visit or train at leading international cancer centres in developed countries.<sup>132</sup> The Global Cancer Institute was founded after the publication of our 2013 Commission as an educational and research foundation “to improve survival and quality of life of cancer patients worldwide”, including Latin America. The Institute has a growing network of collaborating committed oncologists dedicated to mitigate cancer mortality globally, and specifically in Latin America.

Training in palliative care in Latin America has evolved slowly and has many challenges, particularly with a scarcity of specific policies for palliative care. In most medical schools, undergraduate curricula do not include palliative care as a regular subject, although some countries, such as Argentina, offer palliative care as an optional class.<sup>133</sup> In support of our call for improved palliative care,<sup>1</sup> a survey<sup>134</sup> of 58 Brazilian medical schools showed that 79% of those surveyed believe integration of palliative care into medical school curricula is important. Major reasons for choosing not to implement these curricula were: absence of institutional interest, inadequate time, and insufficiently trained teachers. Importantly, initiatives from undergraduate students of medical schools, such as Academic Leagues in Brazil, have increased awareness for the need for palliative care training.<sup>135</sup> However, ten of 19 Latin American countries surveyed have no formal training in palliative care, and roughly 70% of certified professionals practice in Argentina, Chile, and Mexico (table 4),<sup>5</sup> those countries in addition to Costa Rica were classified as having the highest palliative care development in Latin America.<sup>59</sup>

As mentioned in our previous Commission, participation in clinical trials is an important part of continuing medical education and quality of care in oncology. However, clinical trials in Latin America represent only 3–5% of all clinical trials registered at [www.ClinicalTrials.Gov](http://www.ClinicalTrials.Gov),<sup>136</sup> and the migration of clinical trials from the USA to emerging markets in the past decade<sup>109</sup> has declined because of local long bureaucratic regulatory processes and difficulties in the granting of patents.<sup>110</sup> Brazil is the most productive Latin American country as measured by the number of clinical research publications, and its productivity is increasing.<sup>137</sup> However, even with this increment, the effect of Latin American research on research worldwide remains limited (panel 1).<sup>138</sup>

## Part 7: Disparities in cancer control

Although numerous efforts to overcome cancer inequalities have been undertaken in the Latin American region in the past few years, inequities in cancer care persist, which have been discussed in several studies published since 2012 (table 6).<sup>139–154</sup> We report on several initiatives to overcome these inequalities.

### Geographical disparities

Most cancer specialists in Latin American countries practice medicine in tertiary cancer centres in large urban areas offering cutting-edge, complex, multimodality treatments. The inequitable geographical distribution of these centres requires patients outside urban areas to travel long distances, even for simple treatments, and was identified as an issue in our previous Commission. Notably, this issue is not only reported in low-income and middle-income countries, but also in the USA and other high income countries.<sup>1,155</sup>

One important issue which arises with this geographical disparity is waiting times, with reports from Mexico and Brazil describing median waiting times of 7 months or more for patients with breast cancer from symptomatic presentation to initial treatment.<sup>151,156</sup> In both of these studies, the longest delays occurred between initial contact with health services and histopathological confirmation of diagnosis—either relating to poor access to services or poor quality of histopathological tests. A survey<sup>157</sup> of Mexican oncologists confirms these reports, describing delays between patient visits as one of the most important variables that adversely affect patient care. Although data for waiting times for care are not available for all health systems in the region, long delays still seem to be very frequent for patients treated in public institutions.

In order to improve health care in remote and rural regions, telemedicine networks (eg, including teleradiology for histological diagnoses) have been implemented in Peru, Ecuador, and Colombia.<sup>158,159</sup> Although the effect of these programmes on health indicators is still being assessed, their implementation in Peru has decreased the non-reported health cases (those sent by the health establishment that get lost and do not reach the epidemiological department of the regional government) from 29% to 15% since 2010. Additionally, the number of medical appointments from referrals made by telemedicine workers has increased by 50%.<sup>159</sup>

Another strategy to promote the decentralisation of resources is the relocation of specialised facilities in strategic regions that can serve rural populations. In Peru in 2014, the decentralisation of cancer services was included as part of the national cancer control plan, called Plan Esperanza and in January, 2015, the first centre offering chemotherapy for rural patients with cancer in the province of Lamas, San Martin was opened.<sup>160–162</sup>

As another way to decrease geographical disparities, we have previously recommended that nurses, health workers, and general practitioners working in remote areas should be trained, as in Canada, to do specific tasks such as screening, simple diagnostic procedures, and basic chemotherapy administration, which might help to diagnose and treat cancer earlier.<sup>1</sup> In Colombia under the “Ten-Year Plan for Cancer Control 2012–2021”, nurses and health-care providers including gynaecologists from remote areas have been trained in visual inspection

	Cancer site	Country	Year of publication
<b>High mortality</b>			
Low socioeconomic status*	Cervical cancer	Brazil	2014 <sup>139</sup>
Malnutrition (associated with low socioeconomic status)	Childhood acute lymphoblastic leukaemia	Guatemala	2013 <sup>140</sup>
Residence in rural and more marginalised regions	Breast cancer	Brazil	2014, <sup>141</sup> 2015 <sup>142</sup>
Residence in rural and more marginalised regions	Childhood cancers	Brazil	2013 <sup>143</sup>
Residence in rural and more marginalised regions	Childhood and adolescent cancers	Mexico	2012 <sup>144</sup>
Indigenous populations	Gastric cancer	Peru	2012 <sup>145</sup>
<b>Reduced survival</b>			
Low socioeconomic status*	Breast cancer, cervical cancer, non-squamous cell lung cancer, prostate cancer	Colombia	2014 <sup>146</sup>
Public health insurance (in comparison to private schemes)	Breast cancer	Brazil	2013 <sup>147</sup>
Malnutrition	Childhood and adolescent cancers	Costa Rica, Dominican Republic, El Salvador, Guatemala, Honduras, Nicaragua, Panama	2012 <sup>148</sup>
<b>High average years of life lost</b>			
High marginalisation index	Cervical cancer	Mexico	2014 <sup>149</sup>
<b>Advanced cancer diagnosis</b>			
Low education level	Cervical cancer	Brazil	2014 <sup>150</sup>
Low education level	Breast cancer	Mexico	2015 <sup>151</sup>
Public health insurance in comparison to private schemes	Breast cancer	Brazil	2013 <sup>147</sup>
<b>Low prevalence of screening</b>			
Low socioeconomic status*	Cervical cancer	Bolivia, Brazil, Dominican Republic, Guatemala	2013 <sup>152</sup>
Low socioeconomic status*	Breast cancer	Mexico	2013 <sup>153</sup>
Rural residence	Cervical cancer	Ecuador, Nicaragua, Peru, Trinidad and Tobago	2013 <sup>152</sup>
Rural residence	Breast cancer	Mexico	2013 <sup>153</sup>
Indigenous populations	Cervical cancer	Guatemala	2013 <sup>152</sup>
Less comprehensive public insurance scheme (Seguro Popular) versus social security comprehensive schemes	Breast cancer	Mexico	2014 <sup>154</sup>
Public health insurance scheme versus none	Breast cancer	Mexico	2013 <sup>153</sup>

\*Such as Human Development Index, education, household access to electricity and plumbing services, and proportion of individuals living under the poverty line.

