

Cancer Control in Latin America and the Caribbean 2



Perspectives on emerging technologies, personalised medicine, and clinical research for cancer control in Latin America and the Caribbean

Gustavo Werutsky, Carlos H Barrios, Andres F Cardona, André Albergaria, Alfonso Valencia, Carlos G Ferreira, Christian Rolfo, Evandro de Azambuja, Gabriel A Rabinovich, Georgina Sposetti, Oscar Arrieta, Rodrigo Dienstmann, Taiane F Rebelatto, Valeria Denninghoff, Veronica Aran, Eduardo Cazap

Challenges of health systems in Latin America and the Caribbean include accessibility, inequity, segmentation, and poverty. These challenges are similar in different countries of the region and transcend national borders. The increasing digital transformation of health care holds promise of more precise interventions, improved health outcomes, increased efficiency, and ultimately reduced health-care costs. In Latin America and the Caribbean, the adoption of digital health tools is in early stages and the quality of cancer registries, electronic health records, and structured databases are problematic. Cancer research and innovation in the region are limited due to inadequate academic resources and translational research is almost fully dependent on public funding. Regulatory complexity and extended timelines jeopardise the potential improvement in participation in international studies. Emerging technologies, artificial intelligence, big data, and cancer research represent an opportunity to address the health-care challenges in Latin America and the Caribbean collectively, by optimising national capacities, sharing and comparing best practices, and transferring scientific and technical capabilities.

Introduction

Latin America and the Caribbean has approximately 650 million inhabitants and more than 1·3 million new cases of cancer annually.¹ Cancer is the second most common cause of death in most countries in this region, independent of economic status.^{1,2} Cancer control is both insufficient and inefficient, with deficiencies in trained health-care professionals, fragmentation of health systems, limited or inadequately distributed budget allocations, understaffed hospitals, inadequate access to new therapies, geographical and cultural barriers, and a shortage of hospital facilities and technologies—all of which compromise patient outcomes.³ Most people in the region receive health care through public health systems, which are known to have lower rates of cancer screening, more delays in cancer diagnosis, greater proportions of advanced disease at presentation, and limited access to optimal therapies, compared with private health care.^{4,6}

Better health outcomes are driven by cost-effective interventions and can be further improved by the incorporation of innovative technological solutions. Big data, digital innovation, and artificial intelligence are transforming cancer care globally, with a broad vision of leveraging data, technology, and expertise to improve health care. New initiatives such as data-driven algorithms have been successfully deployed to support oncologists' prognostication and therapy response predictions through optimising, harmonising, and adopting digital solutions in electronic health records, which could offer opportunities to upgrade and modernise cancer control strategies in Latin America and the Caribbean. In addition, personalised

medicine has great potential to improve prevention, diagnosis, and patient outcomes in the region, although questions related to cost-effectiveness are unresolved.

Research and innovation are drivers of scientific and economic development. Although Latin America and the Caribbean has been more active in cancer clinical trials in the past few decades, further initiatives in basic, translational, and independent academic cancer research are limited and in need of development throughout the region.

In the second paper of this Series, we aim to describe how emerging technologies, clinical research, and personalised medicine can improve cancer control in the region.

Emerging technologies to improve cancer prevention, diagnosis, and treatment Digital pathology, next-generation sequencing, and liquid biopsy

Pathology is crucial for the prevention, diagnosis, and management of cancer. Challenges to optimising pathology in Latin America and the Caribbean include inadequate infrastructure and centralisation of laboratories, a shortage of pathologists (particularly in public health systems) and subspecialty expertise, reimbursement issues, scarce training opportunities, and limited access to qualified and accredited pathology services.⁷ Digital pathology—which is suitable in a variety of clinical applications such as the acquisition, management, sharing, and interpretation of pathology information—can improve diagnostic capabilities and management of workflow, permit image sharing, enhance pathologist

Lancet Oncol 2021; 22: e488–500

This is the second in a Series of two papers about cancer control in Latin America and the Caribbean

Latin American Cooperative Oncology Group, Porto Alegre, Brazil (G Werutsky MD, C H Barrios MD, T F Rebelatto MD); Oncology Department (C H Barrios), Oncoclínicas Precision Medicine and Big Data Initiative (R Dienstmann MD), Instituto Oncoclínicas, Rio de Janeiro, Brazil (C G Ferreira PhD); Thoracic and Brain Tumor Unit, Clinical and Translational Oncology Group, Clínica del Country, Bogotá, Colombia (A F Cardona PhD); Foundation for Clinical and Applied Cancer Research (FICMAC), Bogotá, Colombia (A F Cardona); Molecular Oncology and Biology Systems Research Group (Fox-G), Universidad el Bosque, Bogotá, Colombia (A F Cardona); Translational Research & Industry Partnerships Unit, Instituto de Inovação em Saúde (i3S), Porto, Portugal (A Albergaria PhD); Institución Catalana de Investigación y Estudios Avanzados (ICREA) and Barcelona Supercomputing Center, Barcelona, Spain (A Valencia MD); Center for Thoracic Oncology, The Tisch Cancer Institute, Icahn School of Medicine at Mount Sinai, New York City, NY, USA (C Rolfo PhD); Medical Oncology Department, Institut Jules Bordet and l'Université Libre de Bruxelles, Brussels, Belgium (E de Azambuja PhD); Laboratory of Immunopathology, Institute of Biology and Experimental Medicine, and School of Exact and Natural Sciences, University of Buenos Aires,

Buenos Aires, Argentina (G A Rabinovich PhD); Instituto de Investigaciones Clínicas Mar del Plata, Buenos Aires, Argentina (G Sposetti MD); Un Ensayo para Mi, Buenos Aires, Argentina (G Sposetti); Department of Thoracic Oncology, Instituto Nacional de Cancerología (INCan), Mexico City, Mexico (O Arrieta MD); University of Buenos Aires - National Council for Scientific and Technical Research (CONICET), Buenos Aires, Argentina (V Denninghoff PhD); Instituto Estadual do Cérebro Paulo Niemeyer, Rio de Janeiro, Brazil (V Aran PhD); Latin American and Caribbean Society of Medical Oncology (SLACOM), Buenos Aires, Argentina (E Cazap PhD)

Correspondence to: Dr Gustavo Werutsky, Latin American Cooperative Oncology Group, Porto Alegre 90619-900, Brazil gustavo.werutsky@lacogcancerresearch.org

education, and facilitate consultation and diagnostic interpretation among pathologists with broader expertise.⁸ Digital pathology holds great promise for the region, but barriers to implementation include technological, infrastructural, and economic limitations. For example, in cervical cancer screening, advanced digital microscopy diagnostics, supported by artificial intelligence, are feasible in resource-limited settings for detection of abnormal cells in Papanicolaou tests.⁹ Digital pathology for primary diagnosis of breast lesions detected via screening prove to be highly accurate, and automated digital pathology algorithms have been developed to support pathologists to quickly determine HER2 status.¹⁰⁻¹²

The emergence of central laboratories as centres of excellence to serve a hospital network or a geographical region represents an attractive solution to facilitate access to new technologies in pathology, improve patient care, and provide widespread coverage in a cost-sustainable approach. Digital pathology is still incipient in the region; nonetheless, some laboratories (eg, in Brazil¹³ and Mexico¹⁴) implemented a clinical digital pathology system as part of their routine.

Next-generation sequencing and targeted therapies are not part of the standard of care in most public health systems in Latin America and the Caribbean. Multigene panel sequencing has been shown to have moderate cost-effectiveness in the USA compared with single-marker genetic testing for the management of certain tumour types.¹⁵ The economic impact of gene sequencing in low-income and middle-income countries has not been adequately studied. In Latin America and the Caribbean, very few cancer centres and laboratories offer next-generation sequencing tests, which are not routinely reimbursed by public or private health insurance.¹⁶ Pharmaceutical companies have been funding biomarker tests that enable indication of targeted agents linked to specific cancer types. However, the availability of industry-funded sequencing varies by country and is driven by industry priorities, making the situation unsustainable. Looking forward, countries will need to generate unique schemes for deployment of next-generation sequencing that relate to locally available drugs.

Liquid biopsy, which was recently approved for analysis of multiple cancers and biomarkers, has the potential to improve patient care.

Currently in Latin America and the Caribbean, access to liquid biopsy, specifically monotargeted tests (eg, PIK3 in advanced breast cancer and *EGFR* Thr790Met [T790M] mutation in non-small cell lung cancer), is only through programmes sponsored by pharmaceutical companies and the capacity to implement this technology in clinical practice in the region is limited.¹⁷

To date, a few tumour driver mutations and targeted agents are available in clinical practice for the most common cancer types—ie, breast, prostate, lung, colorectal, and stomach cancers, which account for approximately 50% of new cancer cases in Latin America

and the Caribbean.¹⁸ Thus, next-generation sequencing and liquid biopsy as a testing strategy for cancer diagnosis and treatment in the region needs to be critically evaluated to determine how they compare with an approach of testing for several markers individually, or whether next-generation sequencing and liquid biopsy could be applied specifically to certain tumour types.

