

SOCIAL DISTANCING AND ECONOMIC CRISIS DURING COVID-19 PANDEMIC REDUCED CANCER CONTROL IN LATIN AMERICA AND WILL RESULT IN INCREASED LATE-STAGE DIAGNOSES AND EXPENSE

Summary Report

Since December 2019, the World has been mired in an infectious pandemic that has displaced other health priorities for 21st-century populations. The social significance and speed of contagion from the coronavirus pandemic have altered criteria for public health prioritization. This has been detrimental to other health problems, including non-communicable diseases (NCDs), which are recognized as the leading cause of preventable illness and premature death.

According to the World Health Organization (WHO), NCDs are responsible for three out of every four deaths in the World. Cancer is the second most frequent, after cardiovascular diseases (1).

Likewise, in Latin America and the Caribbean, cancer ranks second as a cause of death, with 672,758 deaths from cancer recorded in 2018. During 2018, the incidence of new cases rose to 1,412,732. Looking forward, because of the region's aging population and changes in lifestyle, the incidence will increase significantly in coming years (2).

Globally, cancer is one of the leading health challenges. In addition to its importance as a cause of death and suffering, there are increasing incidence rates and rising costs of health care in oncology (3). Several factors appear can explain the increase in cancer morbidity and mortality in the world, in particular the increase in life expectancy and in the exposure to cancer risk factors associated with lifestyle and social and economic development (4).

Worldwide, almost 70% of cancer deaths occur in countries ranking as medium or low on the Human Development Index (HDI). Poverty, including less access to education and health care, exposes residents to greater risk of developing and dying from cancer. According to WHO, in low-income countries less than 30% of patients diagnosed with cancer have access to treatment; in high-income countries, more than 90% of patients diagnosed with cancer have access to treatment (4). At the same time, the development of cancer impacts productivity and family income. This, added to the high costs of treatment, impoverishes families and is an obstacle to the development of countries, helping to widen the gap between the richest countries and those with the lowest incomes.

Modifying this reality is one of the main health challenges and it is possible to face it. Indeed, between 30% and 50% of cancers are potentially preventable if tobacco use and the other main risk factors are controlled- In addition, around 30% are potentially curable if detected early and treated in a timely and appropriate manner (3,5,6). Finally, all patients can benefit from palliative care (3). The failure to promote and develop public policies for prevention, early detection and timely and appropriate treatment, negatively impacts both cancer control and economic development and social welfare.

Published studies on COVID-19 and cancer show that cancer patients with active disease have a higher risk of serious complications and mortality from COVID-19 than the general population,

particularly those with lung neoplastic involvement, myeloid suppressive treatments, advanced age, compromise of their functional status and / or comorbidities (7-11).

Added to the risk of dying from severe complications is the risk resulting from the overflow of the health system in the context of a severe outbreak and the delays in the care of cancer and other diseases as a consequence of the measures implemented to contain the COVID-19 pandemic. Indeed, the immediate demands of the COVID-19 pandemic have required health systems to focus on containment strategies to minimize mortality. Our collective regional prioritization of COVID-19 and implementation of physical distancing as an intervention strategy has impaired cancer health providers' functioning specifically by postponing cancer screening, in-person consultations, and control tests, as well as limiting treatments that might result in significant risk of infectious complications or require critical care. The impact of public health measures to contain the pandemic are interwoven with the changes in habits, behaviors and healthy behaviors and the consequences of the economic crisis, producing an increase in poverty and challenges for patients to access cancer screening and treatment from clinicians in a timely manner (12,13).

Three recent studies from the United Kingdom estimated the possible increase in cancer mortality as a consequence of the pandemic (14-16). Lai et al. reported a 76% reduction in the number of patients referred for a possible cancer diagnosis and a 60% reduction in chemotherapy treatments compared to pre-covid-19 levels. The study concludes that in the 12 months following the pandemic, mortality could increase by 20% -30% in cancer patients (14). Sud et al. used observational studies to generate daily risk rates for cancer progression and applied them to survival by age and disease stage. They estimated that a delay per patient of 3/6 months would cause the attributable death of 4,755 / 10,760 of the 80,406 long-term surviving patients of the total number of patients operated on annually in England for the most frequent invasive cancers in adults (15). On the other hand, Maringe et al. analyzed the possible increase in mortality 5 years after diagnosis for breast (7.9-9.6%), colorectal (15.3-16.6), esophagus (5.8-6.0) and lung (4.8-5.3) cancers with respect to pre-pandemic. As shown, the greatest increase would be observed in relation to colorectal cancer.

