Planning cancer control in Latin America and the Caribbean

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Non-communicable diseases, including cancer, are overtaking infectious disease as the leading health-care threat in middle-income and low-income countries. Latin American and Caribbean countries are struggling to respond to increasing morbidity and death from advanced disease. Health ministries and health-care systems in these countries face many challenges caring for patients with advanced cancer: inadequate funding; inequitable distribution of resources and services; inadequate numbers, training, and distribution of health-care personnel and equipment; lack of adequate care for many populations based on socioeconomic, geographic, ethnic, and other factors; and current systems geared toward the needs of wealthy, urban minorities at a cost to the entire population. This burgeoning cancer problem threatens to cause widespread suffering and economic peril to the countries of Latin America. Prompt and deliberate actions must be taken to avoid this scenario. Increasing efforts towards prevention of cancer and avoidance of advanced, stage IV disease will reduce suffering and mortality and will make overall cancer care more affordable. We hope the findings of our Commission and our recommendations will inspire Latin American stakeholders to redouble their efforts to address this increasing cancer burden and to prevent it from worsening and threatening their societies.

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Part 1: Introduction

Roughly 12·7 million new cancer cases are diagnosed globally each year; without substantial improvement in cancer control, it is predicted that this worldwide annual toll will rise to 21·3 million new cancer cases and 13·1 million deaths by 2030.[1] For the Latin America and Caribbean region, an estimated 1·7 million cases of cancer will be diagnosed in 2030, and more than 1 million cancer deaths will occur annually.[1] The economies of Latin America and the Caribbean are growing rapidly, and the standard of living is increasing. Such growth is accompanied by increases in sedentary lifestyles, unhealthy dietary habits, smoking, alcohol consumption, environmental carcinogenic pollutants, sun exposure, urbanisation, and population ageing. By 2020, it is estimated that more than 100 million people older than 60 years will be living in Latin America and the Caribbean, and that more than half of this group will live beyond 80 years.[2] Worldwide, the contribution of different risk factors to disease burden has changed substantially, with a shift away from risk of communicable diseases in children towards risk of non-communicable diseases, including an increasing burden of cancer, in adults. In 2010, the leading risk factors for global disease burden were high blood pressure, tobacco smoke (including second-hand smoke), alcohol use, household air pollution, diets low in fruits and vegetables, and high body-mass index. Apart from household air pollution, these risk factors are the main causes of chronic disease in adults, particularly cardiovascular disease and cancer. For most of Latin America, the leading risk factors for disease are alcohol use and high body-mass index, whereas tobacco smoke is the leading risk factor in North America and western Europe.[3] Figure 1 shows key cancer demographics in Latin America. A major problem with interpreting these data is that they are generally extrapolated from local hospital or regional databases, and only 6% of the Latin American population is covered by national cancer registries, by contrast with 96% in the USA and 32% in Europe.[7]

Although the overall incidence of cancer is lower in Latin America (age-standardised rate of 163 per 100 000) than in Europe (264 per 100 000) or the USA (300 per 100 000), the mortality burden is greater.[1] This is mainly due to presentation at more advanced stages, and partly related to poorer access to cancer care. In the USA, 60% of breast-cancer cases are diagnosed in the earliest stages, whereas in Brazil only 20% and in Mexico only 10% are diagnosed at an early stage.[8–10] The all-cancer mortality-to-incidence ratio for Latin America is 0·59, compared with 0·43 for the European Union and 0·35 in the USA.[1] All-cancer mortality-to-incidence ratios also vary within Latin America, from 0·39 in Puerto Rico to 0·65 in Belize, Honduras, and Guatemala (figure 1A). Although breast and cervical cancer are the most common cancer types in women in Latin America (figure 1B and figure 2B), and prostate, stomach, and lung cancer are most common in men (figure 1C and figure 2C), our Commission highlights exceptions and unusual regional trends in cancer types.

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There are no publicly available data on how much money is currently invested for cancer control in Latin America; however, there is substantial variation in the percentage of gross domestic product (GDP) spent on overall health care within the region (figure 1D and figure 2D), ranging from around 5% in Bolivia, Jamaica, Peru, and Venezuela to 10·9% in Costa Rica.[6] Average financing from the public sector, as a proportion of health spending, is 50·2% in Latin America, compared with a world average of 62·8%. Figure 1D shows a breakdown of public and private contribution to health-care spending for Latin American countries. Investments are linked to particular disease burdens within specific countries and regions, and are also influenced by social, demographic, and local economic factors.

Overall, Latin America is poorly equipped to deal with the alarming rise in cancer incidence and disproportionately high mortality rates compared with other world regions, underscoring the magnitude of the cancer-control problem. Excluding European and US territories in the region, Latin America encompasses 33 sovereign states with diverse health-care systems, access to care, socioeconomic, geographic, environmental, cultural, and ethnic factors. These factors present many obstacles to optimum cancer care. Our Commission describes strengths and shortcomings of current health-care mechanisms, and identifies ways to overcome barriers to improved cancer prevention and control. We hope this Commission provides ministries of health and other health-care stakeholders a useful framework for discussion and implementation of improved 21st century cancer care and control measures in Latin America.

Part 2: Current health systems in Latin America

All health systems in Latin America face the challenge of epidemiological transition and population ageing, with an accompanying increase in the burden of non-communicable disease and chronic illness.[11] Non-communicable diseases, such as cardiovascular disease, diabetes, and cancer, account for more than 69% of the region's deaths.[12] Further, global and national financial crises have repeatedly adversely affected the region, limiting the progress of its national health systems.

Each country's health system is unique, and many evolved into fragmented or segmented structures that, particularly for poor and unemployed people, provide minimum care and only for urgent needs. Many health systems in Latin America are not well-funded by public or government spending, and require high out-of-pocket spending for health interventions. As a result, there is biased allocation of resources, underinvestment in equipment and infrastructure, and inequities in cancer care across population groups.[13] Segmentation of health systems results in independent institutions that provide all aspects of health care, including insurance or stewardship, and financing and delivery of care to specific populations while excluding others; social security institutions that serve only the salaried workforce are an example. National systems developed as a coexistence of subsystems (public entities, social security, and private providers with varying levels of quality), each with different modalities of stewardship, financing, affiliation, and health-care delivery.[14,15] Segmented health-care systems are typically inefficient in terms of financing and provision of care, and provide fewer services to the poor, thus promoting inequity. The adverse effects of segmented systems on quality, cost, and health outcomes disproportionately affect poor people.[16]

Health-care systems in Latin America are characterised by a lack of health-care coverage for populations excluded from social security or other pooled, public financing mechanisms. Families are exposed to a high risk of catastrophic and impoverishing health payments, and for the poorest families, preventive and health-protective measures are cost prohibitive. Families without access to public insurance can be driven into poverty in an attempt to finance care, particularly for chronic illnesses, and are forced to sacrifice other basic needs such as food, housing, and education.[17,18] In 2008, it was estimated that roughly a third of people in Latin America were considered at high risk of such impoverishment and catastrophic health expenditures.[19]

An alternative model that has evolved in Latin America strives to achieve universal health care and provide equitable care to all citizens.[20–22] Achieving universal health care often involves integration of subsystems, and is being implemented in several countries in Latin America (table 1).[20–24] A key example is Mexico, where health-care reform is leading to universal health coverage through integration of health insurance for poor and uninsured populations, known as Seguro Popular.[25] Health reforms that share aspects of the Mexican Seguro Popular have also been implemented in Colombia, Peru, the Dominican Republic, and Chile.[26] Although many countries' health-care systems have progressed, obstacles for management of chronic, non-communicable diseases remain. It is particularly challenging to meet the range of needs for cancer care, including primary prevention, secondary prevention or early detection, diagnosis, treatment, rehabilitation, long term follow-up and survivorship, palliation, and end-of-life care.[27] Furthermore, fragmented health-care systems cause diagnostic delays and delays in initiating treatment, both of which are associated with advanced-stage disease and contribute to high mortality rates in the region. In Latin America, low screening rates, delayed referrals, and failure to seek medical help when symptoms develop contribute to advanced disease at presentation for breast, cervical, and gastric cancer. For lung cancer, diagnostic work-up requires a multidisciplinary approach, including high-level imaging and an invasive biopsy; most areas do not have the capacity for these assessments, which is a barrier to accurate staging and subsequent treatment. In many areas, access to timely cancer care is impaired by inadequate health-system

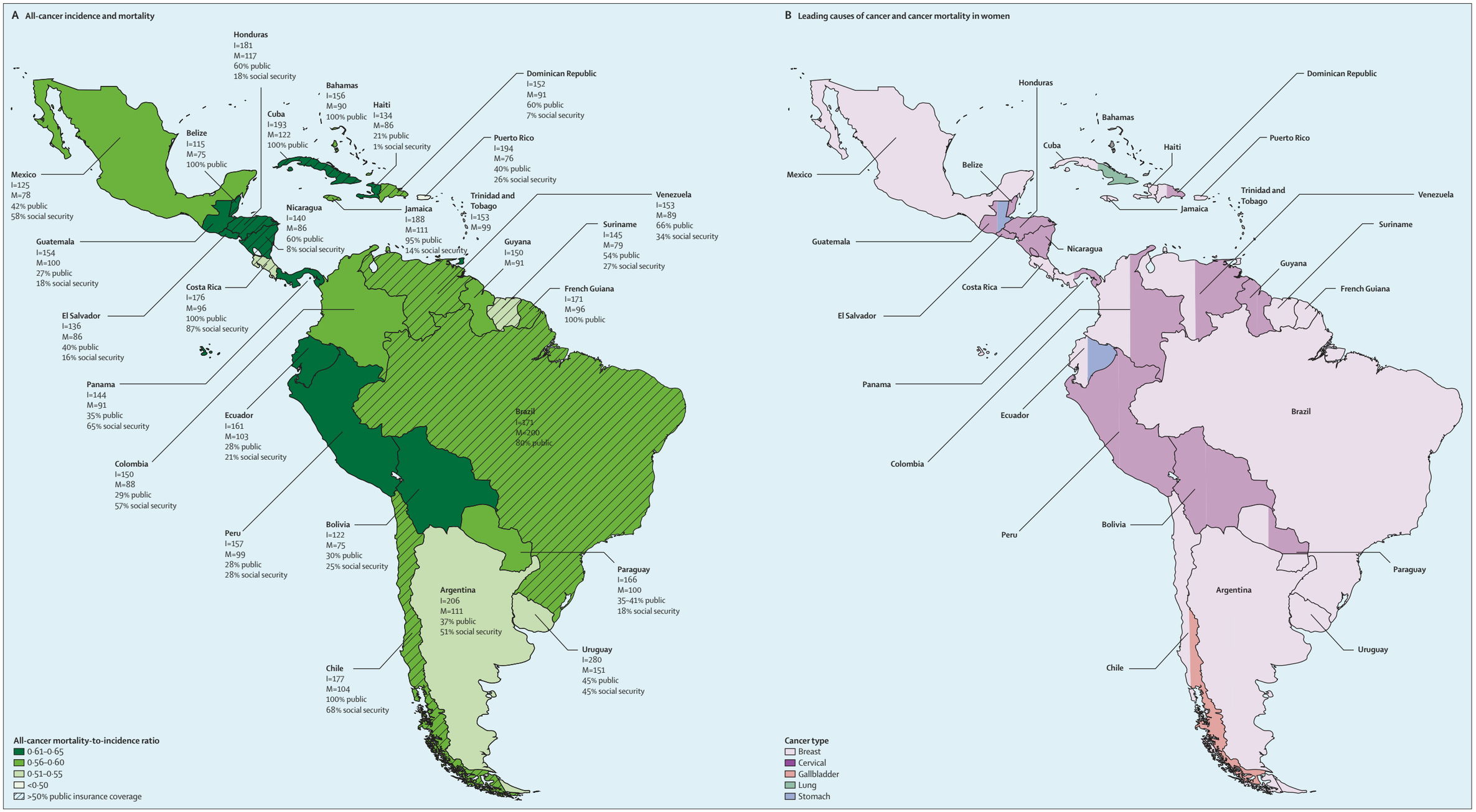

Figure 1: **Cancer and health-care metrics in countries of Latin America**
(A) All-cancer incidence and mortality.[1] Each country is shaded to reflect mortality-to-incidence ratios. All-cancer incidence and mortality per 100 000 people are listed on the map (I=incidence, M=mortality). The percentage of the population covered by public health insurance and social security is listed. (B) Leading causes of cancer and cancer mortality.[1] For each country, the leading cause of cancer is shown by the colour on the left, and the leading cause of cancer mortality is shown by the colour on the right (for Paraguay, breast and cervical cancers are equal leading causes of cancer mortality). (C) Leading causes of cancer and cancer mortality among men.[1] For each country, the leading cause of cancer is shown by the colour on the left, and the leading cause of cancer mortality on the right. Prostate cancer is the leading cause of cancer in all countries. (D) Economic metrics of health care.[4–6] The map shows the total gross domestic product (GDP) per head in gradient colour, and lists total population for each country and total health expenditure as percent of GDP.

C Leading causes of cancer and cancer mortality in men

D Economic metrics of health care

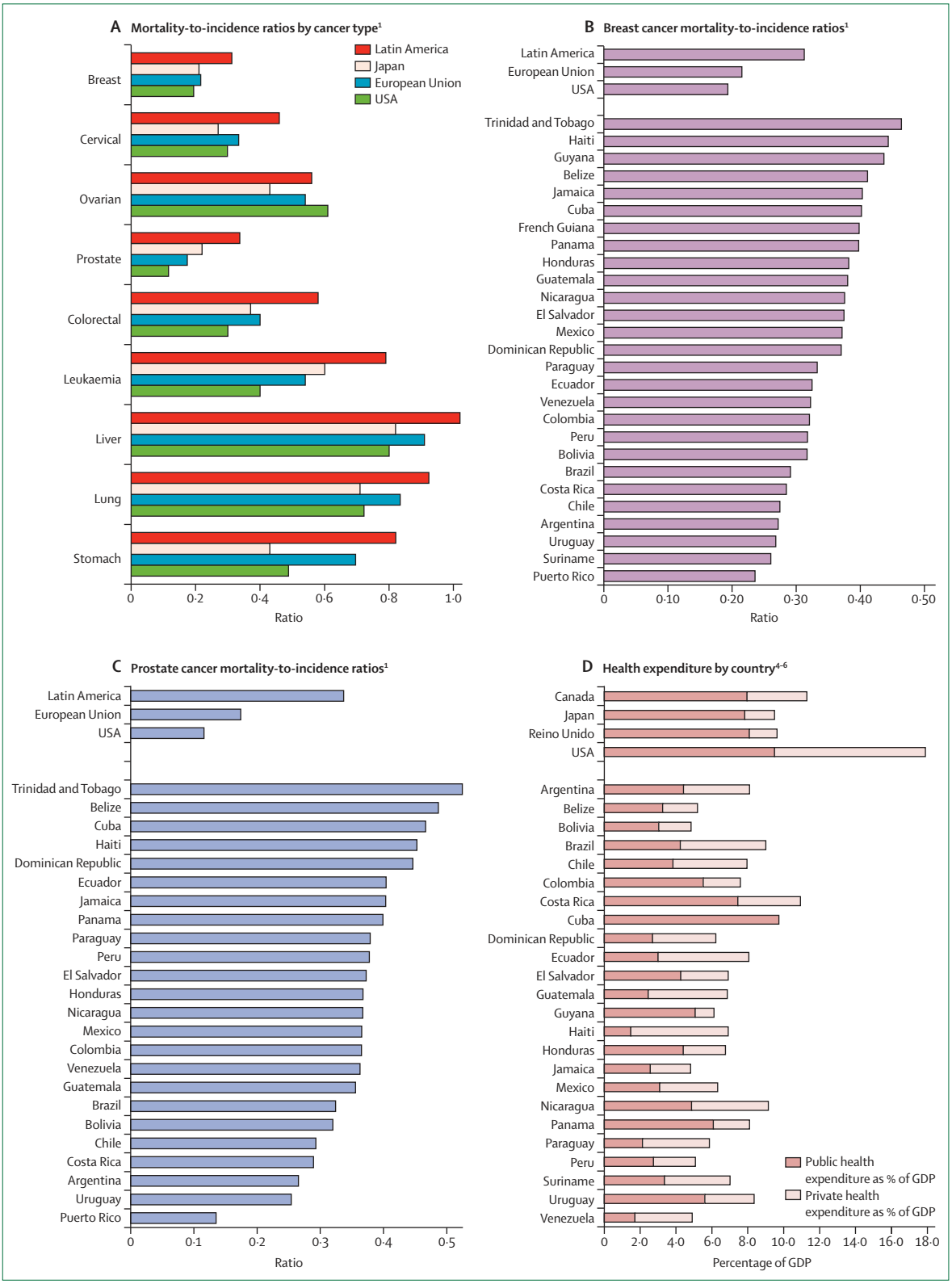

Figure 2: **Cancer incidence and health expenditure by countries in Latin America**
(A) Mortality-to-incidence ratios for different cancer subtypes. (B) Mortality-to-incidence ratios for breast cancer. (C) Mortality-to-incidence ratios for prostate cancer. (D) Public versus private spending on health care in Latin American countries and in other regions.

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	Health-system organisation	Coverage for all citizens
Argentina	A multitier system divided into three large sectors: public, social security, and private	Plan Médico Obligatorio
Brazil	A public health system covers all citizens; roughly 25% of the population has private health insurance	Sistema Único de Saúde (SUS)
Chile	Access to health care for a specific portfolio of diseases (selected by authorities) is guaranteed to all members of the population	For selected diseases
Colombia	Social security system provides health insurance with two main plans: the contributive scheme, which covers a wide range of technologies and diagnostic tests, and the subsidised scheme, which mainly provides coverage for poor citizens	Plan Obligatorio de Salud (POS)
Guatemala	Social insurance provides health-care services for workers and pensioners. The uninsured population has access to free consultations and tests via the public network	Public network
Mexico	Social insurance provides health-care services for workers and pensioners, whereas the uninsured population is covered by public institutions	Seguro Popular (in progress); government organisations provide services for uninsured population
Uruguay	The Nationally Integrated Health System includes a national health insurance regulated by a national health-insurance body (Fondo Nacional de Salud; FONASA) and a national board of health (Junta Nacional de Salud; JUNASA)	Plan Integral de Atención a la Salud (PIAS)
Venezuela	There are two contributive government programmes: the solidario health system with compulsory affiliation, and a complementary system with voluntary affiliation	Solidario

Table 1: **Health systems in Latin America**[23,24]

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infrastructure, especially in low-income, indigenous, and geographically isolated populations.

Full integration of vertical initiatives—ie, stewardship, financing, delivery, and resource generation—into pre-existing health systems has not yet been achieved and would greatly improve cancer care. A key obstacle in most Latin American countries is the lack of a cohesive national cancer plan that includes comprehensive cancer treatment and prevention programmes with ancillary efforts to combat tobacco use and second-hand exposure. According to the National Cancer Control Program Capacity Assessment, undertaken by WHO and the International Atomic Energy Agency (IAEA) in 2009, countries in Latin America that have national cancer plans include Bolivia (in preparation), Brazil (state level), Colombia, Costa Rica, Cuba, Guatemala (in preparation), Honduras, Nicaragua, Panama (in preparation), Peru, Salvador, and Uruguay (in preparation).[28] Several countries, such as Argentina and Chile, have cancer plans designed to address specific malignancies, such as breast cancer, and Mexico is preparing a national cancer plan designed to address control of all cancers. Most national cancer plans focus on breast, cervical, and paediatric cancers. Additionally, most Latin American countries have included cancer prevention, particularly anti-tobacco and obesity, into their overall national health plans. Establishing national cancer plans is a way to integrate existing health systems and apply a diagonal approach to meeting the complexities of cancer prevention and care. Here, we provide examples of different health systems in Latin America that show advances in meeting the challenge of cancer as chronic, high-cost illnesses. Although most continue to struggle with fragmentation and lack of universal health-care coverage, these countries are taking a progressive approach at the health-systems level with regard to cancer prevention and treatment.

Health-system reform: the case of Mexico

Mexico initiated health-care reform in 2003, recognising its problems of low government spending on health care and a predominance of private, out-of-pocket spending, unfair allocation of public resources, inequities in state contributions, and underinvestment in equipment and infrastructure, all legacies of a fragmented health system.[13,25,29,30] The goal of this reform was to achieve universal health coverage that included the uninsured population. The Mexican health-care reform initiative includes a new public health agency, funding for community health services, a new national organisation to monitor and assess health-care quality, and a national public health insurance programme (Seguro Popular), which provides access to essential health services and specialised interventions. Seguro Popular provides funds for catastrophic expenditures, including clinical management of the more common malignancies in adults (cervical, breast, testicular and prostate cancer, and non-Hodgkin lymphoma), bone-marrow transplantation when needed, and all cancer care for children and adolescents younger than 18 years of age.[31] Although full implementation of Seguro Popular has not yet been achieved, it currently covers 52·6 million people and is continuously expanding the number of diseases covered, including malignancies.[25,31] Since its implementation, this new health reform in Mexico has substantially affected cervical-cancer screening. Screening has risen from 30% coverage in 2000 to 48·5% in 2012, DNA testing for human papillomavirus (HPV) has been introduced, and HPV vaccination is now available to all 11-year-old girls. Access to costly breast-cancer treatments has also improved, including access to the monoclonal antibody trastuzumab for HER2-positive breast cancer.