**Table 6: Latin America studies showing persisting cancer inequities and effect on cancer outcome**

techniques for detection of cervical lesions and immediate treatment with cryotherapy (known as the see-and-treat strategy). Since the implementation of this plan in 2012, according to the Health Ministry of Colombia, 9329 women have been screened; of these, 813 were treated with cryotherapy and 247 were referred for tertiary care.<sup>163</sup> Further, about 100 health professionals

including physicians, radiologists, pathologists, and technicians from various urban and rural areas have been trained in quality control techniques for mammographic services.<sup>163</sup> Additionally, a course for general practitioners to strengthen their capacities in early detection of colon and prostate cancer was provided.<sup>163</sup> Other countries, such as Argentina, have increased scholarship programmes, endorsed by their National Cancer Institute which train new cancer specialists to practise in rural areas.<sup>164</sup> In 2014, as part of the Xingu Project in Brazil, local health professionals were trained to collect samples for Papanicolaou (Pap) smear tests in the indigenous population of the Xingu region. These health-care workers performed Pap screening in 76% of the indigenous women living in the area and clarified these women's questions about cervical cancer. During all visits, local leaders provided translation services, which were essential for the success of the programme.<sup>165</sup>

Another strategy to address the scarcity of trained personnel in rural areas is to retrain specialists in rural areas to act as leaders in primary care in order to improve primary care capacity, coordination of care of patients with chronic diseases such as cancer, preventive services, and infrastructure. One particular such effort involves experts in public health care from Cambridge, MA, USA in collaboration with Unimed Mercosul in southern Brazil.<sup>166</sup>

Improving primary care in rural areas is essential to improving cancer care in these locations. To try to increase the number of primary care doctors in small cities, the Brazilian Government has created a programme, the Primary Care Professional Valorization Program, which rewards medical school graduates who work in remote areas for a year with extra scores in their selective process for medical residency. This programme is limited by the fact that these doctors stay for only a year and it doesn't address the fact that rural populations are—because of cultural barriers—in need of long-term patient–doctor relationships.<sup>167</sup> Another Brazilian programme, Programa Mais Médicos (More Medical Doctors Programme), implemented in 2013 to increase the number of primary care physicians in underserved areas, offers placements of foreign-trained doctors in remote locations.<sup>168</sup> This programme has caused intense social and political debate.<sup>169</sup> Likewise, Chile has established the Rural Practitioner Programme, which provides several incentives, such as paid residency in a university hospital plus attractive salaries and benefits proportional to the extent of isolation and clinical responsibility, for physicians to practise in rural areas. Despite low dropout rates in physicians enrolled in this programme, 70% of applicants surveyed do not intend to continue working in underserved areas long term, and would rather go on to a subsequent medical subspecialty.<sup>170</sup>

Another way to counteract inadequate health-care access, is through the integration of health services into

infrastructure that already exists in these rural communities. This process might include use of educational or church-related communities, work related settings or, for the informal employment sector, other types of networks such as microfinance institutions. These microfinance institutions offer loans and financial services outside of formal banks and studies from Latin America, Africa, and Asia show that carefully designed interventions implemented through microfinance institutions might improve health knowledge, change health-related behaviours, and increase access to health services.<sup>171</sup> For example, at a regional health fair held by a microfinance institution in Bolivia in 2013, 24% of attendees stated that this was the first formal medical care they had received.<sup>172</sup>

By use of this model, Pro Mujer, a non-governmental organisation that operates in Argentina, Bolivia, Mexico, Nicaragua, and Peru, has integrated health and microfinance services for women in urban and periurban areas. The components of the Pro Mujer health programme address four dimensions of health-care access: geographical accessibility, availability, affordability, and acceptability. As part of this programme, 116 407 pap smears and 174 314 breast assessments were provided, of which 2·7% pap smears and 0·8% breast assessments needed a follow-up or reference for further assessment and possible treatment.<sup>173</sup> Future research is needed to determine the long-term outcomes, the cost-effectiveness of these programmes, and client perception with respect to access to health services.

### Cultural disparities

We emphasised the challenges of indigenous people with respect to cancer demographics and access to care in our previous Commission. The medical literature shows a shortage of epidemiological and clinical data about cancer in indigenous populations in Central and South America.<sup>174–177</sup> One way to rectify this is the collection and inclusion of data from indigenous populations (including their socioeconomic characteristics) into cancer registries. In addition to epidemiological research, promotion of sociodemographic local research would help to understand and decrease cultural barriers unique to these populations. In Argentina, efforts have therefore focused on social research in indigenous populations as an aid to the National Cancer Control Programme.<sup>178</sup>

In Brazil, a specific health information system, O Sistema de Informação da Atenção à Saúde Indígena, (Brazilian Health Information System for Indigenous Peoples), accounting for cultural and demographical factors, is being used to collect and analyse health data in indigenous populations, and has been updated to include data such as proportion of Pap smears collected.<sup>179</sup>

Indigenous peoples face non-financial barriers to effective treatment including language skills, health literacy, traditional beliefs that may not be compatible with treatment, and other cultural barriers. To address

this, some Latin American countries have focused on the role of the so-called patient navigator and the provision of organisational and financial support sustained by non-governmental organisations for indigenous patients. In Guatemala, the Complex Care Programme of the Maya Health Alliance has a designated full-time staff member (patient navigator) to address the cultural and logistical barriers for indigenous and rural patients to receive care. The navigator helps patients to schedule their appointments, arrange transportation, and ensure that interpreter services are available at each clinical visit.<sup>180</sup> In Mexico, a breast cancer non-governmental organisation called Fundación Cimab has been working with the Mexican National Cancer Institute (Instituto Nacional de Cancerología) in the past 3 years to help rural patients with abnormal screening mammography results navigate from their community to centres in Mexico City. These patients are given logistical and financial support to coordinate the first appointment, to arrange transportation, and to cover initial diagnostic assessments. Once the diagnosis is confirmed, patients can receive treatment through Seguro Popular.<sup>181</sup> If feasible, implementation of schemes such as this one on a large scale should reduce delays in diagnosis and treatment abandonment.

In Argentina, Área de Salud Indígena (Indigenous Health Area), a programme by the Ministry of Health, aims to improve health coverage and access to care for indigenous communities by providing training to health workers belonging to indigenous communities. Since 2005, 900 indigenous health workers across the country have been trained and are part of health teams in their own communities.<sup>182</sup> Integration of screening and early diagnosis programmes into this already established infrastructure could improve cancer outcomes in these communities.