In addition to the negative impact on survival, diagnosis in later stages will determine a significant increase in cancer care costs compared to pre-pandemic. This is not minor given the significant economic impact of cancer. Indeed, the total annual economic cost of cancer in 2010 was estimated at approximately US\$ 1.16 trillion and is increasing (3). Although it impacts all countries, it especially affects those with the lowest incomes.

In this regard, a recent Australian study estimated the excess mortality and also the economic impact resulting of diagnostic and treatment delays for 4 cancers (breast, lung, colorectal and melanoma) due to the COVID-19 pandemic (17). To do this, they used a "stage change" model of the disease (model available at: https://cancerhealthservices.shinyapps.io/oncology_stage_shift/). Considering a 3/6-month delay in diagnosis and initiation of treatment, this study predicts almost 90/350 excess deaths and 12/46 million Australian dollars (8.6 / 33 million USD) in healthcare costs in Australia for 5 years for patients diagnosed with these 4 cancers in 2020. The authors emphasize that more accurate data on disease stage during and after the COVID-19 pandemic is essential to obtain more reliable estimates.

Concerned about this situation, a group of Latin American experts on cancer, under the leadership of Dr. Tabaré Vázquez, and based on experience from Uruguay (Document "Proposals for a National Strategic Plan in response to the impact of the COVID-19 pandemic. Uruguay, May 6, 2020"),

decided in May 2020 to carry out a project with the aim to evaluate the impact of the pandemic on cancer control in the region. Data about the state of cancer control, previous to and during the pandemic, were collected from nine countries in the Latin American region. Concrete proposals were detailed to urgently re-establish the public policies for cancer control and the implementation of cancer prevention interventions post-pandemic.

The project's strategy consisted of convening health leaders from Argentina, Brazil, Chile, Colombia, Honduras, Mexico, Nicaragua, Peru and Uruguay to operationalize country-specific technical teams that would address clinical, economic, health system, and public policy issues for cancer control in what would become this Latin American Report and the Position Paper.

Information from countries reported in public sources/scientific publications on health systems, cancer control prior to the pandemic, the characteristics of the COVID-19 pandemic, the measures implemented by governments and the impact of the pandemic on cancer care and expense in the short and medium-term was collected and analyzed. The proposed measures to prevent/mitigate the negative impact of the pandemic on cancer control and expense were analyzed and detailed.

1.- Characteristics of the health care and cancer control prior to the pandemic, the COVID-19 pandemic and measures implemented by the governments of the region.

The aim of this document is to describe cancer control in nine Latin American countries before the COVID-19 pandemic, the measures implemented by the different governments in the region during the pandemic and healthcare for cancer patients. The percentage of the GNP for health in the region ranges from 6.61% to 2.08% Argentina (6.61%) and Uruguay (6.58%) are the countries with the largest investment in healthcare, whereas Mexico (2.77%) and Guatemala (2.08%) are the countries with the lowest investment levels (18).

Funding for the healthcare systems in Latin America comes mainly from government funds, through taxes, and to a lower extent from both public and private funds, resulting in fragmented healthcare systems which provide coverage for the economically active population (with both public and private funds), and the rest of the population, which translates into a scarcity of resources and inequity in terms of access to healthcare.

The objective of providing universal coverage is not achieved in all the countries 100%. Cancer control in Latin America is characterized by fragmented healthcare systems (19).

Most countries in the region have developed or are going through the implementation phase of National Cancer Control Plans. Uruguay has the most advanced cancer registry in the region, and both local and regional important advances and achievements have been reported such as the population and hospital – based registries in Cali and some provinces in Argentina (20).

As for primary prevention and legislation, the anti-tobacco act and its enforcement in Uruguay, Chile and Colombia, as well as the obesity or malnutrition act in Uruguay, Chile, Colombia and Mexico should be underscored. Most of the countries have national screening programs for breast cancer and cervix cancer, and Uruguay and Argentina for colon cancer.

Most countries have also implemented vaccination programs for the human papilloma virus (HPV) and hepatitis and access to palliative care. The most advanced legislation and the most successful primary and secondary healthcare models in each country might be reproduced in other countries to accelerate cancer control in the region.

The first cases of COVID-19 infection in the region were reported between the last week in February 2020 (Feb 28th in Brazil) and the beginning of the third week (March 17th, 2020) in Guatemala). In most of the countries the first cases were reported between March 3 and 6. To date, September 21st, the most affected countries, in terms of their population, are Brazil and Mexico; Uruguay reports the lowest number of cases.