How to improve a fragmented health system: an example from Argentina

Argentina's health system is financed by three sectors: public health, social security, and private insurance. A fourth subsystem, known as the National Institute of Social Security and Retirement Fund (INSSJP-PAMI), specifically covers retirees, similar to Medicare in the USA. Although this matrix structure is intended to provide universal coverage, its multiple independent systems lack vertical and horizontal integration, resulting in inadequate coverage for many. In the social security and private systems, health care can be contracted from different sources, some of which own their health-care facilities. In the public sector, financing is provided by the provincial or municipal government. The national government has an oversight role, including specific programmes to reduce provincial differences. Financing

of the public system comes from national and provincial taxes, and coverage is open to all; however, it is mainly used by people who lack any other type of health coverage. It is mandatory for employers to provide health insurance for all workers. Additionally, social insurance is mandatory for all government employees and is usually provided by workers unions. This insurance is funded by employers' contributions and can include copayments. The system includes the National and Provincial Social Security and the INSSJP-PAMI. By contrast, the private system consists of direct contributions and prepayments to medical companies. Both the social security system and private insurance are regulated by the Superintendent of Health Services, reporting to the Ministry of Health, and by the Obligatory Medical Program (PMO).

Any resident of Argentina has the right to medical care for catastrophic diseases, including cancer. Funding sources for cancer differ according to the health sector responsible for the patient. If a patient does not have private or social security insurance, the patient's province must cover costs. The national government also has resources to provide coverage for patients, including non-residents, located anywhere in the country. High-cost medications and treatments are covered by a special fund as part of the Special Programs Administration, supported by the Superintendent of Health Services (Korenfeld L, National Cancer Institute, personal communication).

In an effort to overcome this fragmented health system and improve cancer control, the Argentinean Government launched a new National Cancer Institute supported by the Ministry of Health in September, 2012.[32] The National Cancer Institute is responsible for development and implementation of health policies and coordination of integrated actions for cancer prevention and control in Argentina.

A national approach to cancer control: the case of Cuba

Cuba's constitution mandates universal health-care services, based on equity, prevention, scientific and technical evidence, community participation, public institutions, and government participation in medicine. There are no private hospitals in Cuba.[2]

As in other Latin American countries, the Cuban health system is challenged by the burden of non-communicable diseases, which account for 84% of all deaths, with cancer the second most common cause of death overall. Mortality from cancer increased 11% from 2006–10.[33] Cancer will soon become the leading cause of death in Cuba, and is already so in eight of 14 provinces.[34] The challenges faced by Cuba are exacerbated by its rapidly ageing population (17·6% of the population is older than 60 years), adult smoking rates higher than 35%, and obesity in 20% of adults.[35]

Within Latin America, Cuba has one of the highest investments in public health expenditure, at 9·7% of GDP, but cancer incidence is nonetheless high—only Argentina, Barbados, Guadeloupe, Martinique, Puerto Rico, and Uruguay have higher incidences.[1] Also, mortality-to-incidence ratios are higher than the Latin American average (0·63 in Cuba *vs* 0·59 for Latin America overall).[1] In Cuba, it is unclear how much of all public health spending is allocated toward cancer control.

The health system in Cuba is well organised and well staffed. Within the country, there are more than 452 community-based polyclinics that are well integrated into a national health system and offer preventive cancer services. Cuba also has the highest physician-to-person ratio in the world, with one physician per 147 people (compared with one to 388 in the USA).[36] For cancer care, Cuba also offers state-of-the-art radiotherapy services.[37]

Cuba's Ministry of Public Health, which oversees cancer control, reorganised their cancer programme in 2006 to create a single Comprehensive Cancer Control Program within a National Cancer Control Unit. This unit leads public-health strategies for cancer prevention and control, and coordinates the National Cancer Registry, the National Oncology and Radiobiology Institute, and the Scientific Pole, which leads medical research within the country. The National Oncology Group advises the Ministry of Public Health on cancer-control policy, the planning of human and material resources for cancer care, and cancer research. A National Cancer Network is designed to facilitate inclusive decision making and links all institutions working in cancer control at the national, provincial, municipal, and community levels, through a health-system information platform, known as INFOMED.

Health-system reorganisation: the case of Chile

Chile has a high human development index of 0·805, a composite statistic of life expectancy, education, and income indices that reflect people-centred policies (rather than national income).[38] Nevertheless, it has one of the highest cancer mortality rates in the world, at 120 per 100 000 inhabitants. According to national data, the annual estimated incidence of cancer is 240 per 100 000 inhabitants.[39]

Most oncologists in Chile work in the private health-care sector, in the capital city of Santiago, which results in major geographic inequities in access and provision of cancer services. Most secondary and tertiary centres in Chile provide surgical treatment for common cancers, but radiation therapy and chemotherapy units provide few services and have long waiting lists. In the private sector, patients choose their physician and have access to a wide range of surgical, medical, and radiation oncology services. Anecdotally, it seems many oncologists in Chile believe that cancer outcomes differ substantially depending on whether a patient receives treatment in Chile's public or private health system. However, there is no national cancer registry, and available registries (regional or single institution) represent a small portion of the population and often do not consider where a

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patient is treated, so it is unknown whether outcomes differ with respect to place where treatment was delivered.

In response to discrepant health-care coverage, Chile's Ministry of Health declared cancer to be a public-health priority in 1997. Their National Cancer Program now focuses on breast and cervical cancer, with a national anticancer drug programme and programmes in palliative care and radiation oncology, and provides guidelines for safety of patients and staff. Determining which cancers present the most serious threats in Chile has been hindered by the lack of a national cancer registry and epidemiological data; however, a comprehensive review of cancer services and research began in 2010, led by the Chilean Universidad Católica in collaboration with Kings Health Partners (London, UK).[40]

National cancer plan: the Peruvian model

According to the National Institute of Neoplastic Diseases in Peru, the annual incidence of cancer is 150·7 per 100 000 inhabitants, and roughly 55% are newly diagnosed stage IV cancers.[41] There is a shortage of health-care providers, tertiary-care hospitals, radiotherapy units, and diagnostic medical devices (eg, mammograms, endoscopy equipment, and pathological diagnostic equipment). In 2012, Peru proposed the Strategic Program for Cancer Prevention and Control (Plan la Esperanza) to reduce morbidity and mortality from cancer. This programme focuses on prevention of leukaemia, lymphoma, and breast, cervical, gastric, lung, and prostate cancer. The specific objectives are to prevent the development of cancer in about 12 million poor and extremely poor people through promotion of prevention and early detection of cancer; to provide comprehensive, timely, and quality treatment to patients with a new diagnosis of cancer; and to strengthen capacity of cancer services in the public sector. In view of the cancer-related needs identified after a thorough review, the programme created a list of priorities that will form the focus of future interventions to optimise the allocation of resources in the health system and subsequently improve cancer care.[41]

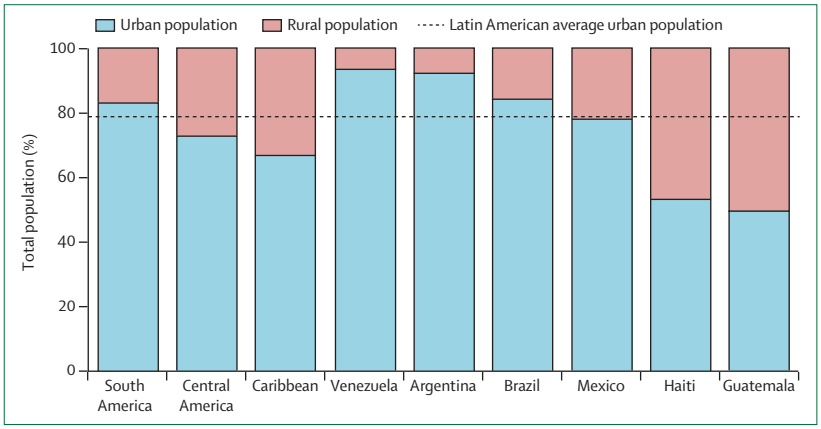

Figure 3: **Urban and rural populations for subregions and countries in Latin America and the Caribbean, 2011**[44,46]

Conclusions

Latin American health systems face many obstacles to providing optimum cancer services, including fragmented health infrastructure, limited health-care coverage, inadequate funding and resources for specific populations, and heterogeneity in distribution of resources. Therefore, there is an urgent need to plan, develop, and better implement national cancer strategies in view of local needs and current deficiencies in cancer care. To have impact, government leaders, health authorities, and the public must show a unified commitment to improve cancer services and care.

Part 3: Urban and rural cancer care in Latin America

WHO defines urban, rural, and remote areas by considering settlement characteristics, such as population density and accessibility to urban areas.[42] Latin America is characterised by concentration of its populations in major cities, which condenses resources, such as wealth, income, government, and health care, in these areas.[43] The reported percentages of people living in urban versus rural areas vary depending on the reference source and measurement methods. Urban and rural populations are defined as the de-facto population living in areas classified as urban or rural according to the criteria used by each area or country.[44–46] The popular perception that roughly 75–80% of Latin America is urban is questioned by several researchers, therefore we present data compiled from WHO and the United Nations Department of Economic and Social Affairs (79% urban), and data collected by NASA based on population density measurements that indicate that 55% of the population is urban (figure 3 and table 2).[49] The NASA data show that Guyana and French Guiana have the highest percentage of people living in remote areas and none in urban areas; whereas in the Bahamas, Puerto Rico, and El Salvador, most of the population resides in urban settings with a population density of at least 1000 people per square mile. Compared with the population distribution in Canada, Great Britain, and the USA, Latin America has around 10% more people residing in rural areas (table 2).

There is consensus, however, that most of the population in Latin America (>50%) resides in urban areas, and that this percentage is increasing.[49] Rural and remote populations are especially vulnerable to adverse cancer outcomes. They often reside in areas where oncologists and experts in cancer care are not available and local health centres cannot provide specialised cancer prevention, screening services, treatment, or survivor care.

There are important disparities between urban, rural, and remote populations with regard to poverty and health-care access. According to 2011 data from Latin America, 24% of urban populations live in poverty, whereas 50% of rural populations do.[50] Here, we discuss

inequities in cancer screening, diagnosis, and treatment in Latin America due to differences in access to care between urban and rural populations, and discuss cancer care in remote populations.

Barriers to health care for urban and rural populations

Of 590 million inhabitants in Latin America,[51] it is estimated that 54%, or almost 320 million, do not have health-care coverage.[52] Language barriers, unemployment, underemployment, geographic isolation, low education levels, and health illiteracy are all factors behind exclusion from health care. For the poorest populations in urban and rural settings, even in the context of free health care, access can be limited by inability to pay medication costs.[53] Lack of affordable transportation, inconvenient hours of clinic operation, and long waiting times are other factors that pose barriers to medical care.[54]

In Latin America, the rural poor are generally even more underprivileged than the urban poor.[55] They are often uninsured and at high risk of having catastrophic health-care expenses.[56,57] Poor availability and lower quality of cancer services, including health personnel, equipment, laboratories, and diagnostic equipment, aggravate the inequality of access to cancer care in rural versus urban areas.[58,59] An analysis of 12 Latin American countries showed that individuals in the lowest quintile of income and those living in rural areas are at highest risk of catastrophic health expenditures.[17]

Inequitable distribution of cancer centres and specialists

According to WHO's medical devices database, the number of physical and technological resources, such as physicians, nurses, and machines, commonly used to diagnose and provide cancer care are insufficient in Latin America.[59] The physician workforce in Latin America varies from 48 per 100 000 in Guyana to 374 per 100 000 in Uruguay (the worldwide average is 101 per 100 000 in lower middle-income countries and 224 in upper middle-income countries).[28] The density of hospital beds, an indicator of the availability of inpatient services and an important aspect of oncology care, ranges from 80 per 100 000 in Honduras to 290 per 100 000 in Uruguay (range 60–760 per 100 000 in low-income countries), compared with an average of 220 in lower middle-income countries and 360 in upper middle-income countries.[28] Radiotherapy units vary from six per 100 000 people in Bolivia and Paraguay to 57 per 100 000 in Uruguay. Data from Brazil, Colombia, Mexico, and Peru show that oncology services are concentrated in major cities, and this pattern is similar in other Latin American countries. These institutions house most of the medical specialists and specialised equipment required to deliver cancer diagnostic and therapeutic services.[28] This inequitable distribution of services, aggravated by accelerating migration into cities, has put pressure on urban resources, further limiting health-care services.[53] The result is that rural poor have been disproportionately affected.

In Brazil, cancer-care services are concentrated in major centres along the Atlantic coast and in the south and southeastern regions. Mexico City, Guadalajara, and Monterrey house most of the cancer care in Mexico. In Peru, services are concentrated in Lima, Arequipa, Trujillo, and Cusco. There are often no oncology centres in rural regions of these countries, or if available, centres lack key services such as radiation therapy or chemotherapy. Radiation therapy units are also concentrated in large cities. For example, in Peru, ten of the country's 18 radiation therapy units are located in Lima, three in Arequipa, and three in Trujillo, whereas 20 of the country's 25 regions lack radiotherapy centres. In Mexico, there are 20 linear accelerators for 32 states, and seven of these are located in Mexico City.

There is a shortage of all types of physicians in Latin American countries. The number of physicians ranges from 48 per 100 000 in Guyana to 374 per 100 000 in Uruguay, and the number of nurses from 41 per 100 000 in El Salvador to 650 per 100 000 in Brazil.[5,28] Physicians are unevenly distributed within countries in rural versus

	Total population	Remote areas (≤50 people/mile²)	Rural areas (≤999 people/mile²)	Urban areas (≥1000 people/mile²)
Argentina	43 497 320	26%	57%	43%
Bahamas	358 604	17%	35%	65%
Bolivia	11 218 101	32%	76%	24%
Brazil	201 388 560	15%	54%	46%
Chile	17 911 492	17%	53%	47%
Colombia	52 641 020	6%	55%	45%
Costa Rica	5 232 714	4%	51%	49%
Dominican Republic	10 136 578	0%	56%	44%
Ecuador	15 935 410	5%	49%	51%
Guatemala	16 328 786	2%	60%	40%
French Guiana	254 892	40%	100%	0%
Guyana	748 499	46%	100%	0%
Honduras	8 700 943	4%	60%	40%
Haiti	10 214 702	0%	56%	44%
Mexico	119 173 456	6%	51%	49%
Nicaragua	7 215 555	8%	68%	32%
Panama	3 451 344	12%	79%	21%
Peru	31 874 954	14%	60%	40%
Puerto Rico	4 389 532	0%	38%	62%
Paraguay	7 772 998	16%	53%	47%
El Salvador	7 979 201	0%	37%	63%
Latin America	576 424 661	12%	55%	45%
Canada	34 417 676	14%	45%	55%
Great Britain	60 565 220	2%	44%	56%
USA	321 195 904	11%	45%	55%

The percentage of the population living in remote areas (arbitrarily defined as ≤50 people/mile²), rural areas (defined according to the US Census Bureau[47] as ≤999 people/mile²), and urban areas (defined according to the US Census Bureau[47] as ≥1000 people/mile²) was determined for different Latin American countries using data predicted for 2015 from the Socioeconomic Data and Applications Center, a division of NASA.[48] The population density was converted from arc min (a unit of angular measurement equal to 1/60th of a degree) to miles, assuming that 1 arc min equals roughly 1·16 miles. At sea level, 1 arc min along the equator equals roughly 1 nautical mile (1 nautical mile=1·16 miles).

Table 2: **Percentage of the population who reside in urban, rural, and remote areas[48]**

urban areas. For example, in Brazil, where the national average is 144 physicians per 100 000 people, there are 60 physicians per 100 000 in the more underdeveloped northern region, compared with 210 per 100 000 in the southeast, where the largest urban cities are concentrated.[5] Similar disproportions are seen in Colombia, Guatemala, and Argentina; moreover, in rural areas, many physicians are young graduates who serve a mandatory period in rural settings.[56] Despite their inexperience, in the absence of specialised oncologists, these graduates are often the first line for cancer diagnosis and patient referral to more specialised centres.[60]

In Latin America, cancer specialists are concentrated in megacities.[61] For example, according to the National Cancer Plans of Mexico and Peru, there are a total of 269 medical oncologists in Mexico, of whom 44% work in Mexico City, 8% in Monterrey, and 8% in Guadalajara. In Peru, 85% of the 130 medical oncologists reside in Lima. In both Peru and Mexico, several states have no medical oncologist.[45,62] In Colombia, 35% of cancer specialists are in Bogotá, and together, Barranquilla, Medellín, Cali, and Bogotá account for more than 60%. With this concentration of specialists in urban areas, access to oncology services is difficult in rural regions with less than 100 000 inhabitants, where the average time for an initial assessment can exceed 200 days.[63,64] In many countries, patients migrate to cities for cancer care, which can affect the demand on cancer services in cities and might skew cancer statistics. For example, in Brazil, the 2012 incidence of cancer in men was 319 per 100 000 in state capitals, and 268 per 100 000 in states overall.[65] Likewise for women, the total incidence was 323 per 100 000 in state capitals versus 260 per 100 000 in states.

Adequate medical infrastructure to undertake prevention, diagnosis, and treatment of cancer is not available or not accessible in several regions of Latin America. Medical device availability per 100 000 inhabitants is as follows: mammography 4·73 (range 0·42 in Paraguay to 12·97 in Saint Vincent and the Grenadines), MRI 0·199 (range 0 in Dominica, Saint Kitts and Nevis, and Saint Vincent and the Grenadines to 1·16 in Saint Lucia), CT scanners 0·68 (range 0 in Saint Vincent and the Grenadines to 1·93 in Saint Kitts and Nevis), PET scanners 0·001 (range 0 in 16 countries to 0·012 in Mexico), and other nuclear medicine devices, such as emission CT for bone scans, 0·032 (range 0 in nine countries to 0·124 in Cuba). Radiotherapy units are available in 0·128 per 100 000 inhabitants (range 0 to 0·57).[66] By comparison, Australia and Switzerland have 0·5 accelerators per 100 000 inhabitants and France has 0·6.[67]

Most countries in Latin America have a list of anticancer medicines considered essential by WHO. In 2008, essential medicines (ie, medicines that satisfy the priority health-care needs of a population, including cancer drugs and vaccines) were available to 57·7% in the public sector and 65·1% in the private sector.[28] In 2010, WHO reported that tamoxifen for breast cancer was not available in Bolivia, El Salvador, Nicaragua, Paraguay, and Saint Kitts and Nevis, despite being available in most countries for USD 0·10 per pill.[68] We were unable to gather information about access to other anticancer drugs, but the lack of universal availability of tamoxifen in Latin America suggests that the problem of drug access is widespread.

Inequities in cancer services and screening that affect outcomes in rural populations

Access to cancer care varies between regions within a country. Data from Deloitte Access Economics, an Australian health economic consulting firm, suggest that the lack of access to health care is associated with worse outcomes in patients living in non-metropolitan areas.[69] Within Latin America, cancer outcomes vary within regions, depending on economic development and infrastructure. For example, in Brazil, breast-cancer mortality trends are stable in states with higher socioeconomic levels and more urban development, compared with rural areas like northeastern Brazil.[70] In Mexico, Colombia, and Brazil, cervical-cancer mortality rates are low in urban areas and high in rural regions, which have lower social and economic metrics.[71–73] Mortality differences between patients with cervical cancer in urban and rural areas have been attributed to less education, underemployment, and lack of social insurance coverage.[73] Possible reasons for patients presenting with advanced cancer in rural areas include low participation in screening programmes and delayed times to diagnosis and initiation of cancer treatment. Low participation in screening has been noted in areas where health services are geographically distant or hard to access.[61,74] For example, a Mexican study showed that it is far less likely for a woman to have a Pap smear and a mammogram if she resides in a marginalised rural community.[75] Similar findings have been reported for childhood cancers, with worse survival rates in regions with poorer socioeconomic conditions, more rural populations, and among those farther away from specialised cancer care centres.[76,77]

In the northern and northeastern areas of Brazil, where a high proportion of the population live in rural areas, roughly 40% of women aged 25 years and older receive mammography screening; in the southeastern region, which has more urban development, 65% of women received screening in 2008.[78] Use of mammographic screening is also highly correlated with level of education, which tends to be higher in urban areas.[78]

Health-care delivery to remote regions

Delivering care to truly remote regions is even more of a logistical challenge than to rural areas (figure 4). In Peru, for example, 2250 communities along the Yanayaku River in the Amazon are isolated, with no road access, and where the main mode of transit is by boat.[79] In this region, which is remote and settled by indigenous communities, 25% of people in a survey reported that

they had not seen a doctor in 5 years, and the major barrier to care was distance to a health centre.[80] In another study, 75% of women with an abnormal Pap finding had no appropriate follow-up because of residence in a remote setting.[81] Likewise, in Honduras, where only 20% of indigenous women had undergone annual Pap testing, lack of screening was attributed to the remote location.[82] In remote areas where patients do not have access to cancer screening and oncology services, patients often present with more advanced cancer and have worse outcomes.[83–85] Remote settings also create obstacles in delivery of high-quality care. For example, in San Martín, Peru, women who underwent biopsy for an abnormal Pap smear had to wait an average of 4–5 months to receive the histology report from Lima.[81] This long delay in diagnosis is a concern, since waiting 5 weeks or more before definitive treatment worsens survival for cervical cancer.[86]

Similar challenges to providing high-quality diagnostics have been described in Colombia. When Pap smears from remote states were evaluated at a national laboratory, local results were found to be suboptimum: up to 61% of negative smears had abnormal findings on central review and 13% had inadequate sampling.[87] When high-grade cytology was detected, 42% of women from one state had no confirmatory testing or treatment due to inadequate health services.[87]

Conclusions

Major health inequities in cancer outcomes between urban, rural, and remote populations in Latin America are partly a result of concentration of infrastructure, human resources, and other resources in urban areas. People in rural and remote areas have a lower socioeconomic status, lower education level, less health-insurance coverage, and face significant barriers to cancer services. Regional research is needed to identify specific reasons for barriers and ways to overcome these. For remote populations, innovative technologies, including teleoncology,[88] should be further explored to improve cancer-care services.