A similar strategy to the Argentinian programme mentioned is to promote community-based participatory research to integrate education and social action to improve health.<sup>183</sup> For example a study<sup>184</sup> in El Salvador determined the acceptability of self-collected versus provider-collected cervical HPV DNA sampling in women participating in a public sector HPV-based screening programme for cervical cancer. The results showed that 38·8% of participants preferred self-collection because of more privacy, less embarrassment, more ease, and less pain than provider-collected sampling. Another study from Peru<sup>185</sup> also showed that self-sampling and HPV DNA testing resulted in high participation rates in a pilot screening programme for cervical cancer.

In Peru, a study<sup>185,186</sup> assessed the usefulness of community-based participatory research, techniques for cervical cancer screening and HPV vaccination, in the Peruvian Amazon region and in a shantytown outside of Lima. As part of the study, community health leaders were

given an educational course on HPV and cervical cancer and designed their own strategies for implementing interventions such as cervical smear self-sampling and HPV vaccination in their villages. The health leaders included a midwife, a physician, a nurse, and three health technicians. These leaders' screening programme relied on self-sampling of cervical cells and resulted in a high participation rate: 98% of 643 registered women submitted a cervical sample over a 10-day period. Furthermore, 10·8% of women were positive for HPV and 87% of these women returned for assessment and treatment, and 74% returned for follow-up at 6 months.<sup>185</sup> In the vaccination programme, the proportion of girls who received one dose was 98%, 90% received the second dose, and 71·5% received the third dose.<sup>186</sup> These results showed that community input is exceedingly valuable to develop effective cancer prevention strategies.

Because many of the initiatives and strategies mentioned in this section have only recently been implemented and changes in definitive cancer outcomes take several years to be measurable in country-wide populations, the long-term effect of these initiatives on decreasing cancer disparities is unknown. It is therefore important to define indices to measure achievements and success of these interventions to guarantee feedback and to allow continuous improvement of these strategies.

## Part 8: Causes of cancer that are of specific concern to Latin America

Among behavioural and environmental risk factors that have a role in the cause of cancer in Latin American populations, several are of special importance because they cause a large proportion of cancer-associated morbidity, particularly in less developed countries in the region. These risk factors include: (1) tobacco use causing lung cancer, which is anticipated to emerge as the main killer in the region if smoking rates do not decrease;<sup>187</sup> (2) indoor smoke (panel 3), which is the leading environmental health threat in Latin America<sup>17</sup> and thought to be responsible for the high rates of *EGFR* mutated lung cancer in Latin America (table 7);<sup>19,192</sup>

(3) HPV infection causing cervical cancer, which is the second most common cause of cancer-related deaths in women in Latin America<sup>15</sup> and projected to increase by 45% in 2030;<sup>187</sup> and (4) *H pylori* infection, which is thought to cause the uniquely high rates of gastric adenocarcinoma and mucosa-associated lymphoma in Latin America.<sup>193</sup>

### Tobacco and indoor smoke

Trends show that overall adult smoking rates have declined in most Latin American countries over the past 15 years (figure 6)<sup>194</sup> with the largest decrease in Panama, where smoking rates decreased by 57% from 15·4% to 6·6% between 2000 and 2015. Most countries in the region (29 of 33 Latin American and Caribbean countries) have also ratified the WHO Framework Convention on Tobacco Control<sup>195</sup> but, most countries still do not have adequate implementation of tobacco control policies as recommended by the Convention.<sup>196</sup> These policies should include six effective interventions (MPOWER):<sup>195</sup> M=monitoring of tobacco use and prevention policies; P=protection of people from tobacco smoke; O=offering of help to quit tobacco use; W=warning about the dangers of tobacco; E=enforcement of bans on tobacco advertising, promotion, and sponsorship; and R=raising of taxes on tobacco.<sup>195,197</sup>

Therefore, although decreased, the proportion of people who smoke is still high in Latin America. In addition, in some countries the proportion of adolescent or young adult smoking is higher than the proportion of adult smokers (eg, in 2010, 48% of young adults aged 15–24 years in Chile were smokers, versus 33% of adults; figure 6).<sup>194</sup> Additionally, only 46% of the population in the PAHO region (which includes the USA and Canada) have protection against exposure to tobacco smoke in indoor public places and at work and only 26% of the PAHO population are protected against tobacco advertisement and promotion.<sup>196</sup> This is particularly important in view of a study<sup>197</sup> that reported that exposure to tobacco industry marketing affects the probability of quitting smoking.

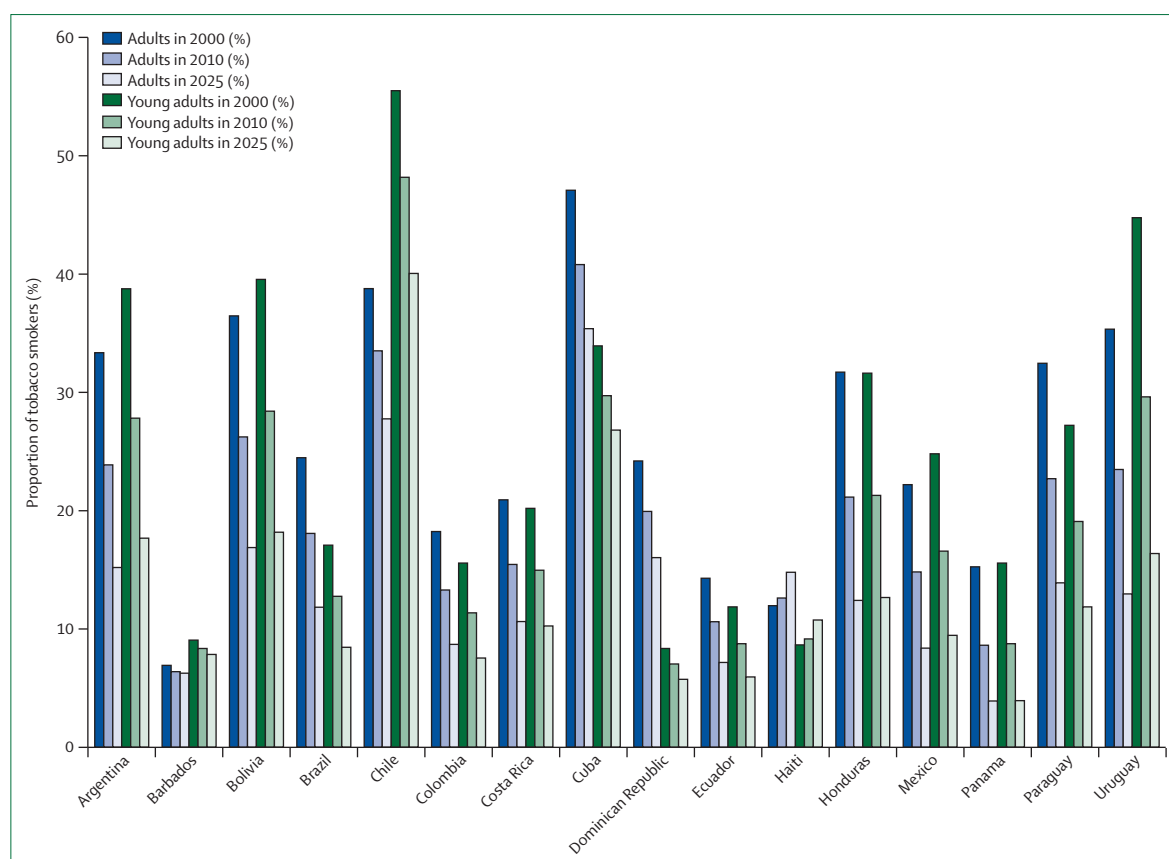
Increases in cigarette prices can encourage smokers to quit and raising prices by increasing taxes by more than 5% between 2008 to 2012 has been adopted by several countries in Latin America (table 8). Although this is an important first step towards tobacco control, the WHO recommends a tax rate of 75% or more of the final sales price,<sup>196</sup> and this has been reached by only two Latin America countries so far: Chile and Cuba (table 8).<sup>196</sup> Additionally, tobacco tax rates below 50% are still in place in: Antigua and Barbuda, Bahamas, Barbados, Belize, Bolivia, Colombia, Dominica, Guatemala, Guyana, Honduras, Jamaica, Nicaragua, Paraguay, Peru, Saint Kitts and Nevis, Saint Lucia, Saint Vincent and the Grenadines, and Trinidad and Tobago.<sup>199</sup> The conflict between countries implementing anti-tobacco campaigns and the tobacco industry is shown in panel 4.