Facing the healthcare emergency, the governments in the region enforced the guidelines drafted by the World Health Organization (WHO), mainly social distancing. Some days later, and considering when the first cases were reported, governments implemented the closing of both air and land borders, and quarantines (Argentina) since mid-March. The quarantine lasted until early June in some countries (Mexico). This lockdown measures were accompanied by either partial or complete suspension of public transportation which limited social mobility, and considerably reduced the flow of patients in healthcare centers (21).

At the end of April, May and June social lockdown was applied only in some cities or regions; on the other hand, social distancing, hand washing, the use of masks, diagnostic tests and case follow –up were the most important prevention measures implemented.

Facing the pandemic, the healthcare systems in the region allocated both economic and social resources and healthcare infrastructure in response to the prevention, diagnostic and COVID-19 patient management challenge.

The healthcare strategy in Uruguay was the most effective action to reduce the number of cases, although the small population and concentration of urban centers certainly played a role. In Mexico, a large number of hospitals were either refurbished or built to provide care for COVID-19 patients exclusively.

In collaboration with governments, medical societies and oncology societies implemented the recommendations and guidelines drafted by the WHO, and international societies like ASCO and ESMO, and in some countries (Argentina, Uruguay, Chile, Brazil, Peru, Colombia, Honduras) local guidelines were drafted for patient care depending on the characteristics of each particular country.

Social lockdown, restriction in travelling and the refurbishing of hospitals had a negative impact on care for cancer patients. From March to June, screening interventions and visits were postponed leading to delayed diagnosis and timely treatment of the new cases; scheduled surgeries were also postponed just like chemotherapy, radiotherapy and palliative care.

Most of the countries implemented telemedicine programs as an alternative option, i.e. phone visits or remote Internet visits). In the coming months and years we will be in a position to have a more objective assessment of the impact of COVID-19 in the region; however, we can state that postponing screening, delays in diagnosis and timely treatment of new cases, will definitely lead to an increased burden of the disease, so much so that governments will have to increase expenditure in cancer care.

2.- Possible regional impact of the pandemic on cancer control and expense

The pre-pandemic public health situation across Latin America, which typically included fragmented health systems, weak social protection for disadvantaged people, and significant percentages of the population living in poverty, will result in this pandemic probably having a greater impact on cancer control in our region than it will have in countries with better public health services and preparation.

In the present report we compared 2019 and 2020 data from our nine countries for March 16 to June 30, 2020 and found a **significant reduction** - variable depending on the country - in the **number of first-time visits to oncology services** (between -28% and -38%) and a corresponding reduction in **pathology** (between -6% and -50%), **surgery** (between -28% and -70%), and **chemotherapy** (between -2% and -54%) for patients with cancer. The available data on radiotherapy showed a significant reduction in the case of Chile (public subsector sample) and Peru (private provider). On the other hand, and in accordance with international recommendations to postpone screening studies in average-risk patients, a **significant reduction in PAP studies** (between -46% and -100%), **mammography** (between -32 % and -100%) and **colorectal cancer screening test** (Uruguay: -73%) was found.

If the significant decrease in screening tests continues as a trend, there will be a corresponding decrease in recorded cases of cancer, but only in the short term. **But, later, there will be an increase in cancer cases, which will unfortunately include detection of more advanced stage cancers, with consequent increase in cancer mortality and in direct expenses associated with care of patients with more advanced disease.**

Most Latin American countries do not have evaluations on the costs of cancer care, either at the aggregate level or associated with the different cancers and the different stages of the disease, and almost none have information on indirect costs, that is, the resulting costs. of productivity and income losses for patients and their families as a result of premature morbidity and mortality. For this report it was possible to analyze data from Brazil, Peru, Uruguay and Mexico, which are summarized below.

In Brazil, spending on cancer care has had a continuous expansion in recent years and it is estimated that total spending (direct and indirect costs) will reach **US \$ 76 billion in 2020**. A recently published study estimates the average cost of cancer as 1.7% of GDP per year, reaching almost US \$ 60 million in 2015 (22).

In Peru, the Budget Program for Cancer Prevention and Control - 024 (PpR) has significantly increased the allocation of budget resources for cancer prevention and control at the national level (23). The budgetary resources assigned to this program **for the 2017-2019 triennium** increased by 29.49% compared to the period 2011 to 2016, reaching **US \$ 588 million**. In addition, it should be noted that there was a reorientation of the allocations, with an increase of 14% in what was **allocated to treatment, which went on to represent 44.4% (US \$ 260 million) for the years 2017 to 2019**.