Electronic health solutions

Regionally, Latin America and the Caribbean has a high rate of mobile phone adoption, with 70% of the population being unique mobile subscribers—equivalent to 444 million connections and 343 million mobile internet users, giving a penetration rate of 55%.¹⁹ This continuous and enormous spread of mobile technologies enables almost instantaneous contact with an ever-increasing mass of consumers and clients, making mobile health (mHealth) an evolved subfield of electronic health (eHealth).

eHealth and mHealth have great potential to improve access to health systems, minimise health problems, and improve health-care delivery, particularly in low-income and middle-income countries (figure 1). Text messaging (SMS) programmes have been used to educate patients, raise awareness, provide adherence and appointment reminders, facilitate data reporting and communication, and assist in data collection and medical records creation.²⁰ SMS has been shown to improve adherence to medical appointments in Colombia independent of a patient's age,²¹ and to improve management of side-effects in patients receiving chemotherapy in Brazil.²² Patients report that they feel more confident with the support, and that the SMS messages stimulate self-care despite economic and social limitations.²³ However, it is estimated that approximately 77 million rural inhabitants in Latin America and the Caribbean have no access to high-quality mobile and internet connectivity.²⁴

A comparison of different mHealth applications finds that 44.3% have been directed to health monitoring and surveillance, and 41.9% to health promotion and awareness.²⁵ Smartphone apps can support self-management of cancer pain, eliminating unnecessary hospitalisations and emergency room visits, thus reducing health-care costs.²⁶

Telemedicine has been applied in multiple clinical settings, increasing access to care and showing at least equivalence to in-person care, high levels of satisfaction among both patients and health professionals, and decreased health-care costs.²⁷ The COVID-19 pandemic spurred rapid availability and adoption of telehealth services in several Latin American and Caribbean countries, especially in the private health sector.²⁸ Argentina initiated use of telemedicine in the public health system (including for cancer care) during the pandemic with more than 130 000 consultations, of which 72% were done via mobile phone.²⁹ In Brazil, telemedicine was adopted by several private hospitals and by the largest

private health provider covering 3·6 million members, which performed more than 111000 teleconsultations in 2020.³⁰ Telemedicine can potentially play an important role in cancer care, especially in areas of limited access to health system structures and, most importantly, in remote geographical areas within large countries.

Despite the potential benefits of eHealth, its incorporation into health systems and patient care remains limited in Latin America and the Caribbean, mainly due to insufficient funding for system development, inadequate equipment and internet-related infrastructure, and little regulatory guidance. To take best advantage of digital innovations, the region must build capacity by training personnel, including medical students.^{31,32}

Artificial intelligence

Artificial intelligence can be applied in several important steps in cancer care, from diagnostic methods to surgery and treatment, by supporting clinical judgement and managing processes to optimise health systems (figure 1).³³

Successful use of artificial intelligence requires precise data collection and data entry, which are highly dependent on training and monitoring as staff transition from legacy systems.³⁴ In Latin America and the Caribbean, it is difficult to ensure high-quality data for harmonised datasets representing large areas, as data capture is fragmented through several health-care organisations or insurance providers. Likewise, making artificial intelligence useful requires qualified personnel to register, collect, and interpret data. In fact, the clinical translation of artificial intelligence approaches in medicine has been limited due to the lack of structured datasets that integrate phenomic, genomic, and environmental determinants of health.³⁵ Once effectively launched, artificial intelligence can be used in Latin America and the Caribbean to integrate additional factors in determining best courses of treatment, such as genetic characteristics that vary substantially throughout the region.³⁶

Artificial intelligence can be applied broadly to promote equity in patient access to high-quality health care, increase transparency of training datasets, and stimulate investments in machine learning and data science, all of which will result in the generation of reliable data so necessary for decision makers tasked with improving the delivery of medical interventions (table 1).³⁷ Future implementation of narrow artificial intelligence solutions, in which a learning algorithm is designed to perform a single non-complex task, can aid public health officials and oncologists in remote rural areas. Examples include medical artificial intelligence technology for early detection of skin cancers based on image recognition, and health-monitoring platforms to avoid overtesting and overtreatment of cancer. In addition, health workers could be trained to use medical artificial intelligence tools to compensate for insufficient numbers of trained physicians, scaling up access to best available health care. Disease mapping and remote consultation could be

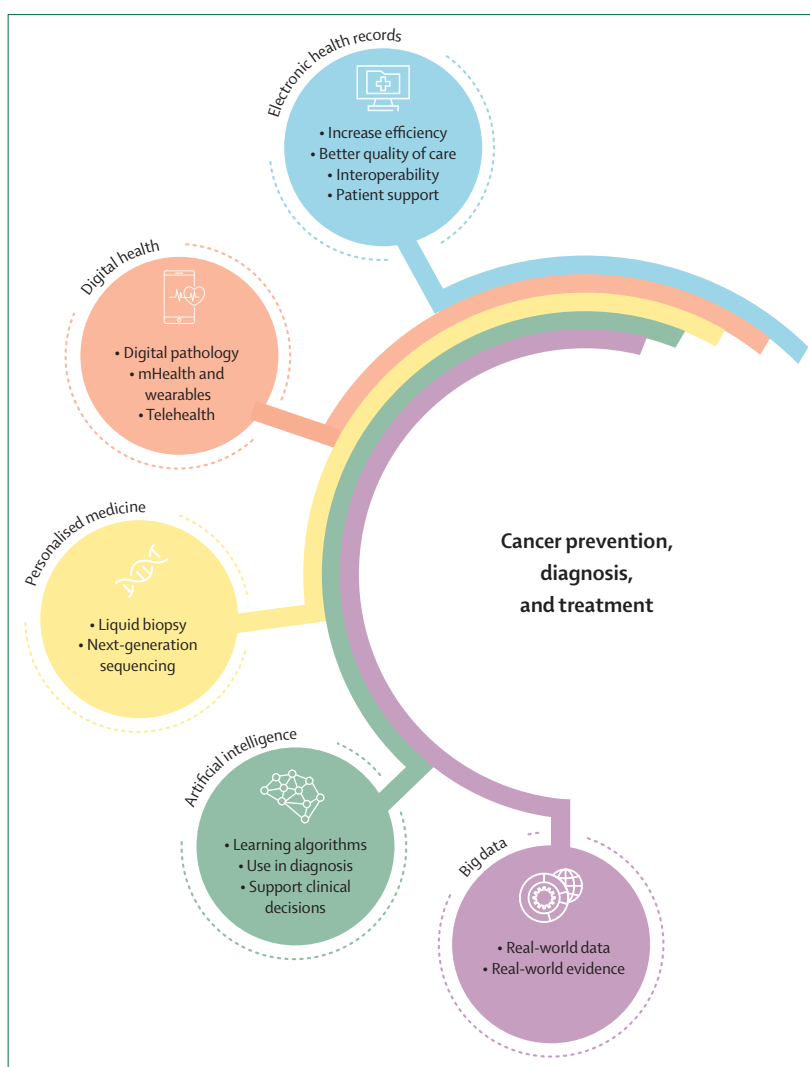


Figure 1: Emerging technologies for the prevention, diagnosis, and treatment of cancer in Latin America and the Caribbean
mHealth=mobile health.

possible since existing and new technologies such as computers, robots, cameras, and mobile phones can be powered with artificial intelligence to generate and send information from remote areas to the main medical centres. In addition, a multilevel medical artificial intelligence service network system could help to decrease the inequality between urban and rural health services.³⁸ To prepare for dissemination of artificial intelligence, which will strengthen health systems, government investments are urgently needed in public-private partnerships.

Big data and real-world evidence to improve cancer care

The growth in ability to gather and store data with digitised medical files, molecular diagnostics, and real-time patient monitoring data from wearables will provide information