Apart from national measures to curb tobacco use, several MERCOSUR countries (ie, Argentina, Brazil,

EGFR mutation frequency % (n)	
Argentina	14% (1713) <sup>189</sup>
Colombia	25% (1939) <sup>189</sup>
Costa Rica	31% (102) <sup>189</sup>
East Asia	51% (1450) <sup>188</sup>
Europe	10% (860) <sup>191</sup>
Latin America	26% (5738) <sup>189</sup>
Mexico	34% (1417) <sup>189</sup>
Panama	27% (174) <sup>189</sup>
Peru	51% (393) <sup>189</sup>
USA	22% (1007) <sup>190</sup>

Table 7: Approximate frequency of *EGFR*-mutated lung cancer in the Latin American region compared with the USA, Europe, and east Asia





**Figure 6: Estimated trends in tobacco use among adults and young adults in Latin American countries in 2000, 2010, and 2025**

Estimations were made based on data from national surveys and when data was unavailable for a given year, the estimated proportions of smokers were projected with well-established models and trends observed in each country. No data were available for Antigua and Barbuda, Bahamas, Belize, Dominica, El Salvador, French Guiana, Grenada, Guatemala, Guyana, Nicaragua, Peru, Saint Lucia, Saint Kitts and Nevis, Saint Vincent and the Grenadines, Suriname, Trinidad and Tobago, and Venezuela for the selected years compared. Young adults are individuals aged 15–24 years, whereas adults are individuals aged 25 years and older. Data obtained from WHO.<sup>194</sup>

Uruguay, Paraguay, Venezuela, Bolivia, Chile, and Peru) have coordinated their tobacco control initiatives to regulate cross-border advertising and illicit tobacco trade between states.<sup>206,207</sup>

Beyond legislative and policy issues, collaborative efforts are underway to better understand barriers and facilitators to prevent smoking initiation and to stimulate smoking cessation in the Latin American population and in smokers diagnosed with cancer. Examples include Project ASPIRE (A Smoking Prevention Interactive Experience) by The University of Texas MD Anderson Cancer Center with colleagues from Mexico and Colombia, piloting tobacco cessation interventions and web-based prevention of smoking targeted at adolescents in Latin America.<sup>208</sup> Another project, Colombia And Mexico Against Tobacco Use (COMET), with the same collaborators, analyses the social and cultural factors that affect continued tobacco use in patients with cancer in Mexico and Colombia.

In contrast to cigarette smoking, awareness of indoor smoke exposure is growing only slowly in Latin American states. Few initiatives to improve the

situation have been taken. For example, supported by the UN Development Programme, Peru's Ministry of Energy and Mining has initiated a programme to provide 125 000 improved cooking stoves, ultimately benefiting 750 000 people. By the end of 2011, the programme had resulted in the construction of 75 000 stoves in various provinces of the country, including those with low human development indicators. However, many more efforts and awareness are needed to address this issue in the Latin American region, and health experts should advocate with respect to this issue.<sup>209</sup> Apart from other detrimental health effects, wood-smoke exposure has been specifically linked to *EGFR*-mutated lung cancer within the Latin American region.<sup>19,192</sup> This association, which is being investigated from an epidemiological perspective at centres in the USA, Bolivia, Mexico, Peru, and Venezuela, would explain the high-rates of *EGFR*-mutated lung cancer in the region.<sup>210</sup> A review of *EGFR*-mutation frequency, updated from our 2013 report, in selected countries in Latin America compared with the USA, Europe, and east Asia is shown in table 7.<sup>188–190</sup>

	Price of a pack of 20 cigarettes in 2008* (PPP†)	Taxes in 2008* (%)	Price of a pack of 20 cigarettes in 2012* (PPP†)	Taxes in 2012* (%)
Antigua and Barbuda	3.20	6.60	3.10	6.60
Argentina	2.11	69.20	2.74	67.83
Bahamas	3.35	31.23	4.58	37.71
Barbados	8.89	47.77	7.96	48.76
Belize	4.69	19.17	4.69	21.19
Bolivia	1.99	41.00	2.34	42.03
Brazil	1.59	57.15	2.26	63.15
Chile	3.56	76.37	4.39	81.24
Colombia	1.48	34.31	2.01	43.77
Costa Rica	2.33	55.72	3.30	71.50
Cuba	..	75.00	..	75.13
Dominica	2.63	25.61	3.13	23.40
Dominican Republic	4.87	57.03	5.36	58.59
Ecuador	3.39	64.29	4.83	73.02
El Salvador	2.79	41.47	3.96	51.75
Grenada	3.87	40.50	..	..
Guatemala	2.26	56.71	2.76	48.98
Guyana	3.02	35.85	3.30	30.15
Haiti	..	..	..	..
Honduras	2.23	45.25	3.50	34.03
Jamaica	9.74	43.88	12.19	46.06
Mexico	3.58	61.17	4.47	66.62
Nicaragua	2.90	19.79	3.06	29.11
Panama	3.32	36.59	5.96	56.52
Paraguay	0.40	18.83	0.65	17.34
Peru	2.65	41.85	3.14	42.14
Saint Kitts and Nevis	2.45	18.20	3.48	19.96
Saint Lucia	4.40	30.08	5.39	19.72
Saint Vincent and the Grenadines	3.78	14.71	3.97	14.88
Suriname	2.59	58.14	3.23	60.96
Trinidad and Tobago	2.17	36.69	3.40	32.58
Uruguay	2.92	65.82	4.00	68.70
Venezuela (Bolivarian Republic of)	4.55	70.79	6.45	71.04
Canada	6.38	64.55	6.80	64.45
USA	4.58	36.57	6.07	42.93
UK	5.44‡	77.00	7.09‡	77.00