Comprehensive assessments at local health centres, regional hospitals, and at the national level will best determine how to optimise cancer care for urban and rural populations. Strategies to alleviate the concentration of cancer centres in major urban cities and to redistribute them more equitably should be sought. Locating specialised facilities in strategic regions able to serve several rural areas, and economic and academic incentives to attract health-care personnel, are measures to consider. Nurses, health workers, and general physicians should be trained to conduct specific tasks—eg, screening, simple diagnostic procedures, and basic chemotherapy administration—with referral to health-care facilities for specialised cancer care. Additionally, in countries with fragmented health systems, institutional collaborations could be established that allow for patients who lack public insurance to be treated at cancer institutions intended for the insured, and vice versa. It is essential to involve local physicians and nurses in proposing solutions to these issues.

Figure 4: **Tambopata River in Peru**
In some regions of Latin America, communities are isolated by limited road access, and travel by boat is the main mode of transit. For example, the Ese Ejja are an indigenous tribe who live along the Tambopata River in Madre de Dios, Peru. Delivering optimum cancer care to this community, who have high rates of exposure to mining contaminants,[79] is a challenge. This photograph is reprinted with permission of the photographer, Ry Tweedie-Cullen.

Part 4: Cancer care for indigenous peoples

There is no universal definition of indigeneity.[89] In Latin America, there is consensus that indigenous refers to the descendants of people who predated European contact. An estimated 400 different indigenous groups live in Latin America, representing 10% of the population or about 60 million people (table 3).[89] Indigenous populations are heterogeneous, but they share many cultural and socioeconomic conditions. The common experience of colonisation, forced migration, marginalisation, loss of language and native land, and suppression of culture unify this group and create similar health inequalities;[90] therefore, we discuss indigenous populations collectively with respect to cancer care. Although the number of indigenous people unable to access cancer services is unknown, this section attempts to describe this population and the challenges they encounter when receiving cancer care. Few studies have investigated cancer outcomes in indigenous populations of Latin America, so we discuss this topic by drawing parallels to other regions of the world where cancer trends have been characterised in indigenous populations.

Epidemiology of cancer and prevalence rates among indigenous peoples

Epidemiological data on the health of indigenous peoples in Latin America is limited. There are no national registries of cancer incidence and mortality that specifically

	Total population	Indigenous population	Percent of population classified as indigenous*
Bolivia	10 290 003	7 305 902	71%
Guatemala	14 099 032	9 305 361	66%
Peru	29 549 517	13 888 273	47%
Ecuador	15 223 680	6 544 660	43%
Belize	327 719	62 693	19%
Honduras	8 296 693	1 243 674	15%
Mexico	114 975 406	16 085 059	14%
Chile	17 067 369	1 365 390	8%
El Salvador	6 090 646	425 736	7%
Suriname	560 157	33 777	6%
Guyana	741 908	44 514	6%
Panama	3 510 045	210 602	6%
Nicaragua	5 727 707	285 813	5%
French Guiana	N/A	N/A	4%
Paraguay	6 541 591	196 248	3%
Trinidad and Tobago	1 226 383	24 773	2%
Colombia	45 239 079	904 782	2%
Venezuela	28 047 938	560 959	2%
Jamaica	2 889 187	57 784	2%
Puerto Rico	3 998 905	79 978	2%
Dominica	73 126	1462	2%
Barbados	287 733	3194	1%
Guadalupe	N/A	N/A	1%
Martinique	N/A	N/A	1%
Bahamas	316 182	3162	1%
Argentina	42 192 494	417 706	1%
Costa Rica	4 636 348	45 436	1%
Brazil	205 716 890	411 434	0%
Uruguay	3 316 328	995	0%
Total for Latin America	580 743 730	59 509 367	10%

Total population statistics for each country, predicted for 2015, were obtained from the NASA Socioeconomic Data and Applications Center.[49] The total indigenous population was calculated using the reported percentage of indigenous people in each country.[90] *Rounded to the nearest percent.

Table 3: **Total population, indigenous population, and percent indigenous determined for 2015 in Latin America**

account for ethnicity and indigeneity. To examine the distribution of cancer types among indigenous Latin Americans, the top five cancers in Bolivia, Guatemala, and Peru, countries with the highest percentage of indigenous people, were compared with Latin America overall.[48] Among women, incidences of cervical, gastric, hepatocellular, and gallbladder cancer are higher in these countries than average rates in Latin America.[1] Among men, incidences of gastric cancer, hepatocellular cancer, and leukaemia are higher in Bolivia, Guatemala, and Peru than for the total region. These findings are consistent with a study from Ecuador showing different cancer patterns among their indigenous population compared with non-indigenous people.[91] As in studies from Australia, New Zealand, Canada, and the USA,[84,92] indigenous people in Latin America have more adverse cancer presentations and outcomes, including more advanced disease at diagnosis and higher mortality rates than non-indigenous populations.[93–95]

Cancers associated with inadequate screening or prevention

Cervical cancer and HPV-associated dysplasia are common among indigenous women and women living in remote locations.[96–99] Although genetic polymorphisms prevalent in some ethnic populations might promote HPV-associated cervical cancer,[100] there is no evidence for this in the indigenous populations of Latin America. The high burden of cervical cancer is explained by limited access to Pap smear screening, HPV vaccination, and early cervical cancer treatment.[96–99] Furthermore, new research suggests that indigenous women might have a higher risk for cervical cancer because of increased wood-smoke exposure.[101–103]

Guatemala has the highest rates of hepatocellular carcinoma in Latin America, in both men and women; with two-thirds of the Guatemalan population being indigenous, this cancer seems to be disproportionately affecting indigenous people in the region. The incidence of hepatocellular cancer in Guatemala and neighbouring Mexico is attributed to high rates of chronic viral hepatitis, alcohol use, and environmental aflatoxin exposure.[104,105] Cholangiocarcinoma disproportionately affects indigenous men and women in Latin America.[106] This could be explained by their limited access to cholecystecomies.[107]

Cancers associated with tobacco use, dietary factors, and environmental carcinogens

Although rates of tobacco-related cancers among indigenous peoples are unknown, indigenous communities in Latin America consider tobacco to be wholesome and sacred. Cigarettes and snuff are often provided as offerings in indigenous ceremonies and rituals,[108] and one study from Peru reported a higher use among indigenous peoples in the Amazon region than the national average.[80]

Gastric cancer mortality is twice as high in Bolivia, Guatemala, and Peru compared with the average across Latin America.[1] A recent study from Peru found socioeconomic and nutritional factors, rather than genetic alleles or Amerindian ancestry, accounted for the high incidence of gastric cancer in indigenous people.[93] Risk factors for gastric cancer specific to indigenous people in Latin America include tobacco and alcohol use, higher intake of salt and nitrate-preserved foods due to a lack of access to refrigeration, and untreated *Helicobacter pylori* infection.

Many indigenous people use biomass fuel for heating and cooking, and many combustion by products (polycyclic aromatic hydrocarbons; eg, benzopyrene) from biomass fuels are carcinogenic. In Mexico more than 50% of people tested in an indigenous community had unsafe levels of carboxyhaemoglobin due to indoor smoke exposure,[109] and 40% of women in the Andes had chronic lung disease from smoke inhalation.[110] These

measurements suggest that many indigenous people are exposed to indoor smoke pollution from biomass fuel use and to carcinogenic combustion byproducts. Indigenous people often live on lands that are environmentally degraded or contaminated with carcinogens.[111] High rates of mercury and DDT exposure are reported in the Amazon of Brazil,[112,113] arsenic exposure in Chile is linked to bladder and lung cancer in non-smokers,[114,115] and, in Ecuador, cancer rates are high in indigenous communities located near areas contaminated with petroleum.[116,117]

Barriers to cancer services and care

Indigenous people in Latin America have poor health outcomes compared with their non-indigenous counterparts,[89] and, in this context, there are many factors that affect optimum cancer prevention, screening, and treatment in this population. One main barrier to cancer care that affects indigenous people is the fact that this population often resides in rural or remote areas with limited access to health services. As described in the previous section, there is a lack of cancer screening for populations living in rural and remote areas. When cancer screening services are available, there are often long waits for screening, follow-up care, and treatment. Poor diagnostic testing and inadequate health services also result in adverse outcomes.

Cultural differences affect how indigenous people interface with modern health and cancer services. Indigenous people often need thorough explanations about the causes of their illnesses, how their drugs work, and why they should keep to the clinical instructions. Many health providers are unaware of these needs or are too busy to fulfil them.[111] Cultural misconceptions, such as misunderstanding of traditions and differences in communication, can undermine indigenous people's experience when they seek oncology services, and understanding these factors could enhance outcomes in these patients.

Research regarding indigenous populations

Over the past decade, the percentage of medical publications from Latin America that address indigenous health has increased from 6·5% in 1995 to 10·4% in 2004; however, only a fraction (8·7%) of these publications addressed non-communicable diseases, and less than 60 were related to cancer in indigenous people.[118] Research specific to indigenous and remote people in Latin America is needed to better characterise the distribution of cancer in these populations and understand how they receive cancer screening and treatment; with this knowledge, sustainable interventions can be designed to improve outcomes.

The burden of cancer in indigenous populations needs to be characterised. Lifestyle factors, including tobacco and alcohol use, diet, and exercise patterns, should also be studied to direct cancer prevention strategies. Environmental exposures that increase the risk of cancer in indigenous populations must also be identified. Indigenous people live in areas exploited for their resources, and these environments negatively affect their health through environmental contamination. For example, hair analysis of indigenous Argentineans living near the Pilcomayo river, in Formosa, showed high concentrations of heavy metals linked to mining spills in Bolivia.[89] In regions where cancer incidence due to leukaemia is high, exposure to environmental carcinogens, such as benzene contamination, warrants close investigation. An inventory of oncology services that serve indigenous populations needs to be compiled, since areas with few oncologists have higher rates of cancer mortality.[119–121] Finally, knowing that poverty is correlated with adverse cancer outcomes and that almost 80% of indigenous people are considered poor,[122] more research is needed to understand how social determinants affect indigenous health with respect to cancer, particularly in Latin America.

Potential solutions

An important first step in improving prevention, screening, diagnosis, and treatment of cancer in the indigenous populations of Latin America is to establish national, regional, and institutional cancer registries that include ethnic data. Our review of existing data shows that many preventable cancers affect indigenous people; therefore, expanding cancer prevention programmes will lower cancer incidence. To reduce cancer in the indigenous population, we recommend public education campaigns, formation of cultural-specific advocacy groups, expanded HPV and viral hepatitis vaccination, cervical-cancer screening, and public programmes to control smoking and environmental carcinogen exposure. In view of the high rates of gastric cancer and cholangiocarcinoma, specific screening for these malignancies might also be appropriate in some regions.

Efforts are needed to bridge language, social, and cultural gaps between patients and oncology providers. Providers who are culturally sensitive to the needs of indigenous people will improve the clinical encounter and patients' understanding of their health and care. In some communities, expansion of the female health-care workforce might be needed since many indigenous women prefer female providers.[123] An emphasis on well-trained interpreters is important. Providing financial incentives and additional training to health-care professionals willing to serve indigenous communities, as Canada is seeking to do,[124,125] could be key to improving cancer outcomes in these communities.

Part 5: Cost of cancer care in Latin America and the Caribbean and future challenges

The global economic cost of new cancer cases in 2009, including medical and non-medical costs, productivity losses, and the cost of cancer research, was estimated to be at least US$286 billion.[16] A major concern is that the

burden of cancer is not equally distributed across nations of the world. Despite the fact that low-income and middle-income countries represent 84·7% of the world population and 61·3% of new cancer cases globally, these areas account for only 6·2% of the financial expenditures on cancer worldwide, exposing the large deficit in investment. Globally, the cancer fatality rate (a ratio of cancer mortality to cancer incidence) is higher in low-income countries than in high-income countries. In 2002, the cancer fatality rate for low-income countries (74·5%) was 1·6 times higher than that of high-income countries (46·3%).[16]

In the introduction, we presented statistics on health-care investment in Latin America and the Caribbean, which are shown in figure 1D and figure 2D. In 2011, total health expenditure in Latin America averaged 7·7% of GDP; however, this percentage varies greatly between countries and regions.[6] Bolivia, Jamaica, Peru, and Venezuela spend roughly 5% of their GDP on health care, whereas Costa Rica spent 10·9% of GDP on health care, which is more than spending in Japan (9·5% of GDP) or the UK (9·6% of GDP).[6] Nicaragua is a standout in the region with low GDP per head (only US$1243 per head; an amount that is lower than GDP per head in Bolivia, Jamaica, Peru, and Venezuela), but nonetheless investing 9·1% of GDP in health care.[6] Brazil, the most populous country in the region, with an emerging economy, invests 9·0% of GDP in health care, whereas Mexico, the second most populous country, invests only 6·3% of GDP.[6]

Figure 2D shows total health expenditure as a sum of public and private health expenditure for selected Latin American countries. Financing from the public sector averages 50·2%, compared with the world average of 62·8%. Out-of-pocket expenditure accounted for 34·3% of health expenditure in 2011, creating a high risk of catastrophic expenditure and impoverishment.[126] WHO has estimated that 15% or lower of out-of-pocket expenditure is needed to reach low risk of catastrophic expenditure.[127] In 12 Latin American countries, the calculated proportion of households with catastrophic health expenditures ranged from 1–25%.[17]

Disparities in health-care spending within countries

Disparities in health-care spending vary across countries in Latin America, and also within countries and regions. In Brazil, for instance, total health-care expenditure represents 9·0% of GDP, but 53% of this amount (4·8% of GDP) is borne by the private sector, which covers less than half of all patients. However, public sector expenditures within the Unified Health System of Brazil (SUS) represent only 40% of total health-care expenditures (3% of GDP), but cover 75% of the population.[6] This contrasts starkly with public expenditures of about 50% in the USA and in excess of 75% in the UK. As such, care in public facilities in Brazil, where overcrowding, lack of access to medications, and limited services and lower quality are typical, often lags behind that of private facilities, with large differences linked to geography and regional income.[128] The situation is similar in other Latin American countries. In 2008, Mexico spent 5·9% of its GDP on health care (52% by the private sector, which covers only 5% of the population).[17]

Latin American countries have focused their health investment on prevention and treatment of infectious diseases, whereas spending on non-communicable diseases, such as cancer, has not kept pace.[129,130] However, many of these countries are now experiencing higher life expectancies and adopting a lifestyle similar to that in developed countries, leading to a rapidly growing number of patients with cancer, a cost burden for which they are not prepared. It is estimated that low-income countries globally would have to spend US$217 billion to achieve the minimum global standard of cancer care, a figure referred to as the funding gap.[16]

Country-specific economic resources for cancer care were not available for all Latin American countries; however, the estimated expenditure gap for cancer (defined by estimated treatment and care costs in the country with the lowest case fatality rate for each cancer site) for middle-income countries globally is between 24–57%, compared with 11% in high-income countries.[59] The total economic burden of cancer in Latin America, including medical and non-medical costs, is estimated to be around US$4 billion (table 4).[16,131,132] However, the overall mean medical expenditure per patient is $7·92, compared with $183 in the UK, $244 in Japan, and $460 in the USA. Latin American figures compare favourably with China (mean expenditure $4·32 per patient) and India ($0·54 per patient). When adjusted by income at current exchange rates, the medical costs of cancer care in Latin America represent 0·12% of gross national income (GNI) per head (ranging from 0·06% in Venezuela to 0·29% in Uruguay), compared with 0·51% in the UK, 0·60% in Japan, and 1·02% in the USA; in India, this figure was 0·05%, and in China it was 0·11%.[16,131,132]

Assessing the cost of cancer care

To assess the cost of any disease, pharmacoeconomic studies are needed that consider the total costs (direct and indirect) incurred from the disease.[133] Direct costs consist of pharmaceutical drugs, medical devices, physician visits, emergency room visits, diagnostic testing services, education, and research. Indirect costs include loss of working days and productivity, travel time and costs, accommodation, and waiting times. Complications that require hospitalisation are the largest contributor to direct costs of cancer, with drug costs being a small fraction. Avoidance of stage IV advanced cancer is the key to reducing costs. Establishing and improving prevention, diagnostic, and basic treatment measures, such as surgery and radiation, are likely to reduce costs the most in Latin America. The large majority of cost-effectiveness studies in cancer are done outside of Latin America. Within Latin America, Augustovski and colleagues[23] identify Brazil as having

	Population in 2009	Predicted cancer cases in 2009	Predicted cancer cases in 2020	Percent increase in number of cancer cases from 2009 to 2020	Total cost (medical plus non-medical) of new cancer cases (2009 US$)	Medical cost per patient of new cancer cases (2009 US$)	GNI per head (2009 US$)	Costs per patient as a percentage of GNI per head
South America	388 211 000	765 155	1 043 388	35·0%	$3 074 936 964·00	$7·92	$5872·67	0·12%
Argentina	40 062 000	111 132	133 451	20·1%	$488 938 632·00	$12·20	$7469·00	0·16%
Bolivia	9 773 000	14 091	19 259	36·7%	$17 759 884·00	$1·82	$1705·00	0·11%
Brazil	193 247 000	365 638	504 824	38·1%	$1 553 826 537·00	$8·04	$8078·00	0·10%
Chile	16 956 000	43 746	60 673	38·7%	$255 943 206·00	$15·09	$8806·00	0·17%
Colombia	4 565 400	88 810	130 969	47·5%	$272 083 689·00	$5·96	$4985·00	0·12%
Ecuador	14 262 000	21 629	30 308	40·1%	$51 207 307·00	$3·59	$3547·00	0·10%
Guyana	753 000	1112	1464	31·6%	$1 422 118·00	$1·89	$2668·00	0·07%
Paraguay	6 342 000	8681	12 110	39·5%	$13 887 221·00	$2·19	$2200·00	0·10%
Peru	28 765 000	56 147	76 373	36·0%	$140 818 954·00	$4·90	$4262·00	0·11%
Suriname	520 000	618	796	28·8%	$2 287 407·00	$4·40	$6281·00	0·07%
Uruguay	3 357 000	13 288	14 914	12·2%	$89 392 385·00	$26·63	$9129·00	0·29%
Venezuela	28 520 000	40 263	58 247	44·7%	$187 369 624·00	$6·57	$11 342·00	0·06%
Central America and Mexico	153 545 000	197 829	279 283	42·3%	$1 454 524 925·00	$7·39	$4117·38	0·18%
Mexico	112 033 000	147 739	208 788	41·3%	$1 284 051 689·00	$11·46	$7724·00	0·15%
Belize	105 000	426	638	49·6%	$1 779 562·00	$16·95	$3870·00	0·44%
Honduras	7 450 000	7433	10 458	40·7%	$12 022 003·00	$1·61	$1831·00	0·09%
El Salvador	6 160 000	9400	12 680	34·9%	$34 673 092·00	$5·63	$3265·00	0·17%
Guatemala	14 034 000	14 043	19 565	39·3%	$33 989 635·00	$2·42	$2606·00	0·09%
Nicaragua	5 710 000	6580	9332	41·8%	$8 591 600·00	$1·50	$1043·00	0·14%
Costa Rica	4 591 000	7173	10 627	48·2%	$47 844 423·00	$10·42	$6175·00	0·17%
Panama	3 462 000	5035	7195	42·9%	$31 572 921·00	$9·12	$6425·00	0·14%
USA	310 383 095	1 646 299	2 078 404	26·2%	$142 830 848 156·00	$460·17	$45 301·00	1·02%
UK	61 652 032	297 747	344 025	15·5%	$11 265 851 099·00	$182·73	$35 714·00	0·51%
Japan	126 552 000	596 253	687 967	15·4%	$30 840 792 562·00	$243·70	$40 861·00	0·60%
China	1 334 908 000	2 627 721	3 536 449	34·6%	$5 786 829 242·00	$4·34	$3833·00	0·11%
India	1 207 740 041	1 023 571	1 369 412	33·8%	$656 216 740·00	$0·54	$1114·00	0·05%

GNI=gross national income.

Table 4: **Cancer cases and expenditures**[16,132,133]

the most experience with use of pharmacoeconomics in decision making, with Chile, Mexico, Argentina, Colombia, Guatemala, Uruguay, and Venezuela beginning to adopt pharmacoeconomic models in decision making. At best, however, efforts are rudimentary and urgent progress is needed to enhance use of pharmacoeconomics in improving cancer care.