	Solutions	Key actions
Emerging technologies and artificial intelligence		
Limited infrastructure, specialisation, and centralisation of pathology laboratories	Implement digital pathology	Optimise central laboratories for hospitals or clinic networks that have geographical barriers or limited access to specialised pathology services; improve efficiencies in workflow, secondary consultations, tumour boards, peer review, clinical trials, research, training, and other areas.
High prevalence of tumour driver mutation and inadequate access to targeted drugs	Provide next-generation sequencing and liquid biopsy for frequent mutations or locally accessible targeted drugs, or both	Adopt cost-effective genotyping platforms that can provide information on the minimum set of genetic abnormalities needed for proper cancer management; partner with the pharmaceutical industry to offer monotargeted testing programmes or next-generation sequencing for use of available targeted drugs
Missed consultations and treatment appointments, low treatment adherence, unnecessary emergency visits or hospitalisation for management of adverse events, long distance from centres	Adopt electronic health and mobile health solutions (eg, text messaging, mobile apps, telemedicine, virtual meetings)	Use text messaging to remind patients of consultations and treatment appointments; use mobile apps to improve treatment adherence and management of adverse events; use text messaging and mobile apps to support self-management of cancer pain; implement telemedicine for consultation, specialists second opinion, and follow-up visits; establish virtual multidisciplinary boards with participation of external experts for treatment planning; use digital health technologies and software to support clinical decision, especially in remote areas, and to manage processes to optimise the health system (eg, increase efficiency of throughputs, improve clinical workflow, decrease human resource costs)
Big data and real-world evidence		
Absence of quality parameters of health care	Adopt electronic health records	Ensure interoperability and standardisation of electronic health record systems; improve and implement national governance; apply interoperability and quality guidelines; build information technology infrastructure and storage facilities; train a specialised workforce (eg, cancer registrars, bioinformatician, and experts in health information technology)
Little real-time information on diagnosis, treatment, and outcomes of cancer population	Generate real-world data	Generate real-world data to evaluate quality parameters, access to optimal treatment, and impact of health-care interventions
Restricted data sharing and interoperability between electronic health record systems, leading to fragmented and unstructured health information	Use big data for health analytics	Construct big datasets to provide analytic data for health authorities and insurers, and to define new policies for national cancer control; use big data to improve health system management and efficiency; regulate, collect, and integrate health information from several resources such as mobile health and electronic health records, and integrate with artificial intelligence
Advances in cancer research		
Enhance participation in clinical trials	Simplify regulation and digitalise all the processes to attract new studies and facilitate clinical trial set-up	Implement fully electronic regulatory and ethics processes, digital signatures for clinical trials contract and documents, and use of electronic trial master file; simplify regulatory processes, use electronic study registration systems, decentralise ethics committee, and build cooperative institutional review boards models to review multicentre trials to avoid duplication in protocol review processes; use digital platforms and websites to improve patient awareness and education about clinical trials; develop apps for finding clinical trials, increasing recruitment and retention rates, and collecting patient-reported outcomes in clinical trials; increase governments support in fostering innovation through translational and clinical research, implementing electronic health records in the public health system, optimising the research process for rapid set-up of clinical trials, and providing fiscal incentives to businesses to increase spending on research and development
Boost cancer innovation through academic clinical trials	Regulate academic clinical trials	Recognise universities, institutions, and academic groups as sponsors for academic trials; require health insurance plans to cover costs of routine patient care in clinical trials (eg, cancer treatments, laboratory tests, imaging, consultations, and other standard-of-care procedures); allow mixed funding and support from commercial collaboration; encourage private funding for cancer research through donation and tax deduction programmes; stimulate philanthropy
Incorporation of personalised medicine into cancer care		
Unknown prevalence of targeted mutations in most Latin American and Caribbean countries; limited access to molecular and genomic tests	Analyse cost-effectiveness of personalised medicine	Generate real-world data on the prevalence of driver mutations and biomarkers for national or specific populations in certain geographical regions; partner with industry to provide tumour driver mutation testing programmes; use centralised laboratories for molecular and genomic tests to decrease costs; study and report cost-effectiveness of incorporating new technologies (including devices, tests, and medicines) into cancer care
Inadequate access to new targeted drugs	Create a precision medicine task force between government, insurers, and experts to evaluate cost-effectiveness data	Define cost-effectiveness criteria in each country to determine priorities for access; consider prioritising curative therapies and the most prevalent disease or biomarkers in the national cancer population; generate real-world data to re-evaluate access and efficacy in its population

Table 1: Challenges, solutions, and key actions to improve cancer prevention, diagnosis, and treatment, both within and between countries in Latin America and the Caribbean

streams for use with powerful analytical tools at a resolution and scale not previously available. The potential uses of biomedical big data analytics might include more complex understanding of health-care inequities at the individual patient, health system, and population levels. At the patient interface, clinicians could use rapid and accurate diagnostics to support specialised clinical decision making or personalised medicine (table 1).

Health systems might see the impact of big data for facilitating access, improving workflow, sustaining long-term operations, as well as tracking and reducing medical errors. Patients are also ready to engage in data generation to promote their own health.

Currently, electronic health records are the most widespread application of big data in medicine and one of the major sources of real-world data.³⁹ Electronic

health record databases represent an emerging data source with the potential to enhance the ability to measure important health outcomes and support clinical decision support systems, and have a positive spill-over effect at the level of research, with comparative effectiveness and cost-effectiveness studies. Promotion of ubiquitous and systematic records of health data for their reuse and ongoing analysis is crucial to improve health-care sustainability through increased biomedical knowledge and results-oriented management.⁴⁰

Among the Latin American and Caribbean countries, Costa Rica and Uruguay are the most experienced with using electronic health records and have advanced coverage of universal and integrated systems.⁴¹ In other countries in the region, use and coverage of electronic health records are increasing, and the quality of cancer registries has improved, but harmonisation of data is challenging because of the variation between countries in the type of data collected and the difficulty in integrating data from various health providers.⁴² Data are typically incomplete, frequently unstructured, non-standardised, episodic, inconsistent, non-accessible, and siloed. These conditions limit linkage between datasets and their potential usefulness in generating real-world evidence, which is the result of analyses of real-world data. Initiatives such as Minimal Common Oncology Data Elements in the USA aim to improve the interoperability of cancer data by proposing data standards that will facilitate transmission of data related to patients with cancer.⁴³

In Latin America and the Caribbean, real-world evidence is mainly used for pharmacovigilance and pure academic research, less so for health technology assessment decision making or pricing negotiations, and not at all to inform early access schemes.⁴⁴ There are many ongoing efforts to collect interpretable data from service providers, insurers, and government agencies, but initiatives are hampered by fragmentation and by inadequate governance and resources.⁴⁵ To obtain generalisable and comprehensive real-world data that can be shared at the national and global level, current health information systems need to improve transferability of routine data collection and patient traceability through the entire continuum of health-care provision. Such improvement includes development and acceptance of common data models, establishing methods to reward stakeholders that share data, and increasing the understanding of the potential value of high-quality datasets to encourage health systems to collect data holistically.

Many countries do not have a central authority to steward health infrastructure with standards that ensure governance, interoperability, and quality guidelines.⁴⁵ National regulation of data is essential to monitor transparency, ensure accessibility, and determine data use criteria. Attention to rigour and reproducibility of results will improve the likelihood of constructing models of collaboration between payers and providers that are

beneficial for all parties. Regionally, delays in the adoption of digital technologies for collection of patients' records can be attributed to uneven access to technology and concerns with security, privacy, and ethical issues. Only recently have legal and standard practice frameworks been established for data anonymisation and linkages that protect patients' rights to confidentiality; Brazil, Barbados, and Panama are the first countries in the region to adopt the General Data Protection Regulation inspired by the EU regulation.⁴⁵⁻⁴⁷ However, the long-term investments needed to use big data in the Latin American and Caribbean context will be challenging. Generally, allocation of resources to build information technology infrastructures, storage facilities, and train a specialised workforce are limited to private health-care settings. Although some countries in the region (eg, Argentina⁴⁸ and Brazil⁴⁹) are embracing a data-driven approach to health care, the generation of big data faces basic issues, particularly due to fragmented sources of data and restrict data-sharing policies by insurance companies, pharmaceutical firms, research networks, and governments.

One example of a big data initiative in oncology is the CancerLinQ platform that integrates electronic health record data from more than 200 oncology practices in the USA.⁵⁰ The purpose is to better understand the clinical decisions and cancer care processes on health outcomes and to provide a platform that supports the design and conduct of further clinical and epidemiological research.

A noted weakness in the biomedical data enterprise is lack of socioeconomic diversity within populations involved in research studies. This problem creates a knowledge gap and represents a unique opportunity for Latin American and Caribbean countries with socioeconomic diversity to contribute to research projects, particularly where high levels of patient involvement and mHealth penetration are required to test individuals' precise self-assessment and monitoring of health outcomes. There is an absolute need, regionwide, to assess the benefits of high-cost interventions for patients with cancer, with sophisticated analyses of high-quality, longitudinal, and integrated data, which in turn will support large-scale research initiatives using big data to advance precision medicine.⁵¹ Strategic investment in true learning health-care systems is needed to achieve the vision of universal population health and personalised medicine for individuals with cancer.

Cancer research in Latin America and the Caribbean

Current status, regulation, and funding

The globalisation of clinical trials has evolved in the past two decades with an increased number of clinical trials occurring outside the USA and Europe.⁵² As of July, 2021, of the 9315 ongoing phase 1-3 cancer clinical trials worldwide registered on ClinicalTrials.gov, 469 (5%) involved Latin American and Caribbean countries, of which 194 (41%) involved Brazil.