Adapted from Pan American Health Organization data.<sup>196,198</sup> PPP: Purchasing Power Parity. \*Most sold cigarette brand in country. †A PPP international dollar has the same purchasing power as the US dollar has in the USA. It does not take into account disposable household income. ‡Recommended retail price.

**Table 8: Taxes and prices for a pack of 20 cigarettes for 2008 and 2012**

### Infectious causes of cancer: HPV and cervical cancer

Despite screening initiatives in many Latin American states over the past decade, the incidence and mortality rates of cervical cancer have not declined as hoped, and show the need to better organise HPV prevention (through HPV vaccination) and screening initiatives.<sup>211</sup>

However, since our previous Commission and as of 2014, 20 countries in the Latin American region have introduced HPV vaccination and include this preventive treatment in their national recommendations: Argentina, Antigua, Barbados, Brazil, Bermuda, Chile, the Caymen

Islands, Colombia, Ecuador, Guyana, Mexico, Panama, Paraguay, Peru, Puerto Rico, Saba, Sint Maarten, Suriname, Trinidad and Tobago, and Uruguay.<sup>212</sup> This increase is steep in comparison to 2011, when only four Latin American countries had included the HPV vaccine in their national vaccination schedules. According to PAHO, 80% of adolescent girls in Latin America theoretically now have access to the HPV vaccine.<sup>213</sup> Since HPV vaccination has only recently been introduced in Latin America, it is premature to assess the success of HPV vaccination in the region with respect to cervical cancer outcomes. As for the proportion of coverage, only a few countries have reported proportion of girls receiving the full dose of the three-dose or two-dose HPV vaccine: 50% in Argentina, and 67% in Mexico and in Panama.<sup>211,214</sup> These statistics, which show whether the vaccine was procured, delivered, and successfully administered, are essential to reporting since this information enables health systems to measure the successes and shortcomings of their endeavours at an early point in time (panel 5).

The second aspect of cervical cancer control is implementation of a comprehensive screening programme (secondary prevention). Cytology-based screening, which is the gold-standard for cervical cancer screening, is incorporated in national or public health care guidelines in almost all Latin American countries today.<sup>211</sup> However, many women in Latin America are not being screened: a report<sup>152</sup> found that less than 55% of eligible women from eight Latin American countries (Bolivia, Brazil, Dominican Republic, Ecuador, Guatemala, Peru, Nicaragua, and Trinidad and Tobago) received appropriate pap smear screening. Barriers to screening depend on the geographical region and population, but disproportionately affect vulnerable populations (eg, indigenous women, the poor, those that live in rural and remote regions, and the uninsured).

Even in the presence of screening, the proportion of patients with cervical cancer will remain high if the quality of screening is poor, or follow-up and treatment of premalignant lesions identified by pap smear is inadequate. In particular, women must receive their test results in a timely manner and when an abnormal finding is detected, women need prompt follow-up care and intervention. These final steps are crucial to a successful screening programme for cervical cancer and are problematic in many Latin American countries with cytology-based screening programmes.<sup>1</sup> This has, for example, been shown in Boa Vista, Brazil, where 86% of eligible women participate in screening, but the incidence of cervical cancer remains high.<sup>217</sup> Poor quality pap smears have also been described in Mexico, Costa Rica, and Colombia.<sup>218–220</sup> To address this problem and improve the education and training of gynaecologic residents in prevention and treatment of gynaecologic cancers in Latin American countries, the Central America Gynaecologic Oncology Educational

#### Panel 4: Tobacco control in Latin America and the tobacco industry

Uruguay was one of the first Latin American countries to introduce a comprehensive anti-tobacco plan in association with WHO Framework Convention on Tobacco Control in 2006.<sup>200</sup> This plan included a 100% smoke-free policy in public places and at workplaces. Uruguay also implemented regulations that required health warnings to cover 80% of packing on tobacco products. Uruguay's strict anti-tobacco policy is already having an effect on the population: between 2005 and 2011, tobacco consumption per person has declined by 23% and the effect is even higher in young people.<sup>201</sup> The effect of these policies on cancer trends in the country is too early to identify but other effects, such as a reduction of acute myocardial infarction by 17.1% within 2 years and an increase in smoking cessation during pregnancy have already been noted.<sup>202,203</sup>

Uruguay's regulation has prompted Philip Morris International, a major tobacco company, to file a legal suit, claiming that Uruguay's antitobacco policies devalue its trademarks and investments in the country.<sup>204</sup> The lawsuit is pending before the World Bank Tribunal,<sup>204</sup> but Uruguay has received accolades from WHO and Pan American Health Organization (PAHO) for their efforts and financial support to defend itself against legal suits from the Bloomberg Initiative.<sup>203</sup> In addition to Uruguay, PAHO has highlighted other examples from the Latin American region where the "tobacco industry has operated (with the) intention of subverting the role of governments and the WHO in implementing public health policies to combat tobacco control".<sup>196</sup> For example, when a comprehensive advertisement ban was discussed in Argentina, the tobacco industry lobbied against it and offered a compromise in which they voluntarily stopped advertising on TV and the radio. As a result, tobacco advertising in newspapers increased.<sup>205</sup>

Programme was established in 2009. So far, this programme has coordinated 13 trips inviting expert gynaecologic oncologists to train residents in Guatemala, Honduras, El Salvador, Nicaragua, Panama, and Costa Rica and on each of these trips, more than 100 residents, fellows, and faculty staff have engaged in the exchange.<sup>221</sup>

These examples show that in resource-constrained environments high level cytology-based screening programmes are difficult to implement because they require the preparation of high-quality pap smears and a trained pathologist or cytotechnologist to interpret the findings. Therefore, there is a general consensus among experts that the approach to cervical cancer screening needs to be modified. Programmes such as see-and-treat screening based on visual inspection with acetic acid (VIA) or a screening strategy based on HPV DNA testing might be more effective in the region than cytology-based screening.<sup>131,222</sup> VIA is now gaining more acceptance in Latin American countries and is now