Drug policies in Latin America and the Caribbean

Over the past decade, many Latin American countries have undertaken profound reforms of their health-care systems concomitant with macroeconomic changes in the region. Panel 1 shows drug pricing policies in Latin America. Brazil, the largest economy in the region, is forecasted to have 15–20% annual economic growth for 2012. Argentina, Colombia, Chile, and Mexico are predicted to have strong economic growth for 2012 and 2013. There is a need for establishing mechanisms that ensure efficient allocation of scarce resources in Latin America, as well as guaranteeing provision of health-care services on the basis of local needs. As health-care systems in Latin America modernise and mature, the region is a promising market for medicines and related products. For example, spending on drugs is predicted to increase from 12% of total expenditure for cancer in 2005, to 28% in 2015, despite tight budget constraints through price referencing and generic substitution.[134]

Lack of access to high-cost cancer medications

Money and access to health-care delivery are associated with cancer outcomes. Breast-cancer survival at 5 years varies from around 80% in high-income countries to 40% in low-income countries.[135] This is partly due to differences in access to care and cancer medicines. In Europe, where patients generally receive timely and adequate primary diagnosis and treatment, there is a difference in cancer survival between countries with fast approval of new cancer drugs versus those with longer time to approval.[136] For the USA, where most patients receive adequate primary diagnosis and treatment, it was shown that new

Panel 1: **Examples of pricing policies for cancer therapies**[23]

Argentina
There is no formal price regulation for cancer therapies; insurance companies negotiate discounted prices with pharmaceutical companies, depending on demand.

Brazil
Drug prices have been regulated since the end of 2000. Policies are defined by the Chamber of Regulation of Drugs Market (Câmara de Regulação do Mercado de Medicamentos), which is composed of five different ministries and led by the Ministry of Health.

Colombia
The Ministry of Commerce defines the top price of each medication. Insurance companies, clinics, and hospitals negotiate with pharmaceutical companies based on the market price of the drug.

Guatemala
There are multilateral agreements for open contracting with the pharmaceutical industry and a bidding process for essential drugs.

Uruguay
The Director of Commerce controls prices in pharmacies and drugstores and permits a maximum 25% discount.

Venezuela
A mixed price system (a system where all essential medicines have their price controlled by the government) has been in place since 1994. The medicines with controlled prices are listed in an official publication by the Ministry of Commerce.

cancer drugs were responsible for more than 50% of the improvement in 5-year survival rates of patients with cancer between 1975 and 1995, contributing more than 10% to the total improvement in life expectancy of US citizens. Furthermore, the number of available cancer drugs has been associated with 1-year and 5-year survival of patients with cancer.[137] These figures should be interpreted with caution. Cancer medications can improve residual risk only after other measures of prevention, diagnosis, and primary care have been optimised. In Latin America, where the main cause of cancer mortality is advanced disease at diagnosis, more emphasis needs to be placed on delivery of state-of-the-art diagnosis, primary surgery, and radiation treatment. Otherwise, increased spending on drugs is unlikely to change national morbidity and mortality statistics.

Providing new cancer drugs can be unaffordable in developing countries. More than 90% of cancer drugs approved in the USA since 2004 cost more than $20 000 for 12 weeks of treatment. Use of these new medications in Latin America would lead to an estimated increased cost of cancer drugs of 15% per year. Therefore, although Latin America is considered to be an expanding market for the pharmaceutical industry, 88% of new drugs launched in 2005–09 were used in North America, Europe, and Japan.[138] Within the public health systems of Latin America, access to expensive medications and technologies is restricted, whereas patients with private insurance (or private funds) have access to many expensive therapies.

Public versus private cancer treatment in Brazil

In Brazil, most patients with breast cancer given adjuvant chemotherapy in public institutions receive first-generation chemotherapy regimens (cyclophosphamide, methotrexate, and fluorouracil) compared with less than a third of such patients in private institutions. The Brazilian Health Ministry reported in 2009 that adding antibody-directed therapy to the list of medications covered by the public health system would increase expenditures for lymphoma treatment by 900%, a prohibitive expense.[139] In 2011, rituximab was incorporated into the list of medications covered, but its use is restricted to first-line treatment of diffuse large B-cell lymphomas.[140] Until recently, patients with HER2-positive breast cancer receiving treatment through the Brazilian public health system had to sue the government to get access to trastuzumab, a common situation in almost all Latin American countries.[141] Women with HER2-positive breast cancer are ten times more likely to receive trastuzumab if they are privately insured (only 6% of patients with HER2-positive breast cancer receive trastuzumab in the public system *vs* 56% in the private sector).[142] In 2012, trastuzumab became available to women with HER2-positive early breast cancer, but not for metastatic disease. This approval will be effective in 2013, 8 years after its widespread approval for adjuvant therapy in the USA.[33,143] The picture is similar in other Latin American countries, such as Mexico, Argentina, and Colombia.[23,141]

Enrolment in clinical trials sponsored by the pharmaceutical industry can be a favourable option for patients in Latin America, by providing access to high-cost medications that are otherwise unavailable. In fact, many Brazilian clinical trial sites have higher enrolment rates than those in the USA or Europe.[144] This situation raises ethical concerns, however, since most patients in Latin America will not have access to the new therapies even if they are approved. One point of view is that trial participation in low-income and middle-income countries is a convenient way for wealthy countries and pharmaceutical companies to gain rapid approval of drugs for use in wealthier markets and enhance company profits at the expense and exploitation of lower income countries.[142,145]

Future challenges

Lack of access to high-cost medications and under-implementation of new technologies needs to be addressed in Latin Amercia, but should not be prioritised over access to primary care. Increased government expenditure and substantial structural changes are needed to diminish inequity within countries, where most people do not have access to a minimum standard of health care, and a small proportion has access to the highest standards. Financial support from developed countries is also important to help Latin America to close the funding gap, which causes inequities in cancer outcomes between developing and wealthy nations.

High-quality research, including cost-effectiveness studies, is needed to understand the optimum allocation of scarce resources. In this regard, Brazil has made great progress with the creation of the Institute of Technology Assessment in Health (Instituto de Avaliação de Tecnologiaem Saúde), an institute which includes collaborations with more than 80 researchers in ten universities from different regions of the country.[146] Mexico, Colombia, Argentina, Uruguay, and Venezuela are also developing similar initiatives. It might not be feasible for every country in Latin America to develop their own cost-effectiveness studies, but taking a regional approach is probably more useful than adopting European and North American guidelines.

Part 6: Medical education: role of the academic and commercial sector

In high-income countries such as the USA, a shortage of oncology services is predicted by 2020, mainly due to the increased incidence of cancer and improved survival.[147,148] Detailed information on the number of cancer specialists in Latin America is limited. In 2010, Peru had 200 oncologists (including surgeons, paediatric oncologists, and medical oncologists), 146 general radiologists, and 72 general pathologists. Therefore, the estimated rate of oncologists per 100 000 inhabitants is 0·67, assuming a total population of 29 549 517 predicted for 2015.[49] In 2012, Mexico had 735 surgical oncologists, 50 gynaecological oncologists, 269 medical oncologists, 151 paediatric oncologists, and 180 radiation oncologists—with an estimated rate of 1·07 oncologists and 0·16 radiation oncologists per 100 000 inhabitants assuming a total population of 112 million.[41,45] These rates are in sharp contrast to those in the USA, where there will be approximately 3·75 oncologists (including medical oncologists, haematologist oncologists, paediatric oncologists, and gynaeco-oncologists) per 100 000 inhabitants in 2020, and considering the growing burden of cancer, it is projected that this ratio will represent a 25–40% shortage of oncologists in 2020 compared with 2005.[149]

By contrast with the USA and European Union, countries in Latin America do not have a unified core curriculum for training clinical oncologists, and each country has its own requirements for specialty certification. The number of clinical oncology training programmes, number of new fellows per year, and annual cancer incidence in several Latin American countries are shown in table 5.

Oncologist education in Brazil

According to WHO, there are about 176 physicians per 100 000 inhabitants in Brazil. Data from the Federal Medical Council (CFM) show that 0·71% of specialists in the country are oncologists and 0·69% are haematologists.[152] As is the case in all Latin American countries, these specialists are concentrated in wealthier urban areas.[152]

Specialisation in medical oncology, under the jurisdiction of the Brazilian Cancer Society (SBC) and the Brazilian Society of Clinical Oncology (SBOC), is a 3-year residency programme preceded by 2 years of training in internal medicine. Trainees increasingly gain medical autonomy, progressing from basic patient assessment in the first year to comprehensive treatment and research abilities by the end of the third year. Trainees work mainly with inpatients in the first year and almost exclusively with outpatients by the third year of residency, allowing exposure to the country's most common cancer types in different clinical settings. The curriculum covers clinical skills, capacity to work as a team member, and ability to organise the oncology assistance process and to plan and execute research. The clinical oncology curriculum is built on the most prevalent cancers, and fellows are trained as general oncologists. Subspecialty oncology training is not common in most centres in Brazil.

Although palliative care has been an established medical discipline for almost 50 years, most Latin American countries lack a formal programme.[153–155] In Brazil, palliative-care specialisation requires a minimum of 1 year of training after completing a fellowship in internal medicine, geriatrics, paediatrics, oncology, anaesthesiology, or family medicine; however, there is no established core curriculum for palliative care training.[156]

Twinning and telemedicine

The objectives of twinning programmes are to establish collaborations between centres with available resources, such as medical technology and specialised personnel, and centres without them. Through twinning programmes, resource poor-centres can have access to specialised training and elaborate strategies and protocols for care of oncology patients using the expertise and guidance of resource-rich centres. Telemedicine is the use of information and communication technologies to improve patient outcomes by increasing access to care and medical

	Number of medical oncology training programmes*	Number of residents in training per year*	Annual cancer cases†	Annual cancer mortality†
Venezuela	4	10–15	36 961	21 249
Colombia	4	8	58 534	34 016
Guatemala	0	0	14 155	9120
Mexico	11	60	127 604	77 708
Ecuador	1	1	20 167	13 280
Panama	1	2	4630	2982
Chile	3	3	36 047	22 123
El Salvador	2	2	7782	5047
Uruguay	1	11	14 584	8644
Brazil	52	103	384 340[150]	172 044[151]

*Barrios C, unpublished data. †Absolute numbers excluding non-melanoma skin cancer (GLOBOCAN 2008).[1]

Table 5: **Number of medical oncology programmes, residents, and cancer cases in selected Latin American countries**

	Disease	Programme	Changes in local cancer care
La Mascota Children's Hospital of Managua (Nicaragua) with the Department of Paediatrics, San Gerardo Hospital (Monza, Italy)[159]	Paediatric non-Hodgkin lymphomas	Creation of a local therapy protocol based on locally available drugs, availability of supportive care, and patient's nutritional characteristics	64% overall survival at 3 years median follow-up[159]
Paediatric oncology centres in El Salvador, Honduras, and Guatemala with St Jude Children's Research Hospital and UTHEI (Memphis, TN, USA)[160]	Retinoblastoma	Establishment of early diagnosis clinics; creation of treatment protocols appropriate for local conditions; establishment of consultation service by use of teleoncology; offering of short rotations overseas for local physicians; donation of equipment	Increase in number of diagnoses; decrease in patient abandonment or refusal of therapy; decrease in patients lost to follow-up; proportional increase of patients alive
Instituto Materno Infantil de Pernambuco (Brazil) with St Jude Children's Research Hospital[161]	Acute lymphoblastic leukaemia	Creation of a specialised paediatric oncology unit	Improvement in mortality rates

UTHEI=University of Tennessee Hamilton Eye Institute.

Table 6: **Examples of paediatric oncology twinning programmes**

information.[89,157] One of the key advantages of teleoncology is that it builds on twinning programmes by connecting centres from high-income countries to those in low-income or middle-income countries; information exchange between centres becomes faster, easier, and cheaper with the use of telemedicine resources, such as web conferencing.[89] Teleoncology can also help to build important partnerships between different centres in the same country or region.[89] In Latin America, paediatric oncology has taken the lead in twinning programmes and use of teleoncology in cancer care;[89,158] several initiatives have improved local cancer care through the use of teleoncology (table 6). A teleoncology collaboration between St Jude Children's Research Hospital (Memphis, TN, USA) and paediatric oncology centres in El Salvador, Honduras, and Guatemala has helped guide treatment decisions and led to improved outcomes in retinblastoma.[160] And an online website created to improve paediatric oncology care through the use of web conferencing in the Amazon region of Brazil allows patients to access care without having to travel to specialised centres in São Paulo.[162]

Role of pharmaceutical industry and clinical research

The quality of clinical trials and the capability of clinical investigation sites and staff have improved in the past decade in Latin America, largely because of collaborations with industry. Trials are a key learning experience because they expose clinicians and trainees to the process of knowledge advancement by allowing them to understand how research protocols are designed and conducted. They also allow exposure to new and emerging technologies. In addition to sponsoring clinical trials, industry has played a pivotal role in supporting or sponsoring mentoring programmes, medical meetings, and research grants. Mentoring programmes are developed in partnership with recognised institutions and have been shown to promote professional growth for young oncologists.[163]

Conclusion

To improve oncology patient care in Latin America, education and training should prioritise prevalent epidemiology and include cancer care from screening to palliation, with local needs emphasised. In view of the oncology workforce shortage, educational initiatives are needed to train general practice physicians and community health-care workers to participate in cancer screening, and to expand their knowledge of cancer diagnostics, treatment, and care. Twinning between centres, mentorship programmes, and promotion of scientific meetings are important learning opportunities that should be encouraged. Several initiatives from organisations such as the American Society of Clinical Oncology and the European Society of Medical Oncology can help trainees from developing countries to improve their knowledge and networking opportunities. Another strategy to stimulate educational growth and optimise available resources is the establishment of cancer centres within institutions focusing on multidisciplinary patient-care approaches. Panel 2 lists strategies that could be implemented to confront the growing cancer demand. Care of patients with cancer and specialised professional education is a growing need worldwide, and Latin America must plan to meet this challenge.

Part 7: Primary and secondary cancer prevention and screening: status, opportunities, and challenges

With the growing cancer incidence in Latin America, the accompanying morbidity, mortality and cost are predominantly attributable to advanced stage cancers. Primary prevention, early detection and diagnosis, and prompt and optimum treatment are leading public health priorities. In this section, we focus on current cancer prevention and detection strategies, particularly for cancers with opportunities for screening and early detection, and we describe challenges in creating optimum cancer prevention and screening programmes across Latin America and the Caribbean.

Primary prevention

The most cost-effective strategy for cancer control is through primary prevention, by reducing the main risk factors and protecting the population's health and wellbeing.

The major modifiable risk factors for cancer are tobacco use, heavy use of alcohol, and obesity. Additionally, some cancers are related to infectious agents, such as hepatitis B virus (HBV), HIV, HPV, and *H pylori*. Environmental and indoor air pollution (ambient particulate matter pollution, household air pollution from solid fuels) in the home, workplace, and community are other preventable causes of cancer. The International Agency for Research on Cancer has identified 415 known or suspected carcinogens;[164] here, we focus on risk factors associated with common cancers.

Tobacco

Tobacco use is the single most important cancer risk factor and accounts for 26% of all cancer deaths and 84% of lung cancer deaths in Latin America, a problem that is getting increasingly worse.[165] In addition to lung cancer, tobacco use has been linked to an increased risk of mouth, larynx, pharynx, oesophagus, liver, pancreas, stomach, kidney, bladder, cervix, and bowel cancer, and possibly breast cancer.[165]

There are around 145 million smokers aged 15 years or older in Latin American. Adult tobacco use varies widely, from 35% in Chile and 30% in Bolivia, to 11% in Panama and 11·7% in El Salvador (table 7). Higher smoking rates are reported in cities (up to 45% in Santiago, Chile, and 39% in Buenos Aires, Argentina) and contribute greatly to second-hand smoke exposure.[166,167] Although tobacco use is highest among men, rates are increasing rapidly among women; in Santiago and Buenos Aires smoking rates are similar for men and women.[167] Chile, Argentina, and Uruguay have the highest rates of female smoking in the region (table 7). Overall, Latin America has the smallest gender gap for smoking globally, with ratio of men-to-women smokers of 3:2.[166] The popularity of smoking among adolescents is particularly concerning. Smoking rates among young people aged 13–15 years are now higher than in adults in many Latin American countries. Prevalence among female adolescents has surpassed their male counterparts in Argentina, Brazil, Chile, Mexico, and Uruguay. Unless these high rates of smoking are curtailed, cancer mortality rates will continue to rise.[166]

Highly effective interventions to reduce tobacco use exist, and anti-tobacco policies offer the greatest opportunity to have an effect on cancer mortality. Potential interventions include tobacco taxation and restrictions on tobacco marketing, labelling and packaging of tobacco products, and smoking restriction in public places; these strategies are detailed in the WHO Framework Convention on Tobacco Control, which has been ratified by 28 countries in Latin America. Currently, 12 countries have adopted legislation banning smoking in all indoor public places and workplaces; another 12 have implemented regulations on the packaging and labelling of tobacco products; and ten countries have introduced bans on tobacco advertising, promotion, and sponsorship. 15 countries now have a tax share of at least 50% of the total price of cigarettes (panel 3).[165,168]

***Panel 2:* Potential strategies to enhance oncology education and training**

- Increase the number of dedicated cancer professionals, including medical, radiation, and surgical oncologists and all allied specialties; this could facilitate interaction and enhance the training of non-specialised professionals that attend to cancer patients.
- Improve training of general physicians and health-care workers to enhance cancer prevention, screening, and early diagnosis.
- Develop strategies to improve geographical distribution of cancer specialists.
- Support cancer education programmes and encourage collaboration between local medical societies, universities, government, and industry to enhance oncology training and care.
- Encourage regional centres in Latin America to collaborate with leading international cancer centres to promote exchange of oncology subspecialty knowledge, skills, and technology.
- Support clinical research and focus research efforts on local needs.
- Provide young professionals with research training, emphasising competency in medical writing and the ability to publish scholarly research findings and reviews.
- Encourage young professionals to participate in international programmes and to develop interactions with leading institutions after initial formal training; build an infrastructure for these professionals to return to Latin America and disseminate their training and skills locally.
- Establish a health infrastructure that supports regional cancer care and allows for multidisciplinary care and a patient-centred approach. Organising cancer care into multidisciplinary centres would allow all the medical professionals involved to exchange knowledge and collectively plan treatment strategies. It would also allow trainees to learn about all aspects of oncology patient care.

Within Latin America, Uruguay is one of the leading countries with respect to tobacco control. In 2006, Uruguay became the first country to adopt a 100% smoke-free policy in public places and workplaces. Additionally, when the price of cigarettes increased to US$4·00 and restrictions were placed on packaging, the adult smoking rate in Uruguay declined from 32% in 2005 to 25% in 2011. Among adolescents, smoking also decreased from 33% in 2005 to 18% in 2011. The prevalence of smoking among physicians fell from 27% to 9%.[169] In Brazil, a national smoking survey done in 2003 showed a decline in the prevalence of smokers and a modest reduction (about two cigarettes per day) in the mean number of cigarettes smoked in recent years.[170] According to the Global Burden of Disease Study in 2010, disease burden attributable to tobacco smoking in Latin America has fallen slightly.[3] These trends could reflect changes in public policy that encourage smoking cessation.