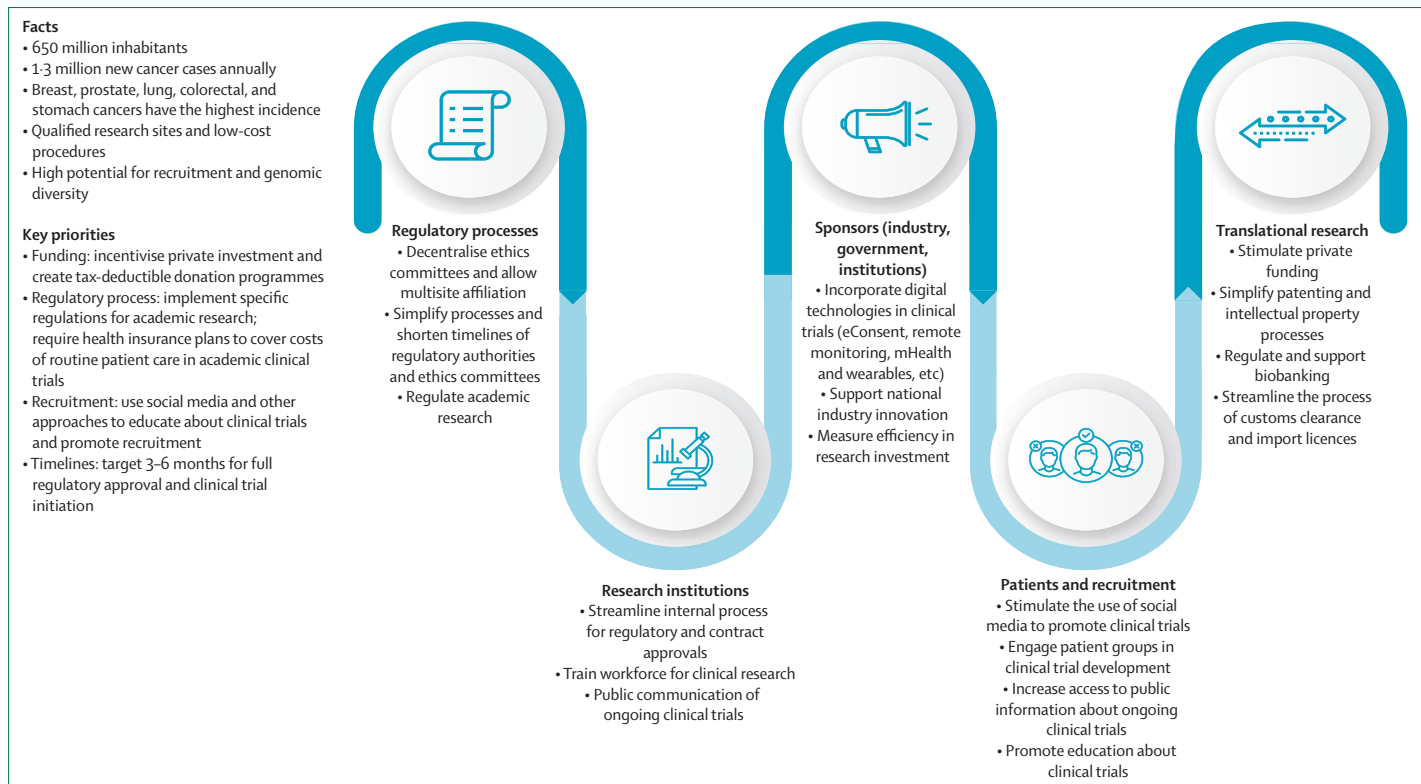


Figure 2: Fostering cancer research and innovation in Latin America and the Caribbean
eConsent=electronic consent form. mHealth=mobile health.

Latin America and the Caribbean is an attractive region to do clinical trials because of its high potential for recruitment, low clinical trial costs, qualified research sites, and improved regulatory timelines in the last decade.⁵³ Nevertheless, there are challenges to overcome, such as a small number research sites that are mostly centralised in specific regions, complex and lengthy regulatory processes in some countries, limited public investment in cancer research, complex processes for customs clearance for research materials, and the lack of educational programmes to train a new generation of cancer researchers.⁵⁴ Clinical research should be considered a priority in the region, and it is crucial to implement procedures to streamline regulatory timelines, decentralise the regulatory process, adopt electronic regulatory submission platforms for clinical trials, and stimulate international collaboration in biobank collection for the discovery of biomarkers related to the Latin American and Caribbean population.

In terms of scientific publication in the region, Brazil is the most productive nation, with 41·8% of identified cancer-related peer-reviewed articles published between 2010 and 2018, followed by Mexico (16·6%) and Argentina (12·9%).⁵⁵ Brazil, Mexico, Cuba, and Argentina were the highest contributors in cancer patent applications, with a total of 12 989 items published and 244 patent applications related to cancer.⁵⁶ Finally, none

of the Latin American and Caribbean countries have an institution listed in the top 200 global institutions ranked in cancer research from January, 2015, to August, 2019.⁵⁷

Investment in research is one of the key pillars to innovation and development. The average share of gross domestic product devoted to research and development is 0·7% for Latin America and the Caribbean, compared with 1·7% globally and 2·5% for North America and Europe.⁵⁸ Funding is not the unique limiting factor associated with innovation. Chile spends less than Brazil does, but has a higher financial efficacy—ie, the relative contribution of each author to an article divided by the country's gross domestic expenditure on research and development.⁵⁹ The science budget for basic and translational research in the region is almost fully dependent on government grants, particularly in federal institutions, and is therefore exposed to economic instabilities. In 2017, during Brazil's economic crisis, there was a resulting 44% decrease in federal investment in research.⁶⁰ More recently, the COVID-19 pandemic impacted scientists and research laboratories due to science budget cuts.⁶¹

By contrast, approximately 70% of clinical trials in Latin America and the Caribbean are sponsored by industry, a proportion similar to that in Europe. Therefore, clinical research on new therapies are infrequently funded by national governments or local institutions.^{62,63}

Among the options to improve funding for cancer research are programmes of donation and tax deduction. Brazil has created a programme (*Programa Nacional de Apoio à Atenção Oncológica*) that allows donors to select a project to fund; in 2020, a total of US\$25 million were invested through this programme.⁶⁴ Philanthropy is still very limited in the region though.⁶⁵ In the past few decades, patient advocacy groups have evolved and more organisations have been established, with a few notable initiatives such as Projeto CURA, which is raising funds for cancer research.

Academic research

Increases in investigator-initiated clinical trials and academic research sponsored by universities, hospitals, or other non-profit organisations (non-commercial sponsors) are crucial to boost and sustain the cancer research agenda in the region (table 1, figure 2). The impact can be substantial; for example, in the USA, results of 45·1% of academic studies sponsored by the National Cancer Institute, including trials with positive and negative findings, affected guidelines of the National Comprehensive Cancer Network or new drug indications by the Food and Drug Administration.⁶⁶

In Latin America and the Caribbean, regulations require that standard-of-care treatment and procedures be fully covered by the study sponsor, making trials expensive and typically unfeasible for academic institutions. As a result, studies addressing important regional research questions with systemic drugs, surgery, or radiotherapy are almost impossible to operationalise.

Globally, there is a trend towards a higher participation of small biotech firms in oncology, creating an opportunity for Latin American and Caribbean countries and institutions to interact with these companies in academic and low-cost clinical trials.⁶⁷ About half of the top 20 pharmaceutical companies operating in Brazil are locally owned and dedicated to the production of generic and, to a lesser extent, biosimilar drugs. However, the high costs associated with drug development and risks of clinical trial failure result in limited research investment and academic interaction.⁶⁸

Partnerships between industry and academic institutions in Europe have led to major scientific breakthroughs that benefitted patients with cancer and can be model for Latin American and Caribbean countries.⁶⁹

Technologies for conducting clinical trials

Incorporating technologies and digitalisation is the next step to increase efficiency in clinical trials through decentralisation and virtual trials (ie, incorporation of digital technologies into clinical trials), especially in Latin America and the Caribbean, to increase widespread participation of sites, including remote areas.⁷⁰

Recruiting and retaining participants in clinical trials remains a challenge. Despite recent efforts, data published in 2017 showed that 40% of trials in the UK

were unable to reach their intended enrolment numbers.⁷¹ Several technological solutions could improve patient inclusion and retention in clinical trials in Latin America and the Caribbean. Digital recruitment approaches could include automated telephone messaging, audio messages, videos, radio and television advertisements, online advertisements, the use of social media, email, and text messages, and automated eligibility screening of electronic health records, data warehouses, or other patient data sources (eg, machine-learning and case-based reasoning models).⁷²

Digital health technologies such as smartphones and wearables can be used in clinical trials to transmit information on participants' symptoms, disease progression, and treatment efficacy in a cost-effective and efficient manner.^{73,74} The use of mobile technologies for data capture offers the possibility of collecting real-time information from study participants, wherever they are (eg, at homes, workplaces, or other settings) in their daily lives, and for a prolonged period. This approach would provide investigators with more complete information about the impact of the investigational product and have been extensively reviewed in the Clinical Trials Transformation Initiative recommendations.⁷⁵

Electronic data capture using validated electronic case report forms could also provide more accurate data capture and allow for automatic queries, thus reducing data management workload and costs. Electronic capture of patient-reported outcome data has many advantages over paper-based data collection. Regulatory agencies have consistently supported the use of such data capture and recommendations have been made by the Electronic Patient-Reported Outcome Consortium.⁷⁶

Social media in clinical trials

Worldwide, patients indicate a belief in the importance of clinical research, but have limited understanding of the research process and availability of information on locations of trial sites.⁷⁷ Improved promotion of education for patients with cancer and communication about clinical trials will mitigate one of the primary gaps preventing access to trials.

In general, the most important sources of information about clinical trials for patients in Latin America and the Caribbean are the attending physician, physicians' reference networks, and advertisements in traditional media. Worldwide, social media is not widely used for trial recruitment; data from the USA suggest that only 25% of cancer investigators in the Southwest Oncology Group use social media to recruit patients for trials.⁷⁸

However, social media is a useful tool for increasing awareness and disseminating information about clinical trials. Social networks offer a nearly inexhaustible source of information for all stakeholders in cancer trials, facilitating recruitment and building awareness of opportunities among patients. Putting opportunities to participate in trials out on social media can allow

For Projecto CURA see <https://projetocura.org/en>

stakeholders to receive feedback from patients, including fears and concerns, and raises awareness, which can benefit clinical research projects.⁷⁹ However, activity on social media might generate uncontrolled risks including issues with confidentiality, privacy, and the integrity of clinical trials. It is important for trial participants to be aware of potential scams and counterfeit goods specific to clinical trial participation, and cross-check information of social media posts.^{80,81}

Although Latin America and the Caribbean faces immense challenges, the room for growth and opportunity in use of social media in cancer research is unparalleled. The immense social media use during the pandemic has allowed marketing strategies not previously experienced. Social network use has grown by 13.2% between January, 2020, to January, 2021, worldwide.⁸² In cancer research, industry, researchers, patient associations, committees, and communities can capitalise on this new way to communicate with different patients with cancer, which might help to build interest among social media users to learn about other serious diseases. The great challenge in the near future is developing ethical uses of social media that are reliably within regulatory requirements.