In **Uruguay**, the **partial information available** (oncological drugs included in universal coverage, radiotherapy, pathological anatomy, PET-CT and spending on high-priced drugs granted in legal actions), show that **direct spending in 2019**, excluding the data that could not be relieved for this report, amounted to **82 million US dollars**. Considering that health spending reaches approximately

9.5% of GDP in 2019, what is allocated to cancer has a weight of at least 1.63% in said spending, a percentage similar to that reported by Brazil.

In **Mexico**, three public institutions focus the attention of more than 96.78% of the national population: Instituto Mexicano del Seguro Social (IMSS), Instituto de Salud y Seguridad Social para los Trabajadores del Estado (ISSSTE) and the operational part known as Seguro Popular (ref: <https://www.inegi.org.mx/temas/derechohabiencia/>). **Between 3 and 11% of the budget of these Institutions is allocated to cancer care.**

Regarding the **costs of studies and treatments for cancer care**, we have data on breast cancer care with **funds from the Seguro Popular de México**, a program that operated from 2003 to 2019, the corresponding public information being available to the latter (24). The total **annual budget per patient was US \$ 135,372** on average.

When direct costs for systemic treatment are analyzed according to the stage and biological profile of breast cancer (hormone sensitive, HER2 positive, HER2 negative or triple negative), it is observed that **for HER2 negative breast cancer, the Stage IV treatment reaches US \$ 6,368 per patient**, doubling the cost of treating patients with stage IIB-III and **tripling that of those with stage IA and IIA**. **If hormone therapy is associated with an inhibitor of cyclin D1/CDK4 and CDK6**, such as ribociclib, **the cost per patient would be 27 times higher than the cost of treating invasive cancer diagnosed in earlier stages** and approximately **600 times the cost of treating non-invasive carcinoma (stage 0)**. For patients with **metastatic HER2-positive breast cancer** (23% of breast cancers in Mexico), the **cost per patient of treatment with Trastuzumab, Pertuzumab and chemotherapy doubles the cost for the treatment of patients with disease in earlier stages** (U \$ 38,796 vs. 21,000) and is **154 times higher than the cost of patients with carcinoma in situ (stage 0)** whose average is U \$ 251.45.

These results are consistent with those published by European and North American countries (25-27), however, the level of resources and economic capacity in Latin American countries is much lower, which allows predicting a more deleterious economic impact for our health systems.

The significant and growing costs of cancer control negatively impact health systems, reducing access with equity and sustainability. This impact is greater in countries with fewer resources and will be even greater in the future due to the presentation in more advanced stages of the disease as a consequence of delays in cancer care during the pandemic.

3.- Proposed prevention/mitigation measures

Health emergencies often have a severe impact on people's lives and well-being. The coordinated response by a country, region, or sector favors preventive and mitigation aspects. Strong, sustainable, and resilient health systems are essential to respond to health challenges for the health, well-being, and economic productivity of populations and their development.

PROPOSALS

To reduce the impact of cancer on populations at the regional level and prevent an uncontrollable situation from being generated in the coming years in public health, we propose the following:

- ✓ Strengthening the planning of actions against cancer through Primary Health Care.
- ✓ Building and development of health policies based on the prevention and care of cancer in its different stages.
- ✓ Design and implementation of a clear, agile, and precise information and statistical instrument for the Americas to develop better cancer prevention and control policies in the region.
- ✓ Linking the region's health systems and seeking intersectoral and inter-institutional collaboration in reducing the impact of cancer in the community.

SHORT-TERM RECOMMENDATIONS

A) Individual dimension

In the particular field, the healthy and sick population must maintain a broad health behavior, avoiding contagion problems by the virus. It would help if you contact your doctor, preferably remotely, asking which situations you can defer and which ones should have immediate attention. Within reason, preventive and control advice for chronic diseases (hypertension, diabetes, obesity, etc.) should be followed, according to the official recommendations and regulations and those of medical societies.

B) Medical dimension

Care modalities adapted to existing conditions, including greater use of teleconsultation and tele-diagnosis should be applied. In the therapeutic area, treatment modalities must be adjusted, implying less mobility and contact between patients and between patients and the healthcare environment; short courses of radiotherapy, outpatient or home chemotherapy, shorter surgical interventions, and less post-surgical stay. In all these cases, the correct evaluation of situations that may be deferred or require external consultation or hospitalization must be agreed with the existing general protocols. In this regard, we understand it necessary to adapt clinical practice guidelines for the management of cancer patients according to local pandemic situations, best available evidence, and with adjustments made to accommodate the level of resources and characteristics of the health system.