Obesity, diet, and physical activity

The relationship between colorectal, kidney, gallbladder, breast, and endometrial cancers with diet, physical activity, and obesity is well established.[171] Diets rich in fruit and vegetables, high in fibre, limited in red meat and processed meat, and limited in alcohol consumption, along with physical activity and maintenance of healthy weight, have been associated with lower cancer risk.[172]

Obesity is an increasing problem in Latin America and is the leading overall risk factor for disease in South

	National cancer plan that includes primary prevention strategies	Cancer age-standardised mortality rates (per 100 000 population)			Prevalence of adult tobacco use (%)			Tobacco use in young people (age 13–15 years; %)			Prevalence of obesity (BMI ≥30) in adults (%)			HPV 16/18 prevalence (%)		
		Total	Male	Female	Total	Male	Female	Total	Male	Female	Total	Male	Female	Cervical cancer	HSIL	Normal cytology
Argentina	Yes	118·5	149·0	98·3	27·0%	32·0%	22·0%	28·0%	26·1%	29·7%	20·5%	22·0%	19·0%	78·2%	67·2%	6·8%
Brazil	Yes	110·7	129·1	96·7	17·0%	22·0%	13·0%	30·1%	28·7%	30·8%	16·9%	16·7%	18·1%	70·7%	54·0%	4·3%
Chile	Yes	120·0	145·0	103·0	35·0%	38·0%	33·0%	35·1%	29·8%	39·8%	25·1%	19·2%	30·7%	50·0%	55·3%*	2·5%
Colombia	Yes	120·7	130·6	114·4	17·0%	23·8%	11·1%	27·6%	27·0%	27·8%	13·7%	NA	NA	57·6%	32·8%	4·5%
Costa Rica	Yes	103·7	120·4	90·1	16·0%	24·0%	8·0%	14·6%	15·9%	13·1%	26·0%	21·2%	31·0%	62·8%	52·8%	3·3%
Ecuador	†	92·2	96·4	89·5	22·7%	36·3%	8·2%	28·6%	31·2%	26·1%	22·0%	15·7%	28·2%	67·7%*	55·3%*	5·2%*
Mexico	Being developed	73·7	79·5	70·2	16·0%	24·0%	8·0%	28·6%	27·8%	28·5%	NA	26·1%	35·6%	67·5%	46·6%	4·2%
Panama	No	97·5	109·2	88·1	11·0%	17·0%	4·0%	8·4%	10·5%	6·5%	3·0%	2·0%	4·1%	62·0%	44·3%*	4·1%*
Peru	Yes	128·0	134·7	123·8	NA	NA	NA	19·4%	21·5%	15·5%	16·5%	11·1%	21·7%	68·3%	55·3%*	3·8%
Suriname	..	80·6	96·7	69·0	NA	38·4%	9·9%	19·2%	20·7%	16·6%	25·8%	16·5%	34·6%	52·5%	55·3%*	5·2%*
Uruguay	No	144·0	197·7	107·7	27·0%	31·0%	22·0%	23·2%	21·4%	24·5%	19·9%	19·4%	20·5%	67·7%*	55·3%*	5·2%*
Venezuela	†	95·6	106·8	87·3	16·9%	20·9%	13·0%	9·4%	11·0%	7·2%	30·8%	26·6%	34·8%	67·7%*	55·3%†	5·2%†
Bolivia	Yes	NA	NA	NA	30·0%	42·0%	18·0%	20·8%	24·7%	16·6%	18·9%	10·0%	27·1%	38·3%	55·3%*	5·2%*
El Salvador	Yes	97·5	91·8	102·0	11·7%	21·5%	3·4%	14·6%	18·2%	11·0%	23·7%	19·9%	27·1%	62·9%*	44·3%*	4·1%*
Guatemala	Yes	90·2	90·3	91·1	13·0%	22·0%	4·0%	16·6%	19·7%	13·3%	21·3%	16·0%	25·8%	62·9%*	44·3%*	5·5%
Guyana	Being developed	85·1	95·4	81·9	16·0%	27·0%	6·0%	20·9%	25·3%	16·0%	22·4%	14·3%	26·9%	67·7%*	55·3%*	5·2%*
Honduras	No	NA	NA	NA	NA	NA	3·0%	20·4%	22·8%	18·2%	19·3%	15·5%	24·5%	53·9%	43·2%	14·6%
Nicaragua	†	88·1	91·1	87·1	NA	NA	5·3%	25·1%	30·4%	20·5%	29·1%	23·8%	34·2%	57·9%	33·4%	4·1%*
Paraguay	Yes	112·4	119·4	108·1	22·0%	30·0%	14·0%	16·7%	20·8%	12·9%	31·3%	28·5%	25·4%	77·9%	55·3%*	5·5%

BMI=body-mass index. HSIL=high-grade squamous intraepithelial lesion. NA=not available. *Regional estimates, no data available. †No response in survey questionnaire.

Table 7: **Cancer plans, cancer mortality, and cancer risk factors in selected countries**

America.[3] Region-wide estimates show that around 139 million people (23%) are now classified as either overweight or obese.[173] Costa Rica, Paraguay, and Venezuela have the highest rates of adult obesity (BMI≥30; table 7). More women are overweight or obese than men in nearly all Latin American countries, but differences are particularly apparent in the Andean region (Ecuador, Bolivia, Peru), where obesity among women is twice as high as among men. Globally, the percentage of people who are overweight or obese is projected to increase, and by 2030, it is predicted that 50% of men and 60% of women in Latin America will be overweight or obese.[174]

In children, the rates of obesity and being overweight have reached epidemic proportions, with roughly 30% of school-aged children in Colombia, Peru, and Ecuador and more than 40% of children in Mexico being overweight or obese.[173] This has emerged as a result of physical and social environments that support unhealthy lifestyle habits, including physical inactivity, large portion sizes, and increased consumption of processed high-caloric foods and sugary beverages.

Opportunities to reverse the obesity epidemic exist. As summarised by WHO, public policies and advocacy efforts are important to support healthy lifestyle changes and raise awareness.[175] Aruba's Call for Action on Obesity is an example of a regional initiative in which health ministers from Latin America are collaborating to create policies that support healthy eating and exercise.[176] Several countries in the region (Chile, Brazil, Costa Rica, Peru, Ecuador, and Mexico) have created, or are developing, policies to encourage healthy eating by requiring food labelling, regulating food advertising, and requiring healthy dietary choices in schools.[176]

Infectious causes of cancer

A recent analysis estimated that 17% of cancers in Latin America (150 000 cases per year) are attributable to infection.[177] Viral hepatitis infections are the primary cause of liver cancer and account for about 82% of all liver cancers in Latin America.[177] Although the highest rates of endemic chronic HBV are found in the Amazon basin, the highest rates of liver cancer occur in Guatemala, Honduras, Ecuador, Dominican Republic, and Nicaragua.[178] In these regions, the pathogenesis of hepatocellular carcinoma is not well-characterised and it is unclear to what extent viral hepatitis infection or other exposures, such as aflatoxins, are contributing to the high incidence. Some evidence shows that the introduction of the HBV vaccine in 26 Latin American countries from the 1980s to 2000 coincided with decreasing incidences of liver cancer.[179]

HPV is the primary cause of cervical cancer and a contributor to other anogenital (vagina, vulva, penis, and anus) as well as oropharyngeal cancers. Studies

show that HPV vaccination is cost effective for cervical cancer prevention in Latin America.[180] HPV vaccination first became available in 2006, and at least six countries in the region have introduced the vaccine (Argentina, Colombia, Guyana, Mexico, Panama, and Peru).[181] The two current vaccines protect against HPV 16 and 18, the two dominant oncogenic types that account for 38·3% (Bolivia) to 78·2% (Argentina) of cervical cancer cases in Latin America (table 7).[182] Wide-scale vaccination is limited by the price of the vaccine and the logistical challenges to vaccinating target populations. To circumvent vaccination at local health centres, HPV vaccination in schools is a feasible option, as a programme in Peru has shown.[183]

H pylori is associated with gastric cancer, and eradication of *H pylori* infection reduces the risk of gastric cancer.[120] Prevalence rates of *H pylori* range from 79·4–84·7% in Latin America.[120] Population-wide eradication programmes, consisting of practical and inexpensive proton-pump inhibitor and antibiotic regimens, offer the most direct approach to reducing consequences of *H pylori* infection.[172] Such programmes, particularly among high-risk populations, could be cost effective in Latin America, where gastric cancer is very common (figure 1A).[1] So far, no such programme has been implemented in the region.[59]

Human T-cell lymphotropic virus type 1 (HTLV-1) is regarded as the cause of adult T-cell leukaemia–lymphoma. The virus is endemic and highly prevalent in some regions of Latin America (Andes highlands, northwest and north regions of Argentina), emphasising a need for systematic screening for HTLV in blood banks, at least in areas with high virus prevalence.[184,185]

Environmental causes of cancer

Exposure to environmental carcinogens in homes, occupational settings, and urban and rural settings is common in many regions of Latin America. These potential causes of cancer merit improved documentation and research, with the aim of eradication and cancer prevention.

An estimated 3 billion people worldwide cook and heat their homes with open fires, including a substantial proportion of people in Latin America.[186] Many of these people are poor, living in rural or remote areas, and regularly burn biomass substances such as wood, animal dung, and crop waste for heating and cooking. In poorly ventilated dwellings, biomass air pollution can result in indoor smoke levels that are 100 times higher than acceptable.[186] Data from in-vitro and in-vivo models provide evidence that woodsmoke and wood byproducts are carcinogenic and promote tumour growth and progression.[187,188] There might also be an association between wood-smoke exposure and EGFR-mutated non-small-cell lung cancer (NSCLC). A study from Mexico showed that wood-smoke exposure was associated with lung adenocarcinoma in non-smoking women,[189] and researchers suggest that wood-smoke exposure might explain the high rates of EGFR-mutated lung cancer in some regions of Latin America.[190,191] This association requires further investigation, since it might explain the high rates of EGFR-mutated lung cancer in Latin America, particularly among women, who are more often than men exposed to cookstove smoke. Studies from Honduras and Colombia provide evidence that wood-smoke exposure increases the risk of cervical neoplasia and invasive cervical cancer.[101,103] The organisation Sembrando has already worked with more than 92 000 families in the Andes of Peru to provide clean cookstoves in an effort to reduce home indoor air pollution.[110]

Exposure to other environmental carcinogens (eg, pesticides and industrial waste), and their role in cancer incidences in Latin America, warrants in-depth investigation. Elevated arsenic concentrations have been detected in drinking water in some areas in Northern Chile and Cordoba Province in Argentina, and have been linked to bladder and lung cancer in non-smokers.[114,115] Lung cancer has been described among coal miners in Brazil,[192] and higher malignancy rates are reported among populations living near mines in Ecuador.[117] Pesticide exposure also increases cancer risk and has been linked to brain and oesophageal cancer in Brazil.[193] In Bolivian farmers, genetic abnormalities were attributed to pesticide exposure.[194] A study from Brazil found correlations between national pesticide sales and prostate, soft-tissue, lip, oesophageal, and pancreatic cancer, and leukaemia mortality among men.[195] Finally, the role of nitrate or nitrite exposure and gastric cancer incidence warrants investigation, considering the high rates of gastric malignancy in Latin America and evidence from Chile that suggests causation.[196] Research collaborations between WHO centres in Italy and Mexico are beginning to investigate health consequences due to

***Panel 3:* Anti-tobacco measures in Latin America**

Countries who have ratified the WHO Framework Convention on Tobacco Control:
Antigua and Barbuda, Bahamas, Barbados, Belize, Boliva, Brazil, Chile, Colombia, Costa Rica, Dominica, Ecuador, Grenada, Guatemala, Guyana, Honduras, Jamaica, Mexico, Nicaragua, Panama, Paraguay, Peru, St Kitts and Nevis, St Lucia, St Vincent and the Grenadines, Suriname, Trinidad and Tobago, Uruguay, Venezuela

Countries with smoking bans:
Argentina, Barbados, Colombia, Ecuador, El Salvador, Guatemala, Honduras, Panama, Peru, Trinidad and Tobago, Uruguay, Venezuela

Countries with regulations on packaging and labelling of tobacco products:
Argentina, Bolivia, Brazil, Colombia, Chile, Cuba, Ecuador, Honduras, Mexico, Panama, Venezuela, Peru

Countries with bans on tobacco advertising, promotion, and sponsorship:
Argentina, Bolivia, Brazil, Chile, Colombia, Ecuador, El Salvador, Honduras, Panama, Uruguay

Countries with a tax share of at least 50% of the total price of cigarettes:
Argentina, Brazil, Chile, Colombia, Costa Rica, Dominican Republic, El Salvador, Guatemala, Ecuador, Jamaica, Mexico, Peru, Suriname, Uruguay, Venezuela

environmental exposures, planning to focus on populations in Mexico that live in mining zones, live near garbage dumps, or work in brick factories.[197] Appropriate control and monitoring of nuclear and radioactive waste is also important to avoid nuclear incidents. In September, 1987, a radiotherapy source was stolen for scrap metal use from an abandoned hospital in Goiânia, Brazil, resulting in accidental contamination of the region. Four people died from acute radiation toxicity, around 130 000 people overwhelmed hospital emergency rooms, and more than 250 people had measurable exposure to radioactive caesium.

Secondary prevention: screening and early detection

Secondary prevention, or the interruption of the disease process at an early, more treatable stage, is a crucial strategy for ameliorating the burden of cancer. Secondary prevention can be achieved by screening asymptomatic people where there is a reasonable time lag between disease onset and clinical progression, and an affordable, accurate, and tolerable screening test.[198] However, some screening methods that are proven to be valuable in high-income countries simply cannot be applied in settings of limited resources.

Breast cancer

Breast cancer is the most common cause of cancer and the leading cause of cancer mortality among women in Latin America. Over the past two decades, breast-cancer mortality in developed countries has fallen, mainly due to mammography screening and early treatment of breast cancer;[199] screening mammography decreases breast-cancer mortality by 20–30%,[200] with the highest benefit in older women.[200,201] By contrast, in Latin America, breast-cancer mortality has increased over the past two decades, and breast-cancer survival is, on average, 20% lower than in the USA and western Europe.[144] High rates of breast-cancer mortality can be attributed to advanced stage at diagnosis; only 5–10% of new diagnoses are made at a stage I disease. The distribution of early and advanced-stage disease varies regionally within each country,[10,202] and differs between public and private hospitals, which might be due to socioeconomic factors.[203,204] The Amazone study[204] from Brazil showed that women who receive treatment at public institutions have more advanced disease at diagnosis. The researchers proposed that high screening rates in the private sector compared with low rates in the public sector could partly explain the stage differences.

Several steps have been taken in Latin America to increase early detection of breast cancer, including guideline development, training of providers, community education, and mammography quality-assurance programmes. Many countries in the region have national recommendations for breast-cancer screening (panel 4).[205] Participation rates for breast-cancer screening in many Latin American countries are low, with only 20% of the eligible population receiving screening (ranging from 5–75%).[206–208] Since data for women that undergo screening through the private system are not available, these numbers might underestimate the total number of women screened. Nonetheless, mammography screening rates are much lower than the 70% coverage recommended by WHO to reduce breast-cancer mortality.[198] With such low numbers of women undergoing screening mammography in Latin America, the ultimate goal of screening, to reduce overall breast-cancer mortality, cannot be achieved with current mammography programmes. Recognising this, a pilot project has been initiated in Colombia to evaluate opportunistic breast-cancer screening. The study involves healthy, asymptomatic women aged 50–69 years, who are attending health services for any medical reason and are allocated to a formal breast-screening programme involving mammography plus clinical breast examination, versus an aged-matched control group who are not offered proactive screening.[209] The objectives are to estimate the effect of the National Cancer Institute of Canada guidelines on breast-cancer downstaging, the effect of opportunistic screening on exposure to mammography and breast examination (ie, number screened), and the costs for implementing opportunistic programmes in the Colombian health system.

Health-system structures have been identified as major barriers to successful breast-cancer screening. In some regions of Latin America, mammography equipment is scarce, with up to 20% of equipment needing repair.[210] Often, there is unequal distribution of equipment within a country, and many women in remote areas do not have access to screening facilities.[211,212] Thus, in many regions of Latin America where women are diagnosed with late-stage breast cancer and resources are limited, mammography screening might not be feasible. By contrast, clinical downstaging could be achieved by screening with clinical breast examinations and education, coupled with enhanced availability of primary care. Several initiatives are underway to test community-based models for extending such screening services to rural women.[209,213] A pilot project is being implemented in La Libertad, in northern Peru, with community workers teaching women about physical signs of breast cancer and trained midwives doing clinical breast examinations. Women with suspicious masses are referred to local hospitals for evaluation and diagnostic fine-needle aspiration biopsies. Women with confirmed cancers are referred to a new regional cancer centre established in northern Peru (IREN-Norte) for further cancer treatment.[213]

In summary, it is crucial to recognise that simply extrapolating the gains from mammographic screening in developed nations to Latin American settings is not appropriate. The benefits and limitations of screening mammography programmes versus clinical downstaging efforts need to be considered. For regions with limited health resources, the Breast Health Global Initiative

Panel 4: **National recommendations for breast-cancer screening in selected countries**[205]

Argentina
- Baseline mammogram from age 35 years, or from age 30 years for women with positive family history of breast cancer (mother or sister)
- Yearly screening mammogram for women aged 50 years and older
- Screening mammogram every 2 years for women aged 40–49 years (depending on risk)

Brazil
- Mammography for high-risk women starting at age 35 years
- Clinical breast examination for women aged 40–69 years
- Mammography every 2 years for women aged 50–69 years

Bolivia
- Periodic clinical breast examination by attending physician
- Mammography screening for women aged 40 years or older, once or twice a year depending on risk

Chile
- Mammography screening for all women, starting at age 50 years

Colombia
- Mammography every 2 years
- Clinical breast examination each year in asymptomatic women aged 50–69 years
- Opportunistic screening offered to all women who attend health services for any reason

Cuba
- Clinical breast examination for women older than 30 years
- Mammography in women aged 50–64 years, every 3 years

Mexico
- Clinical breast examination from age 25 years
- Mammography every 2 years for women aged 40–69 years, and every year for women with a family history of breast cancer

Panama
- Clinical breast examination and breast self-examination
- Mammography every 1–2 years for women aged 40–50 years
- Mammography every year for women aged 50 years and older

Peru
- Clinical breast examination for women older than 20 years
- Identify women at risk and refer them for breast-cancer screening
- Mammography screening is not covered by the public health system

Uruguay
- Clinical breast examination every 3 years for women aged 20–39 years, and every year after age 40 years
- Mammography for women aged 40 years and older, every 1–2 years
- High-risk women should talk with their doctor about mammography screening, starting time, and frequency

Adapted from reference 205 with permission of L M Gonzalez-Robledo.

(BHGI) has developed evidence-based, economically feasible, and culturally appropriate guidelines to improve breast-cancer outcomes. In such settings, BHGI recommends clinical breast examination with or without mammography, coupled with active awareness programmes.[214]

Cervical cancer

Cervical cancer is the leading cause of cancer in ten of 25 Latin American countries, and is a major cause of cancer mortality among women, with 68 220 new cases and 31 712 deaths annually.[1] Cervical-cancer screening can lead to a substantial reduction in incidence and mortality from cervical cancer. In developed countries, cytology screening reduces cervical-cancer mortality by about 50%.[215] Thus, organised screening with appropriate follow-up has been proposed as the main strategy for disease control in Latin America.[216]

Most countries in the region began screening programmes between 1985 and 2005. According to a recent survey, at least nine countries report having an organised screening programme.[217] Despite the introduction of screening, mortality rates from cervical cancer have not decreased in most Latin American countries. Mortality rates have declined in Mexico, Chile, Costa Rica, Colombia, and Puerto Rico, but this change is not necessarily related to nationwide screening programmes.[181] The reduction in mortality might instead be due to improved coverage and accuracy in the certification of deaths.[218] Some reports suggest that quality of screening tests and access to diagnosis and treatment for positive screened women might be factors in the lack of effect seen with cervical screening in Latin America.[181]

High screening coverage, especially among women in the at-risk age group, is essential to reduce cervical cancer mortality. Cervical-cancer-screening coverage varies in Latin America, and reports suggest that roughly 50% of women have received Pap smear screening in the past 3 years.[217] In some countries, including Puerto Rico and Colombia, screening rates are as high as 72%. However, many countries have low screening rates, such as Bolivia with 12% and Nicaragua with only 10% coverage.[217] In Mexico and Paraguay, close to 20% of women have never had a Pap smear, and 50% of women in Guatemala have not had a Pap smear.[181]

Barriers to participation in cervical-cancer screening vary in different countries. In Mexico, Bolivia, Ecuador, Venezuela, Peru, and El Salvador, the main factors

affecting participation are prevailing social and cultural norms that influence women's notions of health and illness, accessibility to health-care centres, and availability of quality services.[61]

Where screening is done, the quality of cytology analysis might be suboptimum for diagnostic purposes. A few studies suggest that Pap smear sensitivity could be as low as 20–25%.[99,219,220] Additionally, when women have abnormal results after Pap screening, there are barriers to receiving appropriate and timely care. An assessment in Peru's Amazonia showed that only 23% of women with positive Pap smears received appropriate treatment.[81] Most programmes overemphasise outreach and coverage of the screening test, without considering the capacity of the health system to deal with diagnoses and treatment.[181] These factors, in addition to low screening rates, probably explain why cytology-based screening programmes have not lowered cervical-cancer mortality in Latin America to the same extent as in developed countries.[181]

To improve the effectiveness of screening in low-resource settings, new alternatives to cytology-based screening have been introduced, including visual inspection techniques and HPV-DNA testing.[181,221] Both screening strategies were shown to be cost-effective alternatives to conventional, three-visit cytology-based screening programmes in resource-poor settings.[181,221] An HPV-DNA test requires less supervision than cytology screening, since it is not observer dependent, lessens the frequency of screening intervals, and allows self-collection of vaginal samples. In India, this test was associated with a significant reduction in the numbers of advanced cervical cancers and deaths from cervical cancer.[222] Currently, Mexico, Argentina, and Colombia have incorporated HPV-DNA testing into their national screening programmes.[217,219] Rapid HPV testing (careHPV) has higher sensitivity than conventional cytology, and can be implemented in low-resource laboratories because it does not require highly qualified personnel.[219] A sample of cells is collected from the cervix or vagina and sent to the laboratory for processing; the result is available in 2–4 h. Because this test has been proven to be simple, rapid, accurate, and affordable, it is a suitable screening method for low-resource settings.[223]

Another approach that has been used with success in resource-limited settings is a single-visit, see-and-treat method based on visual inspection with acetic acid (VIA) and same-visit cryotherapy of eligible lesions. In regions with low access to health care, VIA is an opportunity to overcome barriers for diagnosis and treatment of preneoplastic lesions.[220,224] Visual inspection with acetic acid has a higher sensitivity than conventional Pap smear screening, is easy to implement, less expensive, does not require laboratory evaluation or highly qualified medical professionals to perform the procedure, and allows immediate treatment of precancerous cells. At least eight countries in the region (Bolivia, Colombia, El Salvador, Guatemala, Guyana, Nicaragua, Peru, and Suriname) offer VIA screening as part of the public health system.[220,224]

Colorectal cancer

Colorectal cancer is the fourth most common cancer in men and third most common cancer in women in Latin America.[1] A screening programme with repeated annual or biennial guaiac-based faecal occult blood tests (FOBTs) and endoscopic follow-up of positive test results reduces colorectal cancer mortality by 16%.[225] FOBTs, flexible sigmoidoscopy (with or without FOBT), colonoscopy, and double-contrast barium enema are the standard screening methods recommended by the US Preventive Services Task Force. However, because colorectal-cancer-screening tests can cause harm, are of limited accessibility, are not uniformly accessible to patients, and are all similar in terms of cost-effectiveness, the choice of screening method can be individualised to patients or practice settings.[226]

Although there are national guidelines for colorectal-cancer screening in most Latin American countries, screening programmes are infrequent.[227–229] Studies from Chile and Uruguay looked at the feasibility of colorectal-cancer screening using immunochemical FOBTs in an average-risk population;[230,231] both projects achieved high compliance rates (77–90%) and were able to detect early stage cancers and high-risk adenomas (11–30%). Since these findings were published, a national colorectal-cancer-screening programme has been started in Chile and aims to screen 30 000 people annually over the next 5 years.[230] In Uruguay, a similar study is underway to promote screening in normal and high-risk populations.[232]

Challenges for primary and secondary prevention

There are many reasons why cancer prevention and screening efforts are not more widely available in Latin America, but the main reason is cost. Other socioeconomic factors include individual patient-related financial and cultural barriers, lack of support for appropriate patient counselling, suboptimum health-care infrastructure, poor laboratory quality, and delays in diagnostic testing and interventions once cancer is detected.[233,234]

Supporting patients to implement lifestyle changes to reduce their cancer risk is challenging, even in optimum health systems. Poor and rural populations are particularly disadvantaged in Latin America, because they have less information and fewer resources available, fewer choices about diet, and strong cultural traditions preventing them from adopting new behaviours. In many countries in Latin America, the tobacco industry has substantial political influence, making public health initiatives that involve anti-tobacco policies a challenge.[166,235]

Cancer screening in Latin America presents logistic challenges. With more than 100 million people who lack access to health care for geographic reasons, and 320 million who do not have health-care coverage, it is difficult to establish optimum cancer-screening

programmes.[236] Limited numbers of health personnel and funding in many Latin American health systems means that preventive and screening services are widely unavailable. The cost of HPV vaccine, HPV testing, mammography equipment, and diagnostic tests compete with many other resource priorities. Training sufficient numbers of community health workers to educate and screen populations is a challenge in many settings. Countries with constrained health-care budgets often allocate most of their resources to therapeutic care, despite studies that show that prevention is more cost effective.[237] Health-financing schemes, including health insurance, do not always provide full support for preventive services, further disadvantaging poor populations. Finally, lack of adequate epidemiological data tracking cancer trends in Latin America limits the ability to create optimum cancer prevention and screening programmes. Monitoring trends in cancer burden is essential to improve cancer prevention and screening strategies.