#### Panel 5: HPV vaccination—the case of Brazil

The example of Brazil shows that with proper coordination nationwide immunisation programmes can be successfully rolled out. In March 2014, Brazil introduced the quadrivalent HPV vaccine and within 6 months, 3.4 million girls (83% of the target population) between the ages of 11–13 years had received the first dose.<sup>215</sup> By the end of 2014, 100% of the target population (4.95 million girls) had received the first dose of the HPV vaccine at school or at health centres. The second dose, which was only administered in clinics, reached 58.7% of the eligible population.<sup>216</sup> In 2015, the programme will be expanded to include girls aged 9–11 years (targeting a younger cohort to vaccinate before they become sexually active) and all HIV positive women aged 9–26 years.<sup>216</sup> The aim is to vaccinate 4.94 million girls in 2015 and to achieve this, the Ministry of Health has projected a need to purchase 11 million doses of the vaccine to complete the vaccine series for those who began vaccination in 2014, and to enrol new participants in the programme.<sup>216</sup>

available in the public sector in 15 countries in the region (Costa Rica, El Salvador, Guatemala, Nicaragua, Argentina, Colombia, Venezuela, Antigua and Barbuda, Bahamas, Barbados, Guyana, Saint Kitts and Nevis, Saint Lucia, Suriname, Trinidad and Tobago).<sup>211</sup> Quality problems, however, are noted with this type of screening: in a study<sup>223</sup> from Amazonian Peru, VIA results were highly variable when compared with pap smears, liquid-based cytology, and HPV DNA tests, and these issues were independent of the clinician's experience. Additionally, in a series of workshops hosted between the Centers for Disease Control, PAHO, the Peruvian Cancer Institute, and the Bolivian Ministry of Health, which were aimed at building VIA and cryotherapy capacity in Bolivia, trainees cited national norms prioritising cytology-based screening as a reason for their reluctance to do VIA screening in their practice.<sup>224</sup> Efforts to recruit nurses to receive VIA training proved challenging and was believed to be because historically nurses in Latin American states have not had an active role in doing procedures or making therapeutic decisions.<sup>224</sup> VIA screening programmes in Guatemala and Peru reported concerning proportions of staff turnover and burnout, issues with quality assurance, and insufficient resources contributing to long patient waiting times.<sup>225,226</sup>

Finally, screening on the basis of HPV DNA testing offers a unique approach to circumvent some of the issues of cytology-based and VIA screening programmes, because HPV DNA testing is less demanding in terms of training and quality assurance.<sup>227</sup> Additionally, screening with HPV DNA testing allows women to self-sample, which is preferred by women in Latin America in comparison to a clinical pelvic examination.<sup>184–186</sup> In the USA, HPV DNA testing has been used in parallel with

cytology-based screening for more than a decade for women aged more than 30 years, and new data support the use of HPV DNA testing as a stand-alone test for cervical cancer screening.<sup>226–229</sup> In a screening trial from rural India enrolling more than 130 000 women, HPV DNA testing alone reduced cervical cancer incidence and mortality.<sup>227</sup> Self-sampling with HPV DNA screening has also been assessed in a study<sup>230</sup> in Argentina in comparison to an educational intervention. In the intervention group, 86% of participants had screening (HPV DNA self-sampling) compared with only 20% in the control group, and this difference was independent of socioeconomic variables and the gender of the health-care worker. Based on these results, the Ministry of Health in Argentina is planning to introduce HPV self-sample screening on a national level in the future; additional regional HPV DNA screening initiatives are in progress.<sup>231,232</sup>

#### Infectious causes of cancer: hepatitis and liver cancer

Programmes targeting viral hepatitis B and hepatitis C, which cause most liver cancers in Latin America, have been implemented successfully. In each of the countries with the highest rates of liver cancer (El Salvador, the Dominican Republic, Guatemala, Honduras, and Nicaragua) hepatitis B virus vaccination is offered as part of the national public health plan and the proportion of people vaccinated is very favourable.<sup>233</sup> Based on present trends, the estimated incidence of liver cancer in the region will continue to decline over the next decade.<sup>233</sup>

#### Infectious causes of cancer: *H pylori* and gastric adenocarcinoma

A challenge that needs to be addressed in Latin American countries in the future is *H pylori* infection, which is associated with an increased risk of gastric adenocarcinoma and mucosa-associated lymphoma.<sup>193</sup> Experts believe that the high burden of gastric cancer in the Latin American region is primarily due to *H pylori* infection, whereby populations at highest risk of gastric cancer have low socioeconomic status, high rates of *H pylori* infection at a young age, and are of indigenous ethnicity.<sup>234,235</sup> The very few studies exploring gastric cancer screening, ie, early diagnosis of gastric cancer, in high risk populations in Latin American countries did not have mortality as an endpoint and thus do not qualify as evidence in support of screening, although some early stage gastric cancers were diagnosed.<sup>236,237</sup> Programmes for screening for *H pylori* with subsequent endoscopy or treatment of *H pylori* infection have been proposed, but, similarly, do not contain data on long-term efficacy.<sup>234,238</sup>

### Part 9: Continuing challenges and remaining questions

Although progress has been made, obstacles to Latin American health systems identified by our 2013 Commission remain. There has been progress towards universal health care, but the number of people with a

minimum benefit scheme covering short-term interventions has continued segregating social groups into health-system fragments: a well-funded social security system for employed workers and their families; and a public system providing only basic, poor quality services for the unemployed or the informally employed.<sup>37</sup> For many patients with cancer in need of the full range of quality health services, this segregation of health systems leads to insufficient care. In this concluding section we show the remaining obstacles and suggest future actions to improve cancer care, which are also summarised in panel 6.

To provide accessible, high quality cancer care, Latin American countries need to continue to work towards achieving true universal health care, which means equitable services and coverage for all patients. To achieve this goal, financial and political challenges must be overcome, and inefficient practices must be eliminated.<sup>239</sup> With integration of health-care systems and following successful examples, a unified package of comprehensive cancer care can be attained. This complex transition must be done in cooperation with both national, regional, and global public and private organisations, which should provide funding, guidance, and monitoring.