Translational research

A major drawback in cancer control programmes in Latin America and the Caribbean is the enormous gap between scientific advances and their translation into clinically relevant therapeutics. Public and private funding is scant to support the various stages of the translational process, typically leading to failure either in the technology's transfer from the bench into development or in its clinical application.⁸³

Clinicians are overwhelmed with hospital demands and are not given protected time for clinical research, and basic scientists might be forced to delay translational research activities to focus on publication-generating work to maintain funding and academic positions. In another key link, pharmaceutical entrepreneurs do not give sufficient value to local research done in Latin America and the Caribbean, and technology transfer officers, responsible for connecting the different stakeholders, repeatedly fail in this complex endeavour.⁸⁴ Furthermore, for scientists in drug development, the bureaucracy associated with patenting and licensing processes, managing intellectual property, and the intimidating nature of regulatory requirements, business-related issues, varied perspectives, and different languages present many additional hurdles.

These hurdles might prove insurmountable for scientists attempting to solidify ownership and sales of intellectual property to companies that might acquire it and potentially take the new drug to market. Governmental institutions and non-profit organisations are an alternative source of support and can provide relevant financial and logistical support to overcome these limitations, by supporting basic research; fostering communication of the key players;

encouraging multidisciplinary partnerships between academia, health care, and industry by creating academic-based industry interface offices; and facilitating education of a new generation of scientists with expertise in both basic research and clinical oncology.

Academic institutions should rethink their criteria for assessing scientists, allowing additional years for the complex and lengthy process of translational research. Thus, only collaboration between multiple stakeholders, including public and private entities, will have the breadth of influence and strength to generate a paradigm shift in the development of patient-oriented transformative oncology.⁸⁵

Incorporation of personalised medicine

Personalised medicine is of particular importance in Latin America and the Caribbean, considering the diversity of the population and the varied frequencies of genomic drivers (table 2). For example, *EGFR* mutations are identified, on average, in 26% of patients with lung cancer in the region, but can be present in as many as 51.1% in specific countries, such as Peru.⁸⁶ Differences are likely a result of the admixed population ancestry, and thus a complete understanding of these differences will drive next-generation clinical approaches for the region.⁸⁷ Use of genomic data and cost-effectiveness analyses can improve access to novel treatments and thus reduce the wide gap between precision medicine and standard of care, overcoming disparities in quality of care in the region.⁸⁸

Genomic information has transformed diagnoses in different areas of medicine and improved the diagnoses and treatment of cancer, as well as the development of biomarker-driven oncology trials. These developments are possible due to the combination of in-depth genomic information, larger and more comprehensive databases, and platforms for integrated analyses. The rise of personalised medicine in cancer has led to new trial designs, some of them with deep involvement of academic research institutions.^{69,89}

Assessment of the market value of precision medicine is inconsistent and, in some cases, unclear across different geographies and health technology assessment bodies, although some groups have articulated assessment approaches.⁹⁰ Nevertheless, the size of the precision medicine market in Latin America and the Caribbean was worth US\$5.66 billion in 2021 and is projected to reach \$10.11 billion by 2026, at a compound annual growth rate of 5.66% during this forecast period.⁹¹ This growth projection is due to the expected demand for customised medical solutions, growth in health-care technologies, favourable government regulations, and use of next-generation sequencing in practice.

An important challenge to these projections is the unknown prevalence of targeted mutations in most Latin American and Caribbean countries.

There are conceptual and structural challenges with implementing personalised medicine in Latin America

	Actions	Outcomes
Data: practically all countries in Latin America and the Caribbean have many barriers to access medical information, which is currently the major roadblock for the development of personalised medicine	Promote and implement advanced analytical tools, machine learning, and artificial intelligence; coordinate and share regional information systems and data collection; establish regional agreements for cooperation; harmonise databases at governmental and private organisations (eg, hospitals and health insurance providers)	Availability of large datasets, including electronic health records, with longitudinal data; incorporation of real-world data and real-world evidence into regulatory and health technology assessment processes
Prevention: insufficient research to investigate the potential benefits of personalised medicine approaches in cancer prevention	Propose a coherent governmental approach to personalised health-care prevention; develop and promote clear messages to policy makers, explaining that appropriate interventions need to be quickly implemented to benefit the entire population	Proper use of health-related information for optimised prevention
Diagnostics: limited access to molecular and genetic tests	Do health technology assessments to evaluate the incorporation of new technologies for patients and health systems; establish centralised laboratories that are accessible to multiple institutions	Good-quality research and testing laboratories; availability of next-generation sequencing; good access to cancer-related testing
Therapeutics: insufficient access to novel targeted drugs	Analyse cost-effectiveness of personalised medicine at the local level to demonstrate which interventions are more convenient and feasible according existing resources and health systems context	Real-world data on the prevalence of driver mutations biomarkers for national or specific geographical populations; partnership with industry to provide tumour driver mutation test programmes; use of centralised laboratories for molecular and genomic tests to decrease costs; cost-effectiveness data of incorporation new technologies (devices, tests, and medicines) into cancer care
Health systems: lack of innovation towards personalised health systems	Create a regional or national precision medicine task force between government, insurers, and experts to evaluate data from a cost-effectiveness and real-world data perspective; re-evaluate health systems to create resilient, integrated, and patient-centred models	Clear cost-effectiveness criteria in each country to define priorities for access; prioritisation of curative therapies and the most prevalent disease or biomarkers in national cancer population; generation of real-world data to re-evaluate access and efficacy in the population; patient-centred care that better respond to patient needs
Public and specialist information: insufficient knowledge from public, patients, and specialists	Educate the public, policy makers, medical specialists, and governmental bodies that personalised medicine is not merely applying the concept in diagnosis and treatment of cancer; run explanatory and educational media campaigns through partnerships between scientific societies and governmental institutions (eg, national cancer institutes)	Implementation of best practices related to personalised health care, governance decisions, awareness and attitudes, infrastructure, and financial stewardship
Economics: policy makers must correct preconceptions that personalised health care is too expensive and should invest in health technology assessment processes to ensure informed decision making	Develop health technology assessment studies to evaluate the costs and benefits of personalised medicine interventions; integrate personalised medicine in health systems	Increased public and specialist understanding of the mechanisms, potential, and limitations of personalised health care is needed to help enable its introduction
Politics: Political will remains insufficient or practically inexistent in many Latin American and Caribbean countries	Develop processes and methods for economic evaluations and health technology assessments based on local data and according to the health system capabilities and resources; promote the inclusion of personalised medicine in national cancer plans	Inclusion of personalised cancer care in the political agenda; inclusion of planning of cancer care in national cancer plans, regulations, and norms; a whole-of-government approach, including the executive (eg, the ministry of health), parliament, and judicial power

Table 2: Potential for personalised medicine to reduce health disparities, inequities, and inequalities—a holistic and integrated view

and the Caribbean, including educating physicians on the benefits and limitations of genomic profiling, cooperation between physicians and pathologists, timely reporting of testing results, clinical implications of comprehensive genomic profile, composition of multidisciplinary tumour boards, access to adequate therapies, clinic-genomic databases, and bioinformatics.^{92,93} Financing and counselling will need to be undertaken at local and national levels.

To include personalised medicine within health systems, it is necessary to evaluate differential research needs for decision making—ie, economic evaluations, preparation, delivery, sustainability, and scale-up.

From a diagnostic and therapeutic perspective, disadvantages of implementing personalised medicine in Latin America and the Caribbean include high costs of new diagnostic methods and drugs, which often have modest improvements in survival and the potential to provide cures. A new vision that could change the framework in

the region is to offer personalised screening in cancer prevention, which might have benefits for healthy populations and reduce cancer incidence.⁹²

Looking into the future, all of this progress will be surpassed by a new wave of artificial intelligence-assisted systems, embedded in better-integrated computational infrastructures and fed with higher-resolution data from technologies, such as single-cell genomics and proteomics combined with imaging and personal devices. The participation of Latin American and Caribbean countries in these promising improvements depends on the capacity to overcome the current barriers to generate and access medical information, which are the region's major roadblocks in development of genomic medicine.

Conclusions

The cancer burden in Latin America and the Caribbean is increasing, with a substantial impact on health systems and a growing demand for services in the next

Search strategy and selection criteria

No formal systematic review was done. We searched PubMed focusing on emerging technologies, artificial intelligence, big data, and clinical research on cancer in Latin America and the Caribbean, using the terms “emerging technologies”, “artificial intelligence”, “big data”, “electronic health care”, “digital pathology”, “cancer research”, “Latin America”, “Caribbean”, and “cancer control” from Jan 1, 2000, until Aug 16, 2021. We only considered papers published in English, and selected references according to their relevance to this paper. We searched for relevant information and reports published in websites from Latin American and Caribbean countries published in English, Spanish, or Portuguese related to the topics of this paper.

decades. A comprehensive programme to reduce the incidence and mortality of the most prevalent cancer types in the region should include promoting policies to target risk factors, increasing immunisation coverage against infection associated with cancer, increasing access to screening programmes for early detection, and increasing patient access to timely diagnosis and treatment. In parallel, cancer control will require rapid adoption of new technologies that are currently not widely implemented in the region due to inadequate funding, insufficient human capacity trained to manage new systems, and overall structural deficiencies.