Part 8: Molecular testing and personalised medicine

Human cancer subtypes are traditionally classified according to specific clinical and pathological parameters that include anatomical site of origin, microscopic histomorphology, tumour size, tumour grade, and regional lymph-node involvement. This long-established classification scheme is now being supported by molecular and genetic information that helps to subtype different cancers and predict their behaviour. In clinical practice, testing for specific tumour characteristics can provide prognostic information and direct treatment options. Use of the right therapy, for the right patient, at the right time has implications on risk–benefit ratios of therapies and effects treatment costs. Analysis of tumours at the molecular and genetic level has advanced the field of oncology and ushered in a new era of personalised cancer care. In this section, we discuss the current status of cancer diagnostics in Latin America and how new technologies and targeted therapies are being introduced in the clinic.

Centralised laboratory testing and quality control

Laboratory systems that support cancer diagnostics vary in each country and are not well characterised in the oncology literature. A few studies have compared expert assessment, or centralised laboratory testing, to non-expert or regional evaluations (table 8). In these studies, cancer diagnostic testing, including Pap cytology, cervical, gastric, and prostate biopsy assessments, and immunohistochemistry evaluation for breast cancer, all had low concordance rates. Reasons for differences in assessment between local and reference laboratories might be related to the low-volume load of specific cancer testing at regional health centres and hospitals, inexperience with specific cancer diagnostic criteria, or technical issues related to testing in local laboratories. For example, in a study from Uruguay,[245] investigators reported lower than expected rates of HER2 positivity in women with early breast cancer. Although the reasons for this finding were not fully understood, aspects of the immunohistochemistry testing in the study, such as technician errors in the interpretation of results, variation of antibodies used by test manufacturers, and protein degradation, might have resulted in more false-negative results.[245]

HER2 testing is technically difficult and has been historically problematic.[246] Lack of accurate testing can lead to misdiagnoses or ineffective or inappropriate treatment, which can affect survival. A study from Colombia showed that poor assessment of Pap cytology provided an explanation for why screening efforts in the country had not affected cervical-cancer mortality rates.[241] Several Latin American countries (Argentina, Brazil, Cuba, Mexico, Guatemala, El Salvador, Honduras, Nicaragua, Colombia, Venezuela, Ecuador, Paraguay, Peru, and Uruguay) participate in the International External Quality Assessment Scheme (IEQUAS), which helps to improve and standardise laboratory diagnosis and give measures of laboratory competence.[2,247]

Effect of diagnostic delays

Diagnostic tests for cancer must be timely. Studies from Brazil, Mexico, and Peru suggest that there are delays in pathology assessments that might affect diagnosis and initiation of treatment.[81,248,249] In studies in Brazil and Mexico, the average delay between presentation to a doctor and diagnosis of breast cancer was 6–7 months.[59,248,249] The median time from biopsy to histological diagnosis ranged from 0–68 days in one Brazilian study, and delays up to 299 days were documented for immunohistochemistry results.[250] In a study from Peru,[81] women who had abnormal cytology after a Pap smear screening and who underwent cervical biopsy often waited 4–5 months before receiving definitive diagnoses. When a diagnosis of cancer is delayed, disease stage will be affected and an unfavourable outcome is more likely. Delays in diagnosis of longer than 12 weeks are considered suboptimum for breast cancer, and cervical-cancer survival is affected by delays longer than 5 weeks.[86,251] These delays, causing unfavourable stage migration before the onset of therapy, are considered one of the reasons for higher mortality rates in Latin American countries than in higher resource countries.

Improving cancer diagnostics in Latin America

To improve cancer diagnostics, factors that affect laboratory quality need to be addressed, including availability of laboratory supplies, essential equipment, skilled personnel, resources for appropriate training, and quality-control assessments of the existing systems.[252] At a national level, governments and public health systems should support centralised laboratory networks and establish testing standards.[253] Centralised laboratory networks can improve access to high-level cancer diagnostics and provide regulatory oversight to coordinate operational

	Location	Number of samples	Test	Comparators	Concordance
Wludarski et al (2011)[238]	Brazil	500	HER2 by immunohistochemistry of invasive breast carcinomas	Local and reference laboratories	34·2%
Wludarski et al (2011)[239]	Brazil	500	Hormone receptor status by immunohistochemistry from invasive breast-cancer cases	Local and reference laboratories	κ=0·744 for oestrogen-receptor testing; κ=0·688 for progesterone-receptor testing; false-positive rates were 15·5% for oestrogen-receptor and 16·0% for progesterone-receptor tests in local laboratories
Kasamatsu et al (2010)[240]	Colombia, Mexico, and Paraguay	1056	Gastric biopsies	Pathologists without experience compared with pathologists with experience in gastrointestinal pathology, and experts working in an international reference centre	κ=0·04–0·12 for atrophic gastritis; κ=0·05–0·11 for dysplasia; κ=0·52–0·58 for intestinal metaplasia
Cendales et al (2010)[241]	Colombia	4863	Pap cytology	Original reports from regional cytologists or pathologists compared with a second report made by expert pathologists from the National Cancer Institute of Colombia	κ=0·03
Salles et al (2008)[242]	Brazil	15	Slides representing atypical ductal hyperplasia, ductal carcinoma in situ, and ductal carcinoma in situ with microinvasion	Five pathologists in the community compared with an international specialist in breast pathology	κ=0·15–0·40
Arista-Nasr et al (1996)[243]	Mexico	25	Prostate carcinoma biopsy	Ten skilled pathologists in Mexico City compared with two expert uropathologists from MD Anderson (Houston, TX, USA)	κ=0·32
Lazcano-Ponce et al (1997)[244]	Mexico	40	Pap cytology and cervical biopsy	30 pathologists compared with a standard cytopathologist certified by the Pathological Anatomy Council of Mexico	κ=0·04 for moderate dysplasia on Pap; κ=0·23 for moderate dysplasia on cervical biopsy; κ=0·29 for invasive cancer on Pap; κ=0·64 for invasive cancer on cervical biopsy

Concordance is presented as either a percentage or as Cohen's kappa coefficient. Kappa (κ) is a statistical measure of the agreement between items, where κ=1 if there is complete agreement between the two comparators, or κ=0 if there is no agreement and reflects an association that would occur by chance alone.

Table 8: **Studies of quality of cancer diagnostic testing**

functions and quality control. Diagnostic tests that are not frequently performed, including genetic testing or tumour molecular analyses, should be done exclusively at centralised laboratories. Efforts by the Ministry of Health and the National Cancer Institute in Brazil exemplify this approach. By 2014, the Brazilian Ministry of Health aims to establish ten laboratories throughout the country for molecular testing for lung cancer.[254] Similar initiatives for lung and other cancers are required elsewhere.

At the regional level, initiatives to improve the quality of tissue samples, technical handling of tissue specimens, slide preparation, and special staining need to be supported. Tumour samples should be appropriately preserved (preferably as formalin-fixed, paraffin-embedded tissues) and archived for future diagnostic testing that can affect a patient's subsequent care. In parallel, the establishment of biobanks at national or regional levels is warranted. Initiatives such as the Brazilian National Tumor Bank, which has 38 000 samples stored, or Red de Bancos de Tumores de la América Latina y Caribe (ReBT-LAC), should be encouraged.[255] Appropriately consented tumour archives are also very valuable as a repository for research studies. As advocated for HIV/AIDS care in Africa, another approach to improve quality would be to establish a laboratory accreditation system for cancer in Latin America.[256] Two programmes in Brazil have shown the potential for education to improve accuracy of cancer diagnosis. In Belo Horizonte, concordance between pathologists interpreting premalignant breast lesions increased after a tutorial reviewed the standardised diagnostic criteria and displayed representative images.[242] More recently, an effort in Pernambuco raised the accuracy of diagnosing childhood cancer after the introduction of a focused training programme and the establishment of telepathology in the region.[257]

Genetic predisposition: *BRCA* mutations

Knowledge of cancer genetics in the Latin America population is limited, and most studies from the region have focused on prevalence of *BRCA* mutations. *BRCA* gene mutation, by contrast with many other genetically inheritable mutations for cancer, directly affects clinical management choices. Women found to have a *BRCA* mutation can be educated on modifiable lifestyle factors to reduce their cancer risk and offered more aggressive surveillance, prophylactic surgery, or chemoprevention. From the available studies, *BRCA* mutation rates in Latin America seem to be similar to rates in the USA or Europe, but might be higher in some countries (table 9). The prevalence of *BRCA* mutations from unselected women in the Bahamas is the highest rate detected for any country in the region.[258] The high prevalence of *BRCA* mutation in Latin America might be explained by a historic Jewish migration from modern Spain and Portugal to Latin America during the Age of Discovery in the 15–17th centuries.[268]

In Latin America, genetic testing for *BRCA* or other cancer-predisposing mutations is not widely available,

and is cost prohibitive where it is offered. In low-income settings, genetic testing is often too expensive to be offered on a broad scale, but some form of alternative testing should be considered. Testing for high-frequency mutations as opposed to whole-gene sequencing, or testing a specific population that might benefit from the result could offset the high cost. Testing for *BRCA* mutations in a region such as the Bahamas, where the prevalence is high, could allow for early intervention and save lives, and might be cost saving in the long term.

Expanding cancer genetic research to Latin America

There is growing interest in applying admixture mapping to identify genes that influence complex traits, such as cancer, in populations tracing their ancestry to genetically differentiated populations. This approach has been powerful and more economic than high-density whole-genome association studies, and has led to identifying fixed genetic variants in parental populations.[269–271] This approach has potential value for cancer research, and the Latin American population is an ideal cohort for such studies. Latin American populations are composed of a mix of indigenous Americans, Europeans, and Africans; however, large variation in the number of native ancestries that exist in different Latin American populations implies that the power of admixture mapping varies substantially depending on the geographic region targeted.[272,273] A 2008 analysis[273] reported that the genetic load from Native American ancestors ranged from 70% in north western Argentina to 20% in Brazil, Costa Rica, and Colombia. This study also showed that African ancestors' load was low (less than 5%) in most populations examined, except in the Colombian Caribbean region and in eastern Brazil. This genetic heterogeneity among the continent's populations could modify the pattern of many diseases, particularly cancer, and the response to pharmacological interventions.[273]

Cancer genetic and molecular testing

Few efforts have been made to assess genomic differences with regard to neoplasia in Latin America, and our knowledge of cancer in the mestizo population is largely based on information obtained from the Hispanic population in the USA.[274] However, a few studies aimed at characterising tumour genomics in Latin America have begun. The most thorough study so far characterised *EGFR* and *KRAS* mutation frequency for NSCLC, including 1150 samples from Argentina, Colombia, Peru, and Mexico.[275] Overall, mutation frequency was 33·2% for *EGFR* and 16·6% for *KRAS*. Distribution was homogeneous for Argentina (19·3%), Colombia (24·8%), and Mexico (31·2%); and extremely high in Peru (67%), possibly explained by the influence of Asian migration into the region or by differing rates of wood-smoke exposure.[275,276] The higher percentage of *EGFR*-positive adenocarcinoma lung cancers in Latin America compared with developed countries is unexplained, but differing genetic susceptibility of the population, HPV infection rates, nutritional state, and exposure to wood-smoke have all been implicated.[276,277] Subset analyses of Latin American patients harbouring *EGFR* mutations show a response to targeted treatment; these efforts are informative and show that *EGFR* mutations are not isolated to population cohorts where they were initially described—ie, non-smoking women in Asia.[278] Overturning cancer perceptions such as these are important to improving care. Knowing that *EGFR* mutations are common in lung cancer in Peru will bring attention to this group of patients who might not have access to EGFR-inhibitor therapies. These findings should also promote further investigation into the question of whether *EGFR*-mutated lung cancer is associated with wood-smoke exposure.[136,275,276] If this association is established, it would guide public-health strategies in countries such as Peru.

	BRCA mutation frequency (%) in a cohort unselected for family history	*BRCA* mutation frequency (%) in a cohort selected for family history
Bahamas	23·0% for women with breast cancer[258]	41·0% for women with breast cancer[258]
Brazil	No data available	13·0% for women with breast cancer[259]
Chile	No data available	15·6% for women with breast cancer[260]
Colombia	15·6% for women with ovarian cancer[261]	..
Costa Rica	No data available	4·5% for women with breast cancer[262]
Mexico	No data available	10·2% for women with breast or ovarian cancer (or both)[263]
Hispanic population in the USA	No data available	30·9% for women with breast or ovarian cancer[264]
White population in the USA	5–10·0% for women with breast cancer[265] 10–15·0% for women with ovarian cancer[265,266]	No data available
Age 45 years or younger, in Spain	6·0% for women with breast cancer[267]	No data available

With the exception of two publications (references 259, 263), data are from studies with a sample size of at least 50 patients. Two studies reported novel *BRCA* mutations.[260,263]

Table 9: **Frequency of *BRCA* mutations in cohorts of women with and without family history of breast or ovarian cancer (or both)**

Personalised oncology in Latin America

Characterising the prevalence of predisposing cancer genes, mutations, and molecular markers in different tumours in Latin America is a first step to providing a personalised approach. Regional efforts to achieve such characterisations have begun (tables 9 and 10), and these efforts will ultimately reduce cancer morbidity, mortality, and cost in Latin America. To support these initiatives, pathologists who perform, interpret, and regulate complex molecular and genomic data will need highly specialised training and education in genomic medicine. The diverse genetic ancestry of the Latin American population offers opportunities and challenges. Studies by the Brazilian Pharmacogenetic Network to investigate the genetic heterogeneity of the population are underway.[292] Oncologists, physicians, and all care providers involved in cancer screening, diagnosis, and treatment

need up-to-date training on how to integrate genomic and molecular information into clinical practice. For example, *BRCA* testing in high-risk patients should only be done after comprehensive genetic counselling, as is practice in countries with established testing.

Part 9: Clinical perspectives

Radiation oncology

The IAEA highlights that existing radiation therapy services in Latin America are well below the region's estimated needs, and shows where there are gaps in resources (table 11).[37] Haiti, Belize, and Guyana have no radiation therapy services. In 2007, the IAEA and regional experts from Latin America identified the following problems that need addressing: a deficit of trained personnel; lack of clinical protocols and validated procedural manuals; management of infrastructure not implemented in accordance with international standards; lack or non-adoption of quality management systems; and lack of updated regional databases on infrastructure and personnel in radiation therapy.[293]

Many Latin American governments are aware of the importance of radiotherapy and are investing accordingly. Over the past decade, the region has expanded services and acquired better equipment. However, there remains a severe shortage of radiation specialists, particularly radiation physicists and radiation therapists. The regional professional society for radiation oncology, the Latin American Association for Radiation Oncology (Asociación Latino Americana de Terapia Radiante Oncológica; ALATRO), recently established a regional school with the goal of improving radiation therapy training. This educational effort is supported by national and international organisations, such as the Spanish Society of Radiation Oncology (Sociedad Española de Oncología Radioterápica; SEOR), the European Society for Radiotherapy and Oncology (ESTRO), and the IAEA.

In summary, although Latin American is progressing toward improvement and modernisation of radiotherapy services, the process is slow and varies by region, with some countries needing to urgently prioritise and improve their radiation therapy services. We believe it is important for health ministries in each country to ensure that radiation oncology services are accessible to all of their populations.

Haematological oncology

Diagnosis of haematological malignancies relies heavily on cytology and molecular testing; therefore accurate and reliable pathology is essential. As with solid tumour cancers, outcomes for haematological malignancies in Latin America are affected by socioeconomic, geographic, and cultural disparities in the region. A key challenge is that there are few haematologists in the region; Latin America has 0·9 haematologists per 100 000 inhabitants, compared with 2·2 per 100 000 in the USA.[294] Training programmes need to be improved and haematologists need to be evenly distributed in the region to meet the population's needs. Some countries also lack haematopathologists and the equipment necessary for flow cytometry, cytogenetic and molecular biology testing, and to appropriately diagnose and manage patients with haematological malignancies. A study of chronic myeloid

	EGFR mutation frequency (%) in NSCLC	*KRAS* mutation frequency (%) in NSCLC	*ALK* mutation frequency (%) in NSCLC	*BRAF* mutation frequency (%) in melanoma
Argentina	19·1%[275]	NA	NA	NA
Brazil	25·3%[279]	20·3%[279]	2·5–3·2%[280]	NA
Bahamas	NA	NA	NA	NA
Chile	22·0%[281]	NA	NA	56–58·0%[282,283]
Costa Rica	NA	NA	NA	NA
Colombia	24·8%[275]	17·1%[275]	3·8%[284]	NA
Mexico	31·2%[275]	16·0%[275]	NA	NA
Peru	40–67·0%[275, 285]	16·8%[275]	NA	NA
Hispanic population in the USA	NA	NA	NA	NA
USA	15·0%[286]	20–25·0%[286]	4·0%[286]	NA
Europe	10·0%[287]	16·6%[288]	NA	43–59·0%[289,290]
East Asia	30–60·0%[291]	NA	NA	NA

NSCLC=non-small-cell lung cancer. NA=no data available.

Table 10: **Frequency of *EGFR*, *KRAS*, and *ALK* mutations in NSCLC, and *BRAF* mutations in melanoma**

	Countries	Radiotherapy centres	Linear accelerators	Cobalt-60 units	CT units	Conventional simulators	TPS	LDR manual	LDR remote	HDR Ir-192	HDR Co-60	Radiation oncologists	Medical physicists	Radiotherapy technologists
Caribbean	9	33	25	22	15	13	27	6	2	8	..	79	59	155
Mexico and Central America	7	104	83	74	29	43	106	7	5	23	2	258	74	305
Temperate South America	3	116	126	53	44	35	89	28	1	9	..	276	124	463
Tropical South America	9	348	386	151	102	62	237	40	11	96	1	733	398	1290
Total	28	601	620	300	190	153	459	81	19	136	3	1346	655	2213

TPS=treatment-planning systems. LDR manual=low-dose-rate brachytherapy systems operated manually. LDR remote=low-dose-rate brachytherapy systems operated remotely. HDR Ir-192=high-dose-rate brachytherapy systems using an iridium-192 source. HDR Co-60=high-dose-rate brachytherapy systems using a cobalt-60 source.

Table 11: **Radiotherapy resources in Latin America, as of December, 2012[37]**

leukaemia by the Latin American Leukemia Net showed that although imatinib is available for use as initial therapy to 92% of physicians, only 72% perform routine cytogenetic analysis for monitoring patients on therapy, and only 59% routinely use quantitative PCR monitoring.[295] Necessary blood products to support patients with haematological malignancies are available in most countries, but specialised products, such as irradiated blood products, are limited and require patients to be referred to transplant centres. Although stem-cell transplantation is available in the region, many patients with haematological malignancies face barriers, either access-related or cost-related, that do not allow for immediate transplantation, and these barriers substantially affect patient outcomes.