Although the existence of NCCPs has been reported by many national, regional, and global organisations, information is scarce with respect to the implementation, success, and shortcomings of such plans. Additionally, many NCCPs do not have a comprehensive, systemic approach; have weaknesses in organisation and setting of priorities; and make inefficient use of little resources within small economies.<sup>240</sup>

Compared with high income countries, Latin America in 2015 is far behind in terms of public expenditure on health and cancer care (table 1).<sup>12–15</sup> For most Latin American countries, a redistribution of the health budget is needed to make funding available for cost-effective treatments where they are needed. The first step is to continue development of local data with respect to pharmaco-economic studies to define priorities. We believe ambulatory palliative care should be prioritised, because it decreases costly inpatient, end-of-life care, which is also associated with improved quality of care and quality of life for patients.<sup>61,241</sup> We continue to see inequities between and within countries with high-level palliative care. The continuing low consumption of narcotics, one of few quantitatively measurable indicators of palliation, shows that patients with advanced cancer are still underserved in many parts of Latin America. Therefore, our main recommendation is to continue to focus development in this area and in the interim, to join efforts made by national, regional, and international organisations to promote the inclusion of palliative care into national agendas. Sustained efforts to offer palliative care training to health-care providers are needed. Furthermore, continuing to improve cancer prevention programmes is important because



**Panel 6: Future actions to improve cancer care in Latin America****Fragmented health systems**

- Continued profound segregation between the public and the private health-care sector and between social security systems and basic coverage need to be addressed to overcome inequalities in health-care access
- Efforts towards universal health care need to continue beyond basic coverage and protection against catastrophic health expenditure for poor individuals towards equitable services and coverage including comprehensive care packages for all types of cancer

**Palliative care**

- Programmes of ambulatory palliative care should be prioritised as they are cost-effective and enhance the quality of life of patients with cancer
- National guidelines, which recommend end-of-life use of strong opioids need to be implemented and monitored to overcome the alarmingly low amounts of strong opioid consumption in Latin America

**National cancer plans and cancer registries**

- The implementation and success of the numerous newly signed national cancer control plans have to be monitored and this process should be done in cooperation with international organisations
- Within existing cancer registries, population coverage needs to increase and quality ensured

**Financing cancer care**

- Further redistribution of public expenditure towards health care is needed
- Health technology assessments allowing for local cost-effectiveness thresholds should be done on drugs, screening, diagnostic and therapeutic procedures
- Agencies for health technology assessment should be strengthened and approval guidelines issued by them need to be binding

**Training in oncology and palliative care**

- Efforts towards increasing the oncology workforce need to continue to reduce the patient-to-oncologist ratio
- Initiatives to train health-care personnel in screening and care in remote areas should be extended
- Transcontinental international exchange programmes should continue to be used to improve patterns of practice and adherence to guidelines

- Palliative care training needs to be integrated into medical school curricula in all medical schools in Latin America

**Disparities in cancer control**

- Improvement in poor quality of services and in long waiting times for diagnostic workup in rural and remote regions should be among the top priorities as these issues will subvert any advancements in cancer screening or treatment
- Concentration of cancer services and specialists in urban centres needs to be addressed urgently, eg, through incentive systems or emphasis on primary care training
- Instead of nationwide screening programmes, WHO-endorsed programmes of clinical down-staging and subsequent timely treatment should be promoted
- Programmes with patient navigators and health workers belonging to indigenous communities to overcome language, organisational, and financial barriers should be expanded
- Integration of health services into existing platforms, as done by Pro Mujer with microfinance institutions, seems a promising approach and should be implemented on a wide scale

**Causes of cancer of particular concern**

- Most Latin American countries have ratified the WHO Framework Convention on Tobacco Control, but implementation of tobacco control policies needs to be optimised and monitored, particularly to reduce the high proportion of adolescent smokers
- Protection against second-hand smoke and tobacco advertising should be ensured by specific regulations
- A tax rate of 75% on tobacco products needs to be implemented
- Awareness about the problem of indoor smoke exposure needs to be enhanced and programmes to provide non-toxic cooking stoves need to be expanded
- Strategies for cervical cancer screening need to be customised to local resources and studies identifying optimum screening programmes per region and setting are called for
- Screening and vaccination strategies addressing cervical cancer should be monitored for success and shortcomings
- Timely diagnostic workup and treatment are essential to complement screening, which will otherwise be futile

prevention is often much more cost-effective than treatment and can reduce cancer incidence and mortality rates.<sup>1,242–246</sup> Finally, biosimilars and generics should be used where available.

Restricted access to cancer drugs has resulted in the judicialisation of medicine, which from a health system perspective might actually worsen disparities because only patients who can afford to hire lawyers will benefit.<sup>107</sup> Therefore, an active debate on how to prioritise scarce

resources in the public system in Latin American countries in the long term is urgently needed. In response to this need, Uruguay established the National Dialogue on Health in 2012 with the support of the World Bank. This committee includes members from all stakeholders, including the judiciary, government, the National Resources Fund, medical experts, and patient advocates. Prior to this programme, the number of cancer drugs covered by Uruguay's National Resources Fund increased

considerably, although an estimated two-thirds of high-cost drugs recommended by international guidelines are yet to be covered.<sup>86</sup> Other Latin American states have started to follow Uruguay's example by initiating similar projects.<sup>106</sup> However controversy exists about whether committees of stakeholders will be better suited to decide about new drug approvals and funding compared with health technology assessment agencies, which develop recommendations solely on the basis of local cost-effectiveness analyses.

Despite efforts to address disparities in cancer care, substantial barriers persist in Latin American states. Those living in rural and remote regions are still particularly vulnerable to health-care inequality, which has repeatedly been shown in observational studies.<sup>139–154</sup> These geographic disparities can lead to long delays in obtaining treatment or follow-up and waiting times remain a major issue in the region.

Another issue is insufficient infrastructure and human resources in remote areas. Cancer services and specialists are still concentrated in large urban centres and little has been done to bring oncologists and adequate infrastructure nearer to the patient. Most rural patients still have to travel to large urban centres to receive an accurate diagnosis and have cancer treatment initiated, and in this process, patients often have insufficient or no support arranging consultations with specialists.<sup>81</sup>

In regions where primary care that includes basic diagnostics is available, its quality is often insufficient. This situation is problematic for patients with cancer, for whom early diagnosis and timely referrals are essential for appropriate treatment and favourable outcomes.<sup>247</sup> Although the need to improve primary care is recognised, most Latin American medical schools do not emphasise this training for students and as a result, many students pursue subspecialty training.<sup>248</sup>

Furthermore, many of the region's national cancer plans have focused on early detection in their strategies to control cancer but have neglected strengthening of timely diagnostic and treatment capacities, which is problematic because screening is only useful if timely diagnosis and treatment are subsequently provided (part 8). However, in most Latin American countries, delays between screening, diagnostic workup, and start of treatment impair the success of screening programmes because many patients progress to advanced cancer before they can start treatment.<sup>249</sup>

For disenfranchised populations, a more cost-effective strategy could be early clinical diagnosis, also known as clinical down-staging, which has been endorsed for low-income and middle-income countries by WHO<sup>250</sup> and the Breast Health Global Initiative<sup>251</sup> instead of nationwide, large-scale screening programmes. This early diagnosis approach consists of promotion of awareness of early signs and symptoms in the public, education of first-line health professionals, and

improved referral procedures to enable prompt and adequate diagnosis and treatment of cancer at early stages. A successful example of a down-staging programme was performed in Malaysia where 400 first-line health personnel in hospitals and rural clinics were trained to improve their skills in early detection of breast cancer and to raise public awareness about signs and symptoms of breast cancer through posters and public talks. After 4 years of programme implementation, late-stage breast cancer cases were reduced from 60% to 35%.<sup>252</sup> We believe that, with respect to breast cancer, promotion of early clinical diagnosis will be more effective in Latin American states than screening techniques with low penetrance and low quality screening, such as mammography.