Digital transformation of health care in the region holds tremendous promise and would have beneficial effects, including universal connectivity in the health sector, accelerated progress towards digital public health, and implementation of open, sustainable, interoperable digital information and big data for health analytics. It would mainstream human rights across all areas by digital transformation in health, allowing participation in global cooperative projects that use artificial intelligence, and establishing mechanisms for the confidentiality and security of information in the digital public health setting. Overall, it will generate a renewed public health architecture for the age of digital interdependence.

Research and innovation together have a fundamental role in improving cancer care and control. Cancer research should be considered a priority in Latin America and the Caribbean, with an emphasis on simplification of the regulatory process, regulation and incentives for academic cancer research, and full implementation of electronic health records in health systems that will generate real-world and big data to improve analyses of clinical processes and outcomes for the purpose of providing the best available care with quality and cost-effectiveness.

Ultimately, new and innovative approaches will promote next-generation cancer strategies, which are more firmly centred on each individual's personal

characteristics and will lead to increased effectiveness, economic value, and equitable access for all populations while ensuring the best possible cancer prevention, detection, and care.

Contributors

GW was the lead author of this Series paper and wrote, edited, and reviewed all sections. EC, CHB, and TFR conceptualised the paper, wrote, and edited, and approved the final version. The emerging technologies section was led by CGF, who wrote, edited, and approved the final version of this section. The section on digital pathology, next-generation sequencing, and liquid biopsy were led by CR who, together with VD, wrote, edited, and approved the final version of this section. The section on electronic health solutions was led by AFC, who wrote, edited, and approved the final version of this section. The section on artificial intelligence was led by CGF who, together with VA, wrote, edited, and approved the final version of this section. The section on big data and real-world evidence to improve cancer care was led by RD who, together with AV, wrote, edited, and approved the final version of this section. The section on cancer research in Latin America and the Caribbean and the subsection on current status, regulation, and funding was led by GW, who wrote, edited, and approved the final version of these sections. The section on academic research was led by GW, who wrote, edited, and approved the final version of this section. The section on technologies for conducting clinical trials was led by EdA, who wrote, edited, and approved the final version of this section. The section on social media in clinical trials was led by GS, who wrote, edited, and approved the final version of this section. The section on translational research was led by GAR, who wrote, edited, and approved the final version of this section. The section on incorporation of personalised medicine was led by EC who, together with OA and AA, wrote, edited and approved the final version of this section. GW, CHB, and EC wrote, edited, and approved the final version of the whole manuscript.

Declaration of Interests

CHB reports institutional research grant from Pfizer, Pharma Mar, Polyphor, Henlius Biotech, Merck KGaA, Millennium, LEO Pharma, ImClone Systems, Exelixis, Medivation, Asana Biosciences, AB Science, Abraxis Biosciences, Daiichi Sankyo, Bristol Myers Squibb, BioMarin, Astellas Pharma, AbbVie, Merck Sharp & Dohme, Merrimack, Mylan, Taiho Pharmaceutical, Sanofi, GlaxoSmithKline, Roche/Genentech, Lilly, Boehringer Ingelheim, Novartis, AstraZeneca, and Amgen; advisory board consulting from Boehringer Ingelheim, Sanofi, Lilly, Zodiac, AstraZeneca, Merck Sharp & Dohme, Bayer, Eisai, Roche/Genentech, Pfizer, Novartis, and GlaxoSmithKline; and stocks from MedSIR, Biomarker, and Tummi, outside the submitted work; he declares no relevant conflicts of interests related to this Series paper. AFC declares financial research support from Merck Sharp & Dohme, Boehringer Ingelheim, Roche, Bristol Myers Squibb, and The Foundation for Clinical and Applied Cancer Research (FICMAC); he received honoraria as advisor, participated in speakers' bureau, and gave expert testimony to Merck Sharp & Dohme, Boehringer Ingelheim, Roche, Bristol Myers Squibb, Pfizer, Novartis, Celldex Therapeutics, Foundation Medicine, Eli Lilly, and FICMAC. CR reports grants or contracts from Pfizer–Lung Cancer Research Foundation (for the EMPOWER ME trial); consulting fees (for advisory board) from ArcherDX, Bristol Myers Squibb, Novartis, and Boston Pharmaceuticals; payment or honoraria for educational events from AstraZeneca, Roche, and Merck Sharp & Dohme; participation on a safety monitoring board from MD Serono; leadership or fiduciary role in other board, society, committee or advocacy group, paid or unpaid from the International Society of Liquid Biopsy (Vice President), the International Association for the Study of Lung Cancer (Deputy Chair of the Educational Committee), European School of Oncology (Scientific Board Member), the European Society for Medical Oncology (Faculty of Advanced Lung Cancer), and research support (unpaid) from Guardant Health. EdA reports research support and grants from Roche; and grants from Libbs, Pierre Fabre, Zodiacs, Seattle Genetics, Novartis, Roche, Servier, AstraZeneca, and GlaxoSmithKline, outside the submitted work. OA reports personal fees from Pfizer, Lilly, Merck, and Bristol Myers Squibb; and grants and personal fees from

AstraZeneca, Boehringer Ingelheim, and Roche, outside the submitted work. RD declares advisory role for Roche and Boehringer Ingelheim; speaker's fees from Roche, Ipsen, Amgen, Servier, Sanofi, Libbs, and Merck Sharp & Dohme; and research grants from Merck and Pierre Fabre, outside the submitted work. EC reports honoraria for lectures and consulting or advisory role from Merck outside the submitted work. All other authors declare no competing interests.

Acknowledgments

We thank Linda S Kennedy for revising the text for language and grammar.