Recently, many promising initiatives have been launched that aim to improve and optimise the diagnosis and treatment of haematological malignancies in Latin America. For example, the Hematological Latin American Societies and the American Society of Hematology have been organising annual meetings in Latin America, to provide updates on advances in haematology and to debate challenges for optimum diagnosis and treatment of haematological diseases in the region.[294] These efforts will undoubtedly aid in improving haematological cancer care in Latin America.[296]

Surgical oncology

Despite an era of personalised medicine, molecular diagnostics, and targeted therapy, surgery will continue to be the backbone of control and cure for most solid tumours. The effect of specialised surgeons on reducing operative morbidity and mortality and lowering costs has been reported in many studies of different cancer types.[297–300] There are no data on the distribution of specialist versus general surgeons who treat patients with cancer in Latin America, and this is an area that needs further investigation. Although good surgical quality standards and outcomes are met in some specialised centres in the region, this is certainly less true in remote areas. With the evolution of surgery toward less-invasive approaches, some studies have shown that patients with breast and renal cancer have a higher chance of conservative surgery if they receive treatment at private hospitals in Latin America.[251,301–303] Most of the population is covered by the public health system, and these patients tend to receive more radical surgeries, which might be associated with increased risk of complications, higher costs, and sequelae. Initiatives that focus on implementing quality assurance for surgical management of patients with cancer are urgently needed. Established training programmes with international universities or societies, such as the IAEA sentinel lymph-node biopsy programme, have yielded excellent results, and similar platforms for training in developing countries should be initiated.[304–306] Robotic technology facilitates minimally invasive surgeries, examples of which have been performed in Latin America.[307–310] Although this technology reduces hospital stays, blood loss, transfusions, and use of pain medication, it is currently cost ineffective in the region (though this may change in the future). Robotic-assisted surgery has also paved the way for telesurgery and telementoring that could be highly educational and have a substantial role in providing care in geographically remote areas.

Paediatric oncology

Paediatric cancers are generally highly curable, but effective management is complex and costly. The rise in the number of children with cancer in Latin America is largely due to disease recognition and the development of tertiary paediatric-treatment referral centres.[311] In some areas of Latin America, childhood cancers are not effectively managed because of a lack of adequate hospital infrastructure and expertise. Cancer is now the leading cause of disease-related deaths among children in Latin America.[311] Twinning programmes between regional hospitals and institutions in developed countries have been very successful. An early example was the collaboration between the La Mascota Hospital in Nicaragua and hospitals in Italy and Switzerland in the 1990s.[312] Since then, many other twinning programmes, particularly between St Jude Children's Research Hospital and institutions in Latin America, have demonstrated the feasibility and cost-effectiveness of treating paediatric cancer.[313,314] Although these efforts have benefited children in paediatric hospitals in large urban areas, the rates of abandonment, toxic death, and resistant disease have been high for children from impoverished families or those residing in rural or secluded regions.[315]

In the past several years, some Latin American governments have made commitments to provide additional resources to paediatric oncology, but these efforts remain fragmented and insufficient. Uruguay and Chile are exceptions and have implemented comprehensive, meaningful changes to improve cancer care for children.[316] By contrast, the Brazilian public-health system has not been able to develop a broad partnership with national or regional non-governmental organisations (NGOs) or a cohesive national plan for paediatric oncology care. Similarly, the Mexican public system faces enormous challenges to improve survival of paediatric cancer across different regions of the country.[317] Insufficient numbers of trained paediatric oncologists and oncology nurses, poor hospital infrastructure, and limited psychosocial and economic support for families are crucial barriers to improving paediatric cancer care in Mexico's public health system.[318] As a result, there remains substantial inequality in the cancer care received by children from different geographical regions.[319] The establishment of strong public and private sector partnerships is needed to improve childhood cancer care in the region. Governments and ministers need to have a prominent role not only in funding, but also in efforts to unify and regulate national paediatric cancer programmes.

Clinical oncology nursing

Oncology nurses have an important role in the interdisciplinary oncology team, in terms of patient care and education, communication, research, and adherence to evidence-based practice guidelines. However, nursing shortages have had a negative effect on health care in general in Latin America.[320] The public systems in Latin America are threatened by oncology nurses moving to the private sector or moving to high-income countries for better working conditions and pay. Steps are urgently needed to expand the oncology nursing workforce. Initiatives to stimulate oncology nursing's leadership role in providing education to general nurse practitioners are needed, as well as professional membership nursing societies to develop training and specialisation in oncology and maintaining continuing education programmes.[321] For example, the International Society of Nurses in Cancer Care (ISNCC) serves as a communication network for national and regional cancer nursing societies, and a resource for nurses from several countries, including Latin America, for practice, education, research, and management.[322]

Part 10: Challenges and opportunities at the oncology and palliative-care interface

Data from the Pan American Health Organization show that most patients with cancer in low-income and middle-income countries are diagnosed with disease in advanced stages.[323] These patients need appropriate palliative care, since disease response to anticancer treatment occurs in only a small proportion and symptomatic responses are generally inadequate and short lived. One of the most worrisome and neglected aspects in the care of patients with advanced cancer is the multitude of uncontrolled and distressing symptoms. Palliative care is needed to provide physical and psychosocial relief and to improve the quality of life of patients and their families.[324]

Palliative-care services

Palliative-care services are formally embedded into cancer-care programmes in many high-income countries. In Latin America, there have also been several initiatives to implement palliative services. Since 1998, the Pan American Health Organization has included palliative care as a component of the Non-Communicable Diseases Program and access to palliative care has improved in the region.[325] Nine countries have a national palliative care plan or programme (Argentina, Brazil, Chile, Costa Rica, Cuba, Mexico, Panama, Peru, and Uruguay), and four of these programmes include a monitoring and evaluation system (Chile, Costa Rica, Cuba, Panama). These programmes are often linked to cancer programmes; 17 countries have a national cancer programme, 13 of which include palliative care. Five countries allocate government resources for the development of palliative care (Chile, Costa Rica, Cuba, Panama, and Peru) and four countries provide resources for research (Argentina, Colombia, Cuba, and Mexico).[326] The remaining countries have sparsely distributed palliative services at best. Guyana is the only country in the region that has no palliative services; Belize, Bolivia, the British Caribbean Islands, Nicaragua, and Puerto Rico are in the process of training personnel and building capacity.[326] Compared with Europe and the USA, where most institutions have integrated palliative services and a rate of at least 1000 palliative services per 100 000 inhabitants, Latin American countries generally have 100 palliative care services per 100 000 inhabitants.[327] 777 physicians and nurses from five Latin American nations rated the availability of advanced cancer-care services in their own institutions. 83% of providers reported that pain services were always or often available, and 74% indicated that case management services were always or often available. 50% indicated that psychosocial support services and palliative-care teams were always or often available. Finally, around 30% of respondents reported that home health care, hospital-based hospice services, and volunteer services were always or often available, and only 20% reported that home-based hospice services were always or often available.[328] The diversity of health-care systems, culture, economies, and resources in the region contribute to disparities in access to palliative-care services.[329]

Palliative-care physicians

Although precise numbers and characteristics of palliative-care specialists in Latin America are unknown, a recent survey of physicians affiliated with the Latin American Association of Palliative Care showed a wide distribution of primary specialties among palliative-care providers, including anaesthesiology and pain medicine (27%), internal medicine (26%), general medicine and family medicine (16%), oncology (16%), and other subspecialties (15%).[326] Most physicians have less than 10 years of experience in palliative care and a high proportion (43%) work in community-based facilities without a palliative-care team (ie, home health care or hospitals without palliative-care teams).[330] Education in modern palliative care is inadequate in many parts of Latin America. Examining its current status in Brazil shows the obstacles to optimum palliative care in the region. Brazil's new code of medical ethics mentions palliative care, but does not address palliative-care education.[328] Palliative care is not mandatory in undergraduate medical education in Brazil[331] and few medical schools offer elective courses.[332,333] The Brazilian Federal Council of Medicine recently approved palliative care as an area of specialisation, but did not propose a minimum curriculum.[157] Several multidisciplinary postgraduate courses have recently been created[334,335] based on recommendations by the European Association for Palliative Care.[336] Physician training abroad has improved expertise in palliative care, and has allowed initiatives such as building telemedicine postgraduate courses that can reach isolated regions of Brazil.[335]

Training in advanced cancer care

Medical education for end-of-life care in Latin America is not standardised. Most specialists and general practitioners who provide palliative care have had little formal training.[328] Although most clinicians are adept at providing analgesia according to the WHO three-step ladder, many providers are not comfortable treating other cancer-related symptoms.[328] Similar to the historical development of palliative care in other regions of the world, cancer palliative care in Latin America is distributed between different subspecialties, although largely focused on oncologists.[337]

Practice patterns of advanced cancer-care providers

In Latin America, palliative care for most patients with advanced cancer occurs in the inpatient setting. Survey data from 777 physicians and nurses from Argentina, Brazil, Cuba, Mexico, and Peru show that 55% of patients receiving advanced-cancer care do so in a hospital, 34% receive care at home, and only 10% receive professional end-of-life care at home or in a hospice.[338] This highlights the need to increase providers trained in end-of-life care and to expand palliative-care services. The shortage of providers results in too high a proportion of inpatient acute care beds being occupied by patients receiving palliative care. There is a need to develop capacity for ambulatory, home, and specialty palliative care facilities.

Barriers to advanced-cancer care

Despite continued efforts to provide optimum palliative-care services, the following barriers impede progress: lack of health legislation regarding end-of-life care, socioeconomic disparities, poverty levels, ethnic and cultural diversities, low educational levels, lack of information on diagnosis and prognosis given to patients and families, limited availability of potent analgesics, fear of diversion of opioids to illegal markets, oncologists' concern that palliative care destroys hope, and inadequate palliative-care policies among Latin American countries. These obstacles create disparities in delivery of palliative services and barriers to achieving adequate palliative care.[339,340] In many Latin American countries, resources are mainly directed to curative rather than palliative treatment. Some countries have a small number of palliative centres that are only available in the public-health system; in the private sector, palliative services are often not available because insurance reimbursement mechanisms are not clear.[340,341]

Attempts to implement palliative care are often hampered by a pervasive belief that these services provide only end-of-life care, a lack of training among health-care personnel, and health-care teams that do not include a palliative-care specialist.[342] The result is substandard or ineffective symptomatic therapy and poor social and emotional satisfaction for patients and their families.[342] Patients with terminal illness are managed in two inappropriate manners—abandonment occurs when it is deemed that nothing else can be done, and responsibility is assigned to a family or primary caregiver; and patients are admitted to hospital, using valuable resources needed for acute-care patients.[323]

In many Latin American settings, there is a deeply rooted cultural belief among many patients and doctors that the preferred place to die is at home, in line with many European studies into preferences on place to die. However, a study of older Mexicans with good access to health-care services reported a preference for dying in hospital.[323] Patients with advanced cancer have a variety of uncontrolled and distressing symptoms, often accompanied by limited access to adequate early diagnosis, lack of qualified caregivers and specialised cancer-treatment centres, and late stages of disease at diagnosis. Limitations in the ability to resolve medical issues by the family or primary caregivers and the absence of at-home medical services are the main reasons for providing costly medical attention in the hospital setting at the end of life.

Challenges in managing cancer pain in Latin America

There are many challenges to managing cancer pain in Latin America; implementing effective opioid use is one example.[343] Morphine and other opioids are needed to manage severe pain, and WHO has included them on the list of essential medicines.[344] Aside from their defined medical indications, these drugs have the potential for abuse and have been classified as controlled substances by the Single Convention on Narcotic Drugs of 1961.[345] Most Latin American countries are signatories to this agreement, which stipulates that governments have a dual obligation to ensure the availability of these drugs for medical use, and to control and prevent diversion and abuse (the International Narcotics Control Board is the independent body responsible for monitoring, implementing, and oversight of narcotic distribution).

WHO's Pain and Policy Studies Group reports on opioid use worldwide and has shown that not all countries have the same availability of medicinal opioids.[346] Argentina and Brazil have the highest medical use of opioids, whereas Honduras and Bolivia have very low consumption (figure 5). Additional data reported by physicians from Brazil, Argentina, Mexico, Cuba, and Peru suggest good availability of short-acting morphine and milder analgesics at the institutional level.[328] However, limited availability of long-acting opioids and other step 3 analgesics (according to WHO pain ladder), is of particular concern since they are central to the appropriate management of pain in patients with advanced diseases.[328] Despite some recent advances in opioid use for pain control in Latin America, average consumption remains well below world levels, which translates into inadequate pain management.[342]

Entities such as the Pain and Policy Studies Group (PPSG) and the International Association of Hospices and Palliative Care (IAHPC) have worked to identify barriers to

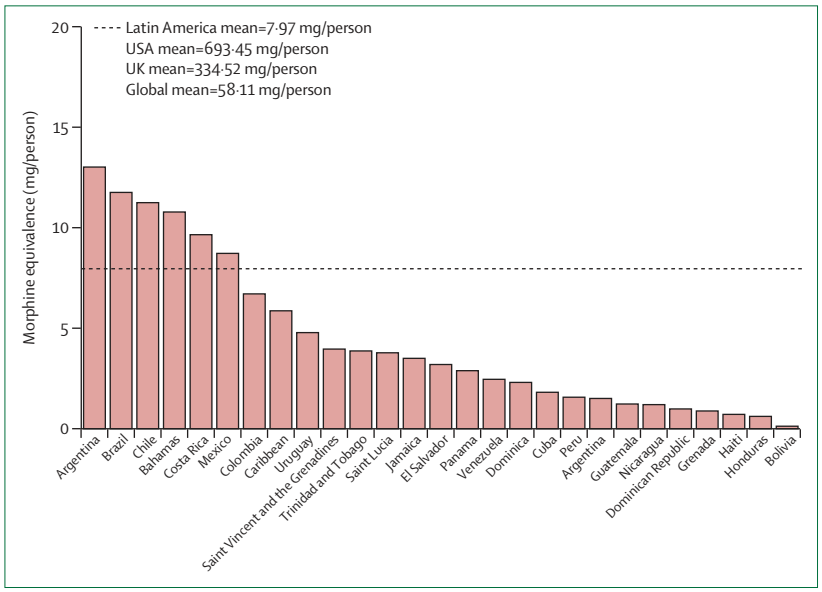

Figure 5: **2010 Latin America opioid consumption**
Reproduced with permission of Martha A Maurer, Pain and Policy Studies Group, University of Wisconsin–WHO collaborating centre.

For more on **opioid consumption data from the Pain and Policy Studies Group** see http://www.painpolicy.wisc.edu/opioid-consumption-data

adequate supply of opioids in different countries. Factors identified include restrictive legislation, inadequate health systems, poor knowledge among health professionals regarding use of these drugs, fear of addiction, adverse drug effects, and excessive regulatory red tape. The PPSG and IAHPC have organised workshops in Colombia, Peru, and Chile with the aim of getting doctors, Ministers of health, insurers, and patients to engage in dialogue about the challenges faced, and to create solutions applicable to each country.[347–349] The training of health professionals in the pharmacology and administration of opioids and other analgesics, and prescription management, are important actions needed to achieve optimum use of these medicines.

Access to palliative radiotherapy varies in Latin American countries. Guyana, Belize, Suriname, and Haiti do not have radiotherapy centres. A survey by IAEA on radiotherapy resources in Latin America showed that 75% of radiotherapy centres are in the biggest cities and that post-graduate training in palliative care and the role of palliative radiation is inadequate, even though the vast majority of physicians take care of palliative patients.[349]

Conclusion

Palliative-care services have progressed in recent years in Latin America; however, there remains limited access to care and medications for patients with advanced cancer. Palliative care must be a priority for health-care policy makers. Education and training in palliative care must be supported and valued. Countries need to improve access to analgesic medications to ease suffering at the end of life, and to do this, they must overcome persistent fears that opioids will be diverted to illegal use.[350] To break these barriers, it is necessary to strengthen the training of health-care providers, to promote research, build capacity, and empower communities with the right to pursue these goals. Health-care administrators should be pressed to ensure safe provision and distribution of opioid analgesics. Continued efforts to promote models of health care that include palliative care with oncology services are essential.

Part 11: Participation, conduct, and corporate responsibility in clinical trials

Latin America clinical-trial experience

Clinical trial research in the Latin American region is scarce.[351] In August, 2012, 35 471 cancer clinical trials were registered worldwide, of which 1665 (4·6%) were registered in Latin America, compared with 21 300 in the USA and 2994 in Canada. Of the registered cancer clinical trials in Latin America, 66% were sponsored by industry and 44% by academic and other sources.[351–353] Wealthier countries with more resources have more experience with clinical-trial research than institutions in Latin America.[351] Peer-reviewed publications from Latin American trials are also uncommon. Only a very small number of all reports on cancer published in peer reviewed oncology journals were led by a Latin American institution.[354] Moreover, a lack of support for clinical-trial research has limited the ability of local physicians to design and run studies that are valuable to their local populations. Unfortunately, results of trials designed by high-income countries do not necessarily satisfy local Latin American needs. There are many barriers to clinical research in Latin America, beginning with limited funding; in 2011, research and development expenditure was 0·65% of GDP, which is 3·4 times less than in high-income countries. WHO advises countries to invest 2% of the overall cost for health in research and development.[344] Other barriers to clinical research in Latin America are lack of time away from patient care and administrative responsibilities for researchers, prolonged times to approval of clinical trials by regulatory agencies, and inadequate allocation and support for research space and other necessary infrastructure in clinical settings.[351]

Despite these obstacles, future Latin American involvement in clinical research is essential. It is important to focus development toward therapies for malignancies that are most common in the region. For example, Brazil has been a key contributor to trials of new anticancer regimens for liver, stomach, and cervical cancer.[351,354–357] Also, large numbers of novel therapies that target infrequent, but specific, tumour mutations or protein-expression patterns are creating an increasing need for international trial collaborations to enrol sufficient patients. This has been increasingly recognised by the pharmaceutical industry, particularly because of the potential market in these countries.

Efforts to promote clinical-trial research are underway. An analysis of Latin American country-of-origin of scientific abstracts submitted to major oncology,

haematology, and radiation meetings in the past decade found that Brazil contributed 51·1% of all abstracts originating from Latin America, with Argentina (19·9%), Mexico (14·1%) Peru (6·2%), and Chile (2·4%) all increasingly contributing.[358] Latin American patient accrual rates are high and the data generated are generally of high quality, although some data-capturing errors have been reported.[359] Despite these errors, most Latin American studies meet the high standards set by regulatory agencies in the USA and Europe for approval of new therapies.[360,361] In Latin America, patients are typically enrolled in phase 2 trials of already approved drugs, or phase 3 randomised clinical trials. Very few of these randomised trials are initiated in Latin American countries.[362]

Overcoming barriers to clinical trials

Clinical research is competitive and interest is increasing in Asia, eastern European countries, and elsewhere. Four Latin American cities—São Paulo, Buenos Aires, Lima, and Mexico City—have a combined population of 60 million people, and such a large patient-base localised within a small geographic area offers the possibility of streamlined logistics and rapid, high-volume recruitment and clinical-trial management. Furthermore, after Portuguese, Spanish is the main language in most Latin American countries, and this is one of the few regions of the world where a single language minimises the need for multiple translations of trial-related documents. Furthermore, English is widely spoken within the medical community throughout Latin America, which further facilitates collaborations outside the region.

Most oncology trials in Latin America have been funded by pharmaceutical companies,[363] and increased funding will probably be needed from government or private foundations. For example, the Breast Cancer Research Foundation recently supported a review and analysis of 3500 patients with breast cancer from Argentina, Brazil, Peru, Mexico, Chile, and Uruguay who had been followed for more than 20 years.[364] These types of retrospective analyses are relatively inexpensive, but large-scale randomised trials that could be of particular importance to Latin America might require substantial non-pharmaceutical support. Running of clinical trials in Latin America can present unique geographical and cultural challenges. Enrolling patients from densely populated urban areas can be straightforward, whereas enrolment to trials that are of specific importance to rural and remote areas is much more challenging because of lack of infrastructure.

There is an inadequacy in most Latin American countries of well-established clinical research units, research personnel, data management, and overall infrastructure. Although trials funded by pharmaceutical companies have resulted in improved clinical trial infrastructure, development of additional clinical research units will need further resources and commitment. Partnerships to provide training to clinic staff and collaborations on research projects will increase access to high-level cancer care.[365] Because clinical trial participation is often considered coercive, particularly among poor patients with low education, it is particularly important that patients are provided with full disclosure of the risks, benefits, and alternatives when they are being offered participation in trials. Adequate supportive care is often needed when novel therapeutic approaches with unwanted toxic effects are studied in low-income countries.[366] Some Latin American countries have already addressed these needs and protections through health-care reform. Examples include Chile's Access of Established Guarantees (Régimen de Garantías Explícitas en Salud Universal; known as the AUGE plan), the Unified Health System of Brazil, Mexico's Seguro Popular,[367] and the improved drug reimbursement for public health systems in Paraguay and Bolivia.