International exchange programmes, which train local oncologists to advocate for underserved patients and identify barriers in their own countries, might raise awareness and help to overcome existing barriers. Provision of patient navigation through complex cancer treatments and improving doctors' patterns of practice through international tumour boards could enhance the quality of cancer care outside of national cancer centres.

Latin America continues to have a shortage of oncologists, a gap that will probably continue or grow because of the rapidly rising cancer incidence in the region. For oncology education, palliative care is of particular concern because almost 50% of Latin American states still have no dedicated training in palliative care within their curricula.<sup>133</sup> Additionally, centralisation of care is widespread in Latin American states, limiting access to patients living outside main cities. For example, one of the main barriers to further implementation of Peru's NCCP is centralisation, with more than 80% of the patients assessed and treated at the National Cancer Institute of Neoplastic Diseases in Lima. We find few systematic strategies to financially incentivise cancer specialists to work in underserved areas despite the benefit of such programmes in Canada and other countries.<sup>253</sup> Therefore, basic training in cancer diagnosis and workup for primary care physicians is a strategy to urgently consider.

Participation in clinical trials to test expensive drugs for first-world markets does not qualify as regional research and seems ineffective at either attracting or educating appropriate clinical researchers in Latin American countries. International exchange programmes can be advantageous in refocusing oncologists to the needs of their communities and train them to be ambassadors of change in the promotion of regional needs to the political and bureaucratic framework in their countries.

Although effective strategies to curb the proportion of people smoking have been clearly outlined, intervention from the tobacco industry threatens these successes, and most Latin American countries tax tobacco products far below the target of 75% set by WHO (figure 6).<sup>194</sup> In many

states this low tax makes a pack of cigarettes far less expensive than a cup of coffee.<sup>199</sup> Strategies to address second-hand smoke exposure in Latin America are also needed. In a study<sup>254</sup> from Argentina, for example, 20·3% of the respondents were exposed to second-hand smoke at home and 38·8% exposed in indoor public places.

The use of electronic cigarettes is gaining popularity, especially in young people worldwide. Experts on the topic advise stringent e-cigarette control until more is known about the long-term effects on health and how they might contribute to cancer pathogenesis. States in the Latin American region should urgently implement suitable measures to ban the sale, importation and advertising of e-cigarettes as initiated in Argentina, Brazil, Panama and other countries.<sup>255–257</sup>

Efforts are needed to identify the most effective and implementable screening strategy for cervical cancer for each region and setting. A particular concern about implementation of HPV DNA testing as a stand-alone screening strategy is that no long-term data are available on its efficacy because this type of screening will miss a proportion of patients who have invasive cervical cancer. A study<sup>258</sup> from China where women with invasive cervical cancer had received pelvic examinations, pap smears, and HPV DNA testing within 3 years of their diagnosis reported that 15·5% had normal HPV DNA screening examinations, 15·5% had a normal pap smear, but only 3·9% had a double-negative result a year before their diagnosis. This study argues in favour of a combination strategy for cervical cancer screening. Health-care politicians should be aware that encouraging data on HPV DNA stand-alone screening from countries with a low cervical cancer incidence might therefore not be applicable to Latin American states. Whether the high false positive rates of HPV DNA screening will overburden health-care systems that are already stressed is still unclear. Before the introduction of HPV DNA testing, Latin American countries need to carefully assess whether they have sufficient resources, personnel, and sustainable funding to support this type of screening. In states where colposcopists and cancer specialists to treat women that have a positive HPV DNA result are rare, introduction of HPV DNA testing will not curb the cervical cancer epidemic. A collaborative effort between the Program for Appropriate Technology in Health, the Bill & Melinda Gates Foundation, the Alliance for Cervical Cancer Prevention, and Qiagen to develop a more affordable HPV test is underway.<sup>259</sup> This test can be used without electricity or running water and results can be offered within hours. A pilot project<sup>260–262</sup> is currently running in El Salvador.

To curb the high incidence of cervical cancer in Latin American countries, comprehensive national and regional reports analysing the status and the shortcomings of cervical cancer screening programmes will be needed. Regional interventional studies, such

as that in Argentina, will need to identify the most suitable screening strategies for different populations, regions, and settings. These studies will need to be done for breast cancer screening, which can be hampered by low coverage, and insufficient quality and follow-up of abnormal results.<sup>263</sup> Therefore, the development of effective screening programmes for cancer emphasises the importance of regional research in the Latin American region.

As authors of this 2015 Commission update to our 2013 report on cancer planning in Latin America and the Caribbean, we have been surprised and gratified that so much progress has been made in only 2 years. Latin American states, some more than others, are in turmoil related to funding, organisation, and execution of cancer programmes. Nevertheless, what is widely evident in Latin America are the steps towards the restructuring of health-care systems, progress on development of cancer registries, adjustments to funding towards universal health care and support of the underserved, and initiation of programmes for primary cancer prevention. We hope and like to believe that our 2013 and 2015 Commissions, our Global Cancer Institute collaborators, fellows and scholars, along with our tumour boards, projects, and publications, have all contributed in some small way towards this progress.<sup>132,264</sup> As a growing worldwide network of oncologists, we are dedicated to contributing towards better outcomes from cancer and better quality of life for cancer patients and their families in Latin America than at present, and we hope that future updates we undertake will show even greater alleviation of the overall cancer burden in Latin America.

#### Contributors

KS-W was the lead author of the Commission and participated in the writing, editing, and review of all sections. Part 2 lead author was YC-G. Co-authors ES-P-d-C, EC, and GdLL participated in the writing, editing, and approved the final version. Part 3 lead author was YC-G. Co-author ES-P-d-C participated in the writing, and editing, and approved the final version. Part 4 lead author was YC-G. Co-authors ES-P-d-C, EC, and GL participated in the writing, and editing, and approved the final version. Part 5 lead author was MD. Co-authors DT and GdLL participated in the writing, and editing, and approved the final version. Part 6 lead author was PERL. Co-authors JSN, JSL, CV, and AB participated in the writing, and editing, and approved the final version. Part 7 lead author was CV-G. Co-authors BLB, PR-E, KU-S, DFB, and MEF participated in the writing, and editing, and approved the final version. Part 8 lead author was BLB. All co-authors participated in the writing, and editing, and approved the final version. PEG wrote the Abstract, Introduction, and Conclusion and participated in the design, writing, and editing of all sections of the Commission.

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