References

- Sung H, Ferlay J, Siegel RL, et al. Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA Cancer J Clin* 2021; **71**: 209–49.
- Kielstra P. Cancer control, access and inequality in Latin America. A tale of light and shadow. London: Economist Intelligence Unit, 2017. https://eiperspectives.economist.com/sites/default/files/Can cercontrol%2CaccessandinequalityinLatinAmerica_0.pdf (accessed July 17, 2021).
- Strasser-Weippl K, Chavarri-Guerra Y, Villarreal-Garza C, et al. Progress and remaining challenges for cancer control in Latin America and the Caribbean. *Lancet Oncol* 2015; **16**: 1405–38.
- Rosa DD, Bines J, Werutsky G, et al. The impact of sociodemographic factors and health insurance coverage in the diagnosis and clinicopathological characteristics of breast cancer in Brazil: AMAZONA III study (GBECAM 0115). *Breast Cancer Res Treat* 2020; **183**: 749–57.
- Martinez-Cannon BA, Zertuche-Maldonado T, de la Rosa Pacheco S, et al. Comparison of characteristics in Mexican women with breast cancer according to healthcare coverage. *Womens Health* 2020; **16**: 174550652094941.
- De-la-Cruz-Ku G, Luyo M, Morante Z, et al. Triple-negative breast cancer in Peru: 2000 patients and 15 years of experience. *PLoS One* 2020; **15**: e0237811.
- Shcolnik W, Chaves C, Ferreira CE dos S, Sanches C. Clinical Laboratories Accreditation Program of the Brazilian Society of Clinical Pathology/Laboratory Medicine (PALC/SBPC-ML): 15-year experience. *Am J Med Qual* 2015; **30**: 294–95.
- Evans AJ, Salama ME, Henricks WH, Pantanowitz L. Implementation of whole slide imaging for clinical purposes issues to consider from the perspective of early adopters. *Canada Arch Pathol Lab Med* 2017; **141**: 944–59.
- Holmström O, Linder N, Kaingu H, et al. Point-of-care digital cytology with artificial intelligence for cervical cancer screening in a resource-limited setting. *JAMA Netw Open* 2021; **4**: e211740.
- Ibrahim A, Gamble P, Jaroensri R, et al. Artificial intelligence in digital breast pathology: techniques and applications. *Breast* 2020; **49**: 267–73.
- Williams B, Hanby A, Millican-Slater R, et al. Digital pathology for primary diagnosis of screen-detected breast lesions – experimental data, validation and experience from four centres. *Histopathology* 2020; **76**: 968–75.
- Roche. Roche launches two digital pathology image analysis algorithms for precision patient diagnosis in breast cancer. 2021. <https://www.roche.com/investors/updates/inv-update-2021-01-11c.htm> (accessed Aug 15, 2021).
- Lab Network. Grupo Dasa investe em digitalização e inteligência artificial e inicia uma nova Era na Patologia do país. Lab Network, 2018. <https://www.labnetwork.com.br/noticias/grupo-dasa-investe-em-digitalizacao-e-inteligencia-artificial-e-inicia-uma-nova-era-napatologia-do-pais> (accessed Oct 7, 2021).
- Philips. Tecnología Philips IntelliSite en el primer laboratorio de patología digital completamente automatizado en México. Philips, 2021. <https://www.philips.com.mx/a-w/about/news/archive/standard/news/press/2021/20210421-philips-intellisite-technology-in-first-fully-automated-digital-pathology-laboratory-in-mexico.html>.
- Steuten L, Goulart B, Meropol NJ, Pritchard D, Ramsey SD. Cost effectiveness of multigene panel sequencing for patients with advanced non-small-cell lung cancer. *JCO Clin Cancer Inform* 2019; **3**: 1–10.
- Torres Á, Oliver J, Frecha C, et al. Cancer genomic resources and present needs in the Latin American region. *Public Health Genomics* 2017; **20**: 194–201.
- Mascarenhas E, Gelatti AC, Araújo LH, et al. Comprehensive genomic profiling of Brazilian non-small cell lung cancer patients (GBOT 0118/LACOG0418). *Thorac Cancer* 2021; **12**: 580–87.
- The Global Cancer Observatory. Latin American and the Caribbean. 2021. <https://gco.iarc.fr/today/data/factsheets/populations/904-latin-america-and-the-caribbean-fact-sheets.pdf> (accessed Aug 15, 2021).
- GSM Association. The Mobile Economy Latin America 2020. <https://www.gsma.com/mobileeconomy/latam/> (accessed June 6, 2021).
- International Telecommunication Union. Question 14-2/2: Mobile eHealth solutions for developing countries. Geneva: International Telecommunication Union, 2010.
- Palacios U, Hernández-Rendón M, Gaviria-Lopez A, et al. Effectiveness of text messages, calls and e-mail on adherence to medical appointments. Review of systematic reviews and meta-analysis. *Ces Med* 2018; **32**: 14–22.
- Rico TM, dos Santos Machado K, Fernandes VP, et al. Use of text messaging (SMS) for the management of side effects in cancer patients undergoing chemotherapy treatment: a randomized controlled trial. *J Med Syst* 2020; **44**: 193.
- Rico TM, dos Santos Machado K, Fernandes VP, et al. Text messaging (SMS) helping cancer care in patients undergoing chemotherapy treatment: a pilot study. *J Med Syst* 2017; **41**: 181.
- Ziegler S, Segura JA, Bosio M, Camacho K. Rural connectivity in Latin America and the Caribbean: a bridge for sustainable development in a time of pandemic. Inter-American Institute for Cooperation on Agriculture, Inter-American Development Bank, Microsoft. <https://repositorio.iica.int/bitstream/handle/11324/12896/BVE20108887i.pdf> (accessed Oct 7, 2021).
- Abaza H, Marschollek M. mHealth application areas and technology combinations: a comparison of literature from high and low/middle income countries. *Methods Inf Med* 2017; **56**: e105–22.
- Kamdar M, Centi AJ, Agboola S, et al. A randomized controlled trial of a novel artificial intelligence-based smartphone application to optimize the management of cancer-related pain. *J Clin Oncol* 2019; **37** (suppl): 11514 (abstract).
- Sirintrapun SJ, Lopez AM. Telemedicine in cancer care. *Am Soc Clin Oncol Educ Book* 2018; **38**: 540–45.
- Villela PS, Aguiar RR, Macieira GB, et al. Nota Técnica N° 3/2020/DIRAD-DIDES/DIDES. Agência Nacional de Saúde Suplementar, 2020. http://www.ans.gov.br/images/stories/noticias/pdf/Nota_Tecnica_3.pdf (accessed July 12, 2021).
- TELAM. Telemedicina: del 72% que usó el sistema a través del celular, 52% consultó por Covid. 2020. <https://www.telam.com.ar/notas/202012/537914-telemedicina-del-72-que-uso-el-sistema-a-traves-del-celular-52-consulta-por-covid.html> (accessed June 6, 2021).
- Bradesco Seguros. Telemedicina: mais de 111 mil atendimentos online em 2020. Barueri: Bradesco Seguros, 2021. <https://www.bradescoseguros.com.br/clientes/noticias/noticia/telemedicina-mais-de-111-mil-atendimentos-2020> (accessed Oct 6, 2021).
- Carter J, Bababekov YJ, Majmudar MD. Training for our digital future: a human-centered design approach to graduate medical education for aspiring clinician-innovators. *NPJ Digit Med* 2018; **1**: 26.
- Curioso WH. Building capacity and training for digital health: challenges and opportunities in Latin America. *J Med Internet Res* 2019; **21**: e16513.
- Reddy CL, Mitra S, Meara JG, Atun R, Afshar S. Artificial intelligence and its role in surgical care in low-income and middle-income countries. *Lancet Digit Heal* 2019; **1**: e384–86.
- Alami H, Rivard L, Lehoux P, et al. Artificial intelligence in health care: laying the foundation for responsible, sustainable, and inclusive innovation in low- and middle-income countries. *Global Health* 2020; **16**: 52.
- Hosny A, Aerts HJWL. Artificial intelligence for global health. *Science* 2019; **366**: 955–56.
- Norris ET, Wang L, Conley AB, et al. Genetic ancestry, admixture and health determinants in Latin America. *BMC Genomics* 2018; **19**: 861.
- Paul AK, Schaefer M. Safeguards for the use of artificial intelligence and machine learning in global health. *Bull World Health Organ* 2020; **98**: 282–84.
- Guo J, Li B. The application of medical artificial intelligence technology in rural areas of developing countries. *Heal Equity* 2018; **2**: 174–81.