Increased training in clinical-trial management has begun for clinicians, research nurses, data coordinators, and regulatory staff. One successful method has been for Latin American investigators to train in strong academic centres in the USA or in Europe, and maintain scientific collaborations after returning to their home countries. To this end, further training scholarships are needed. Delays in initiating Latin American trials have been a substantial challenge, particularly in Brazil, but regulatory agencies have become more proficient.[185,295] Increasing the number of local and international certified institutional review boards will expedite the research approval process and reduce cumbersome delays in initiating clinical trials. In 2005, a group of regulatory representatives from various Latin American countries released the Good Clinical Practice: Document of the Americas guideline, based on an the International Conference on Harmonisation–Good Clinical Practice standards.[368] This document has resulted in a substantial improvement in the regulatory approval process and is widely used by regulatory agencies across Latin America. A fully electronic process for regulatory submissions, such as Plataforma Brasil, is further alleviating the regulatory burden on research teams. Although the regulatory process remains longer than in the USA or Europe, in general, accrual to trials is rapid once they are open to enrolment.

To improve appropriateness of clinical cancer trials in Latin America, young investigators should be trained in cost-effectiveness and health-outcomes research.[369] Decision makers involved in health coverage and payment are increasingly developing policies that seek information about every day clinical-care outcomes that are not collected in conventional randomised controlled trials.[370] For example, an estimate of effectiveness of a drug (effect of a drug in a real-world setting) rather than the efficacy (effect of a drug in a highly controlled randomised trial) is being assessed.[371] Pharmaco-epidemiological data on the net effects of clinical, economic, and patient-reported outcomes after implementation of health coverage or payment policies should

be used by public authorities to guide rational resource allocation.[372] For example, the global Tykerb Evaluation After Chemotherapy (TEACH) trial was designed to evaluate delayed anti-HER2 therapy in patients who had been previously diagnosed with early stage HER2-overexpressing breast cancer but, because of limited access, had not been able to receive standard trastuzumab at the time of their diagnosis.[373]

Although challenged by lack of public or alternative funding sources, academic studies can provide more valuable information to Latin American patients than industry-sponsored trials of high-technology therapies that might not be immediately available to patients because of cost constraints.[374] One example of a trial with regional relevance was an investigation of gemcitabine added to standard chemoradiation for cervical cancer, led by a Latin American investigator as the global principal investigator.[375]

Pharmaceutical companies worldwide are engaging in partnership models with academic centres and researchers, increasing the participation of cooperative groups in registration trials, and strategically expanding drug discovery to key academic institutions around the world. Investigators in Latin America could capitalise on this shift in the coming decade, and rather than perpetuating the individual model, where investigators compete to be the highest enroller in phase 3 trials, develop cooperative groups at local and regional levels. A key initiative is the recently incorporated Latin American Oncology Group (LACOG), which shortly after its foundation was able to launch a multinational randomised clinical trial.[376] Another example is the South American Office for Research and Treatment of Cancer (SOAD), which was created in 1993 in southern Brazil with the support of the US National Cancer Institute (NCI) and the European Organization for Research and Treatment of Cancer.[377–379] For several years, semipurified plant extracts identified by the SOAD in-vitro screening programme were submitted to an in-vitro screening programme at the NCI. This collaboration screened compounds isolated from South American medicinal plants for potential use as anticancer treatments.[380,381]

A simplified legal framework to allow institutions in Latin American countries to sign master agreements with pharmaceutical companies, rather than having to duplicate regulatory work in each participating country, would facilitate rapid group conduct of oncology trials. Patients and advocacy groups also have an increasing role in supporting clinical research. In summary, there is tremendous scope for an increase in clinical cancer trials in Latin America, and substantial effort should be invested to overcome barriers to change the clinical-trial research environment in Latin America.

Part 12: Patient advocacy

Cancer non-governmental organisations in Latin America

Cancer awareness among the public in Latin America has traditionally been low, but NGOs have had an increasingly important role in cancer prevention and control, by increasing awareness, patient support, patient care, and advocacy for cancer policy.[382,383] Breast and paediatric cancer groups have led the advocacy movements so far, with breast-cancer advocates being most active. Breast-cancer NGOs in Latin America have typically been founded by survivors of breast cancer from upper socioeconomic settings who are motivated by altruism to help others. Their initial intent was to destigmatise cancer and to give hope to patients and families.[384] Paediatric cancer advocacy groups have raised awareness and funds and strengthened facilities and services for children with cancer. Smaller paediatric advocacy groups have focused on individual patient access to treatment; this narrow focus has made addressing and rectifying issues easier for policy makers.[159]

Although advocacy groups are increasingly aware of the need to change policy, their impact in this regard has been limited, largely due to lack of funding, resources, and advocacy expertise. Additionally, because public health services are often inadequate, advocacy groups find themselves filling a void and navigating patients to existing services, or fighting in courts for access to treatments for individual patients, rather than striving to shape policy. Recognising these limitations, NGOs in Latin America have begun organising themselves to take on a more comprehensive approach to cancer advocacy. In a few of the middle-income countries in Latin America, coalitions of advocacy groups are beginning to emerge. Promising examples are the Brazilian Federation of Philanthropic Breast Health Institutions (Federação Brasileira de Instituições Filantrópicas de Apoio à Saúde da Mama; FEMAMA) in Brazil,[33] and the Cancer Network (Red Contra el Cancer) in Mexico.[385] These groups are beginning to show the power of collaborative strategic advocacy and are increasingly encouraging other cancer NGOs to speak not only as one voice for one patient, but as one voice for all patients.

Focusing on disease awareness and early detection

Advocacy groups in Latin America are developing several key goals. Among these is the intent to raise widespread awareness of cancer among the general public. The first aim is to destigmatise cancer, since there is a pervasive, deeply rooted cultural view of cancer as taboo and fatalistic in Latin America. Other key goals include linking patients to services such as breast and cervical-cancer screening programmes, and encouraging primary prevention programmes such as cigarette and smoke avoidance. For example, educational and clinical examination programmes aimed at finding smaller tumours and seeking prompt medical attention are being developed. This relatively inexpensive pathway to diagnose and clinically downstage breast cancer has been identified as a feasible way to reduce the burden of advanced cancer and improve survivorship.[385] By contrast, screening mammography programmes are cost prohibitive in many

settings, and only in high-income and educational settings where population compliance reaches at least 70% has it been shown to reduce breast-cancer mortality.[386] In this regard, Knaul and colleagues[387] have advocated linking breast-cancer and cervical-cancer screening to antenatal, maternal and child, or reproductive-health interventions, although invasive breast cancer and preinvasive breast lesions are generally infrequent in this age group.[388]

An example of a successful awareness campaign is the Avon Breast Cancer Crusade launched in the UK in 1992, and in Mexico in 1994.[388] The Crusade works with NGO partners to hold awareness events related to breast cancer, educate and link women to screening services, and help patients obtain treatment after diagnosis. Future awareness campaigns plan to expand public-health messaging beyond breast-cancer screening; they will include messages about primary prevention, risk-reduction strategies, increase cancer screening through policy advocacy, and train community partners to become effective advocates.

Alliances with research collaborative groups

Cancer research is increasing in Latin America, and there is a growing role for NGO advocacy in research.[389] The connection between advocates and the medical research community is a favourable partnership with regard to lobbying for research funding, and has the following goals: improve patients' understanding of clinical trial participation, ensure scientifically appropriate endpoints and cultural appropriateness of trials, increase patient accrual by sharing experiences among research participants, and enhance communication of clinical research concepts in lay-language for patients, families, and communities.[389] Through alliances, researchers and advocates in Latin America are gaining the ability to learn from and assist each other with the common goal of improving patient wellbeing and reducing the morbidity and mortality of cancer.[389]

Developing an action plan for advocacy and legal rights

Public policy is crucial in creating the best environment for cancer survival, and identifying political leaders able to effect change is a key strategy. For example, the American Cancer Society published *Political Mapping of Health Policy in Brazil: a Resource For NGOs working in Breast Cancer,*[390] which explains the health decision-making landscape in Brazil and provides a plan for more strategic and effective cancer advocacy. Insights from political mapping have been integrated into advocacy training and technical assistance provided to FEMAMA, now an affiliate NGO of the American Cancer Society.

Enhanced advocacy resources and training have also begun to help NGOs develop effective strategies for participation in health councils and health conferences, and to undertake legislative and judicial advocacy. An example is increased participation and advocacy by FEMAMA and affiliated NGOs in national health conferences, which lead to the inclusion of resolutions in the *14th National Health Conferences Report* (2011) in Brazil.[391] These resolutions support improved control of breast and cervical cancer through integrated approaches, ensuring existing rights to mammography for all women aged 40 years and older, and measures to reduce the time between diagnosis and treatment. There are also indications of regional progress in efforts to strengthen awareness and education of policies and rights. The Oncological Institute (Instituto Oncoguia),[392] a leader in cancer information and advocacy in São Paulo, Brazil, has developed online and print resources about patient rights, to support their patient navigator programmes.

In summary, although cancer NGOs in Latin America have not yet had the same prominent role in cancer control as in the USA or western Europe, with the growing awareness of the scope of cancer as a public health issue in the region, it is important that patient organisations continue to strengthen their role in cancer-control advocacy, research, and raising of awareness of cancer prevention and early detection.

Part 13: Summary and conclusions

This Commission describes how countries of Latin America are currently overwhelmed by the challenge of cancer control and how this burden is poised to increase substantially. It is estimated that the annual incidence of new cancers will increase by 33·3%, to around 16·8 million cases by 2020.[1] Review of cancer control in Latin America suggests that it has arisen in a piece-meal, largely reactive manner to serve educated and wealthy urban constituents, whereas poorer populations have been neglected. As in all countries worldwide, cancer incidence is increasing in Latin America, and without proactive planning, it will severely tax the resources of the region. Failure to act promptly will have dire human and economic consequences.

A statistic underscoring the problem facing Latin America is that overall mortality-to-incidence rates from cancer are almost twice those of the USA—ie, 0·59 versus 0·35.[1] This discrepancy mainly reflects problems with access to care among poorer people. Also, Latin America spends roughly 0·12% of GNI per head on cancer care (ranging from 0·06% in Venezuela to 0·29% in Uruguay), compared with 0·51% in the UK, 0·60% in Japan, and 1·02% in the USA.[6] In addition to low overall investment, allocation of finances is highly inequitable. Estimates are that of the 590 million inhabitants in the region, 320 million (54%) lack adequate or any health-care coverage.

This Commission emphasised relatively inexpensive, key areas for primary prevention of some common cancers in Latin America. Tobacco use is the most important cancer risk factor in Latin America, accounting for 26% of all cancer deaths and 84% of lung-cancer deaths, and is associated with several other solid tumour malignancies. There are roughly 145 million smokers age 15 years or older in the region, which also has the lowest gender gap for

Panel 5: **Identified goals for cancer control and prevention in Latin America**

Reduce cancer occurrence

- Implement primary prevention measures
  - Develop tobacco control and antismoking policies with emphasis on children and adolescents
  - Reduce obesity and encourage physical activity, with emphasis on children and adolescents
  - Decrease environmental and occupational carcinogen exposure: discourage use of wood or combustible fuel sources by promoting education efforts and providing clean stove options; reduce and eliminate exposure to agricultural and industrial carcinogens (International Agency for Research on Cancer Group 1 and Group 2)
  - Develop early vaccination programmes for hepatitis B and HPV
- Increase awareness of cancer and combat stigma among health ministries, doctors, nurses, and the general population

Avoid late diagnosis of stage IV advanced cancer to reduce morbidity, mortality, and financial cost

- Optimise early detection
  - Develop targeted screening programmes—eg, breast imaging, Pap smear
  - Implement clinical early diagnosis programmes
- Optimise treatment of primary cancer
  - Reduce delays to treatment
  - Improve the quality of surgery and radiation
  - Provide access to essential medicines and clinical trials

Improve treatment of stage IV advanced cancer to reduce morbidity, mortality, and financial cost

- Avoid late intervention in stage IV advanced cancer
- Improve availability and quality of anticancer therapies: anticancer drugs, radiation, and surgery
- Incorporate early, comprehensive palliative and supportive care

smoking in the world with a male-to-female ratio of 3:2. Inexpensive and immediate regulatory interventions, such as tobacco taxation, restrictions on marketing, labelling, and packaging of tobacco products, and smoking restriction in public places could have a substantial effect. Increasing the price of cigarettes should result in immediate declines in adult smoking rates, as was shown in Uruguay when the price of a packet was increased to US$4.

Indoor air pollution, most often due to burned biomass for heating, continues to pose serious risks in Latin America. There are around 87 million people who burn biomass as their main source of fuel, and this is associated with an increased risk of lung and other cancers. Simple provision of clean cookstoves can substantially reduce the risk of indoor home pollution, as shown by the Sembrando programme in Peru. Finally, many other environmental and occupational carcinogens that contribute to new cases of cancer each year in Latin America need to be addressed; examples include mercury and DDT exposure in the Amazon of Brazil, and arsenic in Chile, which are linked to bladder and lung cancer in non-smoking indigenous people. Ministries need to work with industry to find safer alternatives for many agricultural and chemical products.

Obesity is another major public-health issue in Latin America, and is destined to worsen the cancer burden. With the transition to a lifestyle that mirrors developed countries, increasing obesity and concomitant cancer risk is becoming a greater disease burden than infectious diseases in the region. Roughly 139 million people (23%) are classified as overweight or obese, and this proportion is predicted to rise to 50% by 2030.[173,174] More public policies and advocacy efforts to raise awareness of the dangers of obesity are needed. Regulations aimed at controlling obesity have been implemented in Chile, Brazil, Costa Rica, Peru, Ecuador, and Mexico to encourage healthy eating, improve food labelling, regulate food advertising, and require healthy dietary choices in schools.

Around 17% of cancers in Latin America (150 000 cases per year) are attributable to infections, including hepatitis B and HPV.[177] Cervical cancer and HPV-associated dysplasia are common among indigenous women and women living in remote areas. Widescale vaccination is limited mainly by cost, and provision of low-cost vaccines and additional resources are needed. Availability of early vaccination in schools should be considered, as done in Peru.

The limitations of expensive, specialised screening programmes need to be considered. It is crucial to recognise not only disease burden, but also stage at presentation and available resources, to provide the most successful screening strategy for a particular region. For example, in some populations of Latin America, where women are diagnosed with late stage breast cancer and resources are limited, screening with clinical breast examinations can achieve valuable clinical downstaging, whereas screening mammography programmes among these women are unlikely to be feasible or effective. Along these lines, several promising pilot projects have been launched in some regions of Latin America. For cervical cancer, new alternatives to cytology-based screening, such as visual inspection with acetic acid and quick HPV testing, have been introduced that provide a simpler, quicker, and less-expensive approach.

Without adequate demographic data, it is difficult to proactively plan cancer-control programmes. Available cancer incidence statistics cover only 10% of Latin America, and we recommend that health ministries increase investment in cancer registries that include geographic, socioeconomic, and ethnic data. Similarly, further research is needed in cancer epidemiology, health economics, and cost-effectiveness. More doctors, nurses, and other health-care workers are needed to prevent future shortfalls. Investment in, and fostering, a research culture in Latin America should be recognised as cost effective.

Cancer morbidity, mortality, and related medical and non-medical financial costs stem mostly from death from advanced cancer. We have outlined goals to reverse the current trends (panel 5) and recommend several actions (panel 6). Two key changes would change the future. First, total health-care expenditure needs to be

Panel 6: **Recommended actions to improve cancer care**

Increase financial resources for cancer control
- Increase the percentage of gross domestic product assigned to health care, and specifically to cancer services
- Improve balance of resource allocation for cancer control, with particular attention to disenfranchised populations
- Solicit philanthropy for patient care and policy lobbying

Restructure health-care systems
- Move towards universal health-care coverage
- Emulate changes leading to universal health care
- Emulate policies that promote financial protection for health and extend coverage to the uninsured

Optimise oncology workforce to meet regional needs
- Increase the number of cancer specialists, in view of current shortages and future demands
- Geographically redistribute doctors, nurses, and other cancer-care professionals to address the population's needs

Improve technical resources and services for cancer prevention and treatment
- Optimise pathology evaluation and laboratory diagnostics
- Improve imaging availability, accuracy, and efficiency to achieve timely communication of results to providers and patients
- Establish centralised laboratory testing so that state-of-the-art testing and personalised cancer care can be offered

Invest in research and evidence-based cancer care relevant to the region
- Characterise the epidemiology of national and regional cancers
- Create and strengthen national cancer registries
- Monitor cancer outcomes and study the cost-effectiveness of specific interventions
- Build a clinical-trials infrastructure that is sustainable and will support innovative research and educational opportunities for trainees
- Promote laboratory research in cancer biology

Invest in education
- Improve and expand training of doctors, nurses, and other health-care workers
- Fund and organise multidisciplinary health-care workshops
- Implement teleoncology and novel methods for treatment and education
- Raise public awareness and education
- Increase and fund organised advocacy

increased and reallocated to cover disenfranchised populations. Fortunately, Brazil, Argentina, Colombia, Chile, and Mexico are forecasted to have strong growth in their economies, which should afford them the opportunity to channel more resources into cancer control. When the incidence of advanced cancer and mortality is reduced, cost savings could flow back into prevention and treatment of earlier stages of disease to further alleviate the disease burden. Second, countries in Latin America should continue to aggressively upgrade and restructure their health-care systems. Examples of progressive health systems in the region include the SUS in Brazil, the SNIS in Uruguay, and Mexico's Seguro Popular. As part of curbing mortality rates and creating cost savings, urgent reallocation of finances should focus on urban poor as well as rural, remote, indigenous, and other disenfranchised populations.

We recognise the many limitations of our Commission in trying to capture all elements that factor into cancer control in a region as large as Latin America and the Caribbean. However, we hope it will encourage policy makers to continue their efforts, and health-care practitioners to join advocates of changes in cancer control. These actions are needed to avoid a potential cancer crisis. In his second inaugural address, in 1937, US President Franklin D Roosevelt said: "The test of our progress is not whether we add more to the abundance of those who have much; it is whether we provide enough for those who have too little". We hope this Commission will provide an impetus to apply this admirable aspiration to cancer control in Latin America.

Contributors

PEG was the lead author of the Commission, and he wrote the abstract, introduction, and conclusion, and participated in the concept design, writing, and editing of all sections of the Commission. BLL, JS, KSW, and TBC participated in the writing, management, and editing of all sections, and produced figures 1 and 2. LF participated in the management of all references, figures, tables, and panels. Part 2: lead author was YCG. Coauthors EC, CV, AM, FK, HA, RB, SL, RS, and DF participated in the concept development, writing, and editing of the manuscript, and approved the final version. Part 3: lead authors were CVG and KU. Coauthors SS, AM, and CB participated in the concept development, writing, and editing of the manuscript, and approved of the final version. Part 4: lead authors were BLL and MF. Coauthors RK, AG, and VB participated in the concept development, writing, and editing, and approved the final version. Part 5: lead author was MD. MD was responsible for the concept development and writing of the manuscript. Coauthors GL, SSt, and MBl participated in the concept development, writing, and editing, and approved the final version. Part 6: lead author was PERL. Coauthors FH, FSS, AK, EDA, AFCZ, and CB participated in the concept development, writing, and editing, and approved the final version. Part 7: lead author was TBC. Coauthors RM, JJ, SL, and VT participated in the concept development, writing, and editing, and approved the final version. Part 8: lead author was DT. Coauthors AC, CF, CS, ADG, DS, MC, AFCZ, RF, and RMR participated in the concept development, writing, and editing, and approved the final version. Part 9: lead author was GW. Coauthors GM, RG, RR, RK, GI, ER, BR, and LV participated in the concept development, writing, and editing, and approved the final version. Part 10: lead author was ALS. Coauthors MXL, ITV, ACG, AH, MBe, and BR participated in the concept development, writing, and editing, and approved the final version. YCG reviewed and amended the section. Part 11: lead author was MH. Coauthors GS, SSa, FE, LFe, MM, and HG participated in the concept development, writing, and editing, and approved the final version. Part 12: lead author was CVa. KSW and BLL reviewed and amended the section. MHu, AD, and GA participated in the concept development, writing, and editing, and approved the final version.

Conflicts of interest

EC holds leadership positions with SLACOM and UICC; has consultant and advisory roles with Bayer and Schering Pharma; has received

honoraria from Bayer, Bristol-Myers Squibb, and Fresenius; and has received research funding (paid to his institution) from Poniard Pharmaceuticals, Daiichi Sankyo Pharma, and the Breast Cancer Research Foundation. ITV has received support from the National Cancer Institute. FK is a breast-cancer survivor and the founder of Tomatelo a Pecho, a Mexican non-profit association dedicated to promoting early detection of breast cancer in Latin America. She is also lead economist at the Mexican Health Foundation, and a principal investigator for a study on age of onset of breast cancer sponsored by GlaxoSmithKline. She is the wife of former Secretary of Health of Mexico, Julio Frenk, and participated in research and design of Seguro Popular. MBl is a consultant for Bayer Pharmaceuticals, and serves on advisory boards for Sanofi-Aventis and Genomic Health. FHS is an employee of Roche Diagnostics. LV is a member of the international board and consultant for Merck, Sharp, & Dohme, for the quadrivalent HPV vaccine, and a consultant for BD, Qiagen, and Roche for HPV DNA test development. SS is an employee of, and owns stock in, GlaxoSmithKline. All other authors declare no conflicts of interest.

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