- 39 Booth CM, Karim S, Mackillop WJ. Real-world data: towards achieving the achievable in cancer care. *Nat Rev Clin Oncol* 2019; **16**: 312–25.
- 40 Guinn D, Wilhelm EE, Lieberman G, Khozin S. Assessing function of electronic health records for real-world data generation. *BMJ Evidence-Based Med* 2019; **24**: 95–98.
- 41 PAHO. eHealth in Latin America and the Caribbean: interoperability standards review. Washington, DC: Pan American Health Organization, 2017. <https://iris.paho.org/handle/10665.2/28189> (accessed May 22, 2021).
- 42 The Economist Intelligence Unit. Cancer preparedness in Latin America: the need to build on recent progress. London: Economist Intelligence Unit, 2019. <https://worldcancerinitiative.economist.com/pdf/Roche-cancer-preparedness-in-latin-america/CANCER%20PREPAREDNESS%20IN%20LATAM.pdf> (accessed April 29, 2021).
- 43 Osterman TJ, Terry M, Miller RS. Improving cancer data interoperability: the promise of the Minimal Common Oncology Data Elements (mCODE) initiative. *JCO Clin Cancer Informatics* 2020; **4**: 993–1001.
- 44 Justo N, Espinoza MA, Ratto B, et al. Real-World evidence in healthcare decision making: global trends and case studies from Latin America. *Value Heal* 2019; **22**: 739–49.
- 45 Torres-Grimaldo A. Personalised healthcare in Latin America—universalising the promise of innovation. London: The Economist Intelligence Unit, 2020. https://www.rocche.com.br/content/dam/rochexx/roche-com-br/roche-brazil_rwd/pt_BR/Documentos/PT%20EUI%20Personalised%20medicine%20report.pdf (accessed June 10, 2021).
- 46 Martinez A. Latin American data privacy in 2020: what should employers consider when requesting background checks? Jersey City, NJ: Forbes Media, 2021. <https://www.forbes.com/sites/alonzomartinez/2020/01/02/latin-american-data-privacy-in-2020-what-should-employers-consider-when-requesting-background-checks/?sh=10b2a6dd9c8d> (accessed Oct 7, 2021).
- 47 Rodriguez K, Alimonti V. A look-back and ahead on data protection in Latin America and Spain. San Francisco: Electronic Frontier Foundation, 2020. <https://www.eff.org/deeplinks/2020/09/look-back-and-ahead-data-protection-latin-america-and-spain> (accessed Oct 7, 2021).
- 48 Red Hat. Argentina's Ministry of Health achieves agile infrastructure. Raleigh: Red Hat, 2021. <https://www.redhat.com/en/success-stories/Argentine-Ministry-of-Health> (accessed Oct 7, 2021).
- 49 Oliveira S, Monteiro EL. Medicina de dados: as promessas (e os desafios) do big data na saúde. Galileu, 2019. <https://revistagalileu.globo.com/Ciencia/Saude/noticia/2019/11/medicina-de-dados-promessas-e-os-desafios-do-big-data-na-saude.html> (accessed Oct 7, 2021).
- 50 Potter D, Brothers R, Kolacevski A, et al. Development of CancerLinQ, a health information learning platform from multiple electronic health record systems to support improved quality of care. *JCO Clin Cancer Informatics* 2020; **4**: 929–37.
- 51 Denny JC, Collins FS. Precision medicine in 2030—seven ways to transform healthcare. *Cell* 2021; **184**: 1415–19.
- 52 Drain PK, Parker RA, Robine M, Holmes KK. Global migration of clinical research during the era of trial registration. *PLoS One* 2018; **13**: e0192413.
- 53 Franzoi MA, Procter M, Emond O, et al. Abstract PS7-21: timelines to initiate an adjuvant phase III trial across the globe: a sub-analysis of the APHINITY trial. San Antonio Breast Cancer Virtual Symposium; San Antonio, TX, USA; Dec 8–11, 2020 (abstr PS7-21).
- 54 Angel MO, Colombo Bonadio R, Harada G, et al. Mentoring as an opportunity to improve research and cancer care in Latin America (AAZPIRE project). *ESMO Open* 2020; **6**: e000988.
- 55 Ruiz-Patiño A, Cardona AF, Arrieta O, et al. Scientific publications in cancer: in Latin America, strong scientific networks increase productivity (the TENJIN study). *J Clin Epidemiol* 2020; **126**: 1–8.
- 56 Perez-Santos M, Anaya-Ruiz M, Bandala C. Contribution of Latin American countries to cancer research and patent generation: recent patents. *Recent Pat Anticancer Drug Discov* 2017; **12**: 81–93.
- 57 Nature Index 2020 Cancer. Top 200 institutions in cancer research. <https://www.natureindex.com/supplements/nature-index-2020-cancer/tables/overall> (accessed June 5, 2021).
- 58 UNESCO Institute for Statistics. Global investments in R&D. Fact Sheet No. 59, June 2020, FS/2020/SCI/59. Montreal, QC: UNESCO Institute for Statistics, 2020. <http://uis.unesco.org/sites/default/files/documents/fs59-global-investments-rd-2020-en.pdf> (accessed June 5, 2021).
- 59 [No author listed]. Global overview. *Nature* 2014; **515**: S56–57.
- 60 Angelo C. Brazilian scientists reeling as federal funds slashed by nearly half. *Nature* 2017; published online April 3. <https://doi.org/10.1038/nature.201721766>.
- 61 Pérez Ortega R, Wessel L. 'We're losing an entire generation of scientists.' COVID-19's economic toll hits Latin America hard. <https://www.sciencemag.org/news/2020/08/we-re-losing-entire-generation-scientists-covid-19-s-economic-toll-hits-latin-america> (accessed Aug 14, 2021).
- 62 da Silva RE, Amato AA, Guilhem DB, de Carvalho MR, Novaes MRCG. International clinical trials in Latin American and Caribbean countries: research and development to meet local health needs. *Front Pharmacol* 2018; **8**: 961.
- 63 Dombrowsky T, Hædersdal M, Lassen U, Thomsen SF. Development in the number of clinical trial applications in Western Europe from 2007 to 2015: retrospective study of data from national competent authorities. *BMJ Open* 2017; **7**: e015579.
- 64 Ministério da Saúde. Portarias definem critérios de classificação e teto de recursos para projetos no âmbito do Pronon e do Pronas/PCD em 2020. Ministério da Saúde, 2020. <https://www.gov.br/saude/pt-br/assuntos/noticias/portarias-definem-criterios-de-classificacao-e-teto-de-recursos-para-projetos-no-ambito-do-pronon-e-do-pronas-pcd-em-2020> (accessed Oct 11, 2021).
- 65 The Economist. The difficulty of doing good in Latin America. London: The Economist, 2020. <https://www.economist.com/the-americas/2020/11/05/the-difficulty-of-doing-good-in-latin-america> (accessed May 28, 2021).
- 66 Unger JM, Nghiem VT, Hershman DL, Vaidya R, Leblanc M, Blanke CD. Association of National Cancer Institute-sponsored clinical trial network group studies with guideline care and new drug indications. *JAMA Netw Open* 2019; **2**: e1910593.
- 67 IQVIA Institute. Global oncology trends 2018: innovation, expansion and disruption. Danbury: IQVIA Institute, 2018. <https://www.iqvia.com/insights/the-iqvia-institute/reports/global-oncology-trends-2018> (accessed May 22, 2021).
- 68 IQVIA Institute. The global use of medicine in 2019 and outlook to 2023. Danbury: IQVIA Institute, 2019. <https://www.iqvia.com/insights/the-iqvia-institute/reports/the-global-use-of-medicine-in-2019-and-outlook-to-2023> (accessed April 27, 2021).
- 69 Broes S, Saesen R, Lacombe D, Huys I. Past, current, and future cancer clinical research collaborations: the case of the European Organisation for Research and Treatment of Cancer. *Clin Transl Sci* 2021; **14**: 47–53.
- 70 Inan OT, Tenaerts P, Prindiville SA, et al. Digitizing clinical trials. *NPJ Digit Med* 2020; **3**: 20.
- 71 Walters SJ, Dos Anjos Henriques-Cadby IB, Bortolami O, et al. Recruitment and retention of participants in randomised controlled trials: a review of trials funded and published by the United Kingdom Health Technology Assessment Programme. *BMJ Open* 2017; **7**: e015276.
- 72 Frampton GK, Shepherd J, Pickett K, Griffiths G, Wyatt JC. Digital tools for the recruitment and retention of participants in randomised controlled trials: a systematic map. *Trials* 2020; **21**: 1–23.
- 73 Badawy R, Hameed F, Bataille L, et al. Metadata concepts for advancing the use of digital health technologies in clinical research. *Digit Biomarkers* 2019; **3**: 116–32.
- 74 Cox SM, Lane A, Volchenboum SL. Use of wearable, mobile, and sensor technology in cancer clinical trials. *JCO Clin Cancer Informatics* 2018; **2**: 1–11.
- 75 Clinical Trials Transformation Initiative. CTTI recommendations: advancing the use of mobile technologies for data capture & improved clinical trials. Durham, NC: Clinical Trials Transformation Initiative, 2021. https://ctti-clinicaltrials.org/wp-content/uploads/2021/06/CTTI_Digital_Health_Technologies_Recs.pdf (accessed April 29, 2021).
- 76 Ly JJ, Crescioni M, Eremenco S, et al. Training on the use of technology to collect patient-reported outcome data electronically in clinical trials: best practice recommendations from the ePRO Consortium. *Ther Innov Regul Sci* 2019; **53**: 431–40.

- 77 Anderson A, Borfritz D, Getz K. Global public attitudes about clinical research and patient experiences with clinical trials. *JAMA Netw Open* 2018; **1**: 182969.
- 78 Sedrak MS, Sun CL, Hershman DL, et al. Investigator use of social media for recruitment of patients for cancer clinical trials. *JAMA Netw Open* 2020; **3**: e2031202.
- 79 Thompson MA, O'Regan RM. Social media and clinical trials: the pros and cons gain context when the patient is at the center. *Cancer* 2018; **124**: 4618–21.
- 80 Kreidler J. COVID-19 clinical trial: real or fake? Learn how to tell the difference. Federal Trade Commission, 2020. <https://www.consumer.ftc.gov/blog/2020/10/covid-19-clinical-trial-real-or-fake-learn-how-tell-difference> (accessed Oct 7, 2021).
- 81 Vazquez J. Researchers see an increase in fraudulent COVID-19 posts on social media. San Diego, CA: UC San Diego Health, 2020. <https://health.ucsd.edu/news/releases/Pages/2020-08-25-researchers-see-increase-in-fraudulent-covid-19-posts-on-social-media.aspx> (accessed Oct 7, 2021).
- 82 Chaffey D. Global social media research summary 2021. Leeds: Smart Insights, 2021. <https://www.smartinsights.com/social-media-marketing/social-media-strategy/new-global-social-media-research/> (accessed June 6, 2021).
- 83 Investigators of the US–Latin America Cancer Research Network. Translational cancer research comes of age in Latin America. *Sci Transl Med* 2015; **7**: 319fs50.
- 84 Seyhan AA. Lost in translation: the valley of death across preclinical and clinical divide – identification of problems and overcoming obstacles. *Transl Med Commun* 2019; **4**: 1–19.
- 85 Miranda JJ, Castro-Ávila AC, Salicrup LA. Advancing health through research partnerships in Latin America. *BMJ* 2018; **362**: k2690.
- 86 Arrieta O, Cardona AF, Martín C, et al. Updated frequency of EGFR and KRAS mutations in NONSmall-cell lung cancer in Latin America: the Latin-American consortium for the investigation of lung cancer (CLICaP). *J Thorac Oncol* 2015; **10**: 838–43.
- 87 Carrot-Zhang J, Soca-Chafre G, Patterson N, et al. Genetic ancestry contributes to somatic mutations in lung cancers from admixed Latin American populations. *Cancer Discov* 2021; **11**: 591–98.
- 88 Gerson R, Zatarain-Barrón ZL, Blanco C, Arrieta O. Access to lung cancer therapy in the Mexican population: opportunities for reducing inequity within the health system. *Salud Publica Mex* 2019; **61**: 352–57.
- 89 Garralda E, Dienstmann R, Piris-Giménez A, Braña I, Rodon J, Tabernero J. New clinical trial designs in the era of precision medicine. *Mol Oncol* 2019; **13**: 549–57.
- 90 Faulkner E, Holtorf AP, Walton S, et al. Being precise about precision medicine: what should value frameworks incorporate to address precision medicine? A report of the Personalized Precision Medicine Special Interest Group. *Value Health* 2020; **23**: 529–39.
- 91 Market Data Forecast. Latin America precision medicine market research report—segmented by technology, application, by country (Brazil, Argentina, Mexico, Chile and rest of Latin America)—size, share, trends, growth opportunities assessment, industry forecast (2021 to 2026). Hyderabad: Market Data Forecast, 2021. <https://www.marketdataforecast.com/market-reports/latin-america-precision-medicine-market> (accessed June 5, 2021).
- 92 Vicente AM, Ballensiefen W, Donertas D, et al. The ICPerMed vision for 2030. How can personalised approaches pave the way to next-generation medicine? Cologne: DLR Project Management Agency, 2019. https://www.icpermed.eu/media/content/Vision_Paper_2019.pdf (accessed April 26, 2021).
- 93 Westphalen BC, Bokemeyer C, Büttner R, et al. Conceptual framework for precision cancer medicine in Germany: consensus statement of the Deutsche Krebshilfe working group 'Molecular Diagnostics and Therapy'. *Eur J Cancer* 2020; **135**: 1–7.

© 2021 Elsevier Ltd. All rights reserved.