C) Health Systems Dimension

In this regard, it is necessary:

- ✓ Guaranteeing access to oncology services, including support for patient transportation, elimination of economic barriers (out-of-pocket payments), and the use of communication technologies for remote patient assessment and monitoring.
- ✓ Developing communication and education programs that appropriately guide cancer patients to understand the risk of infection by Sars-Cov-2 versus the risk of inappropriate control of their disease such as missing treatments for fear of the virus.
- ✓ Enabling various levels of care and non-specialized professionals to be involved in oncology and the care of cancer patients, through the appropriate use of communication tools, the

constitution of care networks, and structuring of clinical referrals with different levels of responsibility.

- ✓ Developing strategic operational plans for phased reintroduction of activities for early detection of cancer with the aim of reducing the risk of late diagnoses without overwhelming the capacity of oncology services
- ✓ Promoting the development of research on the intersection of COVID-19 and cancer, including its impact on patients, oncology services, and health personnel.

D) Government Policies Dimension

Government and legislative policies are complex issues that will force a discussion on the understanding that societies have of the concept of the "right to health" understood as a broad space, which is related to the comprehensiveness of socioeconomic requirements that determine the possibility that all people - full of dignity - can develop their full potential and enjoy maximum well-being.

In this regard we propose:

- ✓ Developing measures that reduce the pandemic's impact on conditions related to poverty, including strategies for reducing the economic impact of cancer on patients through establishment of ongoing dialogue between the health sector and other sectors of the economy. The desired result is balanced measures protective of health and life, as well as protective of the economic infrastructure.
- ✓ Generating normative operational and economic frameworks that enable and facilitate the implementation of telemedicine.
- ✓ Maintaining, or resuming as soon as possible, measures for control of risk factors, particularly tobacco use, the harmful consumption of alcohol, obesity, sedentary lifestyles, and vaccination against HPV and Hepatitis B.
- ✓ Fast-tracking regional registry systems to assess the impact of the pandemic on cancer care.
- ✓ Promoting regional collaboration and the exchange of learning among government, academic, and health care institutions.

MEDIUM- AND LONG-TERM RECOMMENDATIONS

Initiatives to respond to the pandemic must consider universal access to quality essential health services, both those associated with the coronavirus and other health needs. Health systems and institutions must guarantee access to comprehensive services and incorporate public health criteria that act as axes for strengthening and transforming systems towards universal health coverage. For both agencies, it is clear that these transformations require the strengthening of essential public health functions and governance and financing models that are adequate, effective, equitable, and consistent with a primary health care approach and prioritize populations in vulnerable conditions.

A standard care model is necessary for all public and private providers, which surpasses the market relationship for cooperation, which prevents people from going directly to a specialist or that the gateway remains the emergency of acute hospitals. The care model must ensure that everyone has access to an interdisciplinary family team focused on individuals, families, and communities. For this, new outpatient solutions must be developed in people's habitat; promote the creation of highly complex outpatient and hospital establishments for extended stays, and develop effective networks of social and health care for managing the requirements of older adults, rehabilitation, home management of people without self-sufficiency and palliative and long-term care. It is also necessary to incorporate new management and governance elements in the networks for the effective integration of the actors, ensure intersectoral work and continuity of care; and substantially increase investment in the first level of care. The constitution of an integrated health system implies the definition of a universal health plan that provides a comprehensive response to the main current health problems -among them cancer- and of the future and the generation of a mechanism that unites all sources of financing.

In particular, it is necessary:

- ✓ Ensuring the necessary infrastructure for the prevention, early detection, and treatment of cancer
- ✓ Guaranteeing access to and coverage of essential cancer-related services
- ✓ Empowering patients, their families, and civil society groups to advance cancer prevention, diagnosis, treatment, and rehabilitation.
- ✓ Developing, promoting and implementing National Cancer Control Programs in the face of the new public health realities; defining financing mechanisms, which will protect cancer care in the face of new priorities in public health; and developing flexible operational tools in preparation for inevitable and increasing health threats.
- ✓ Strengthening the implementation of population-based cancer registries using publicly available information to enable real-time planning, monitoring, and evaluation of Cancer Control Plans and agile adjustment and deployment of cancer prevention and control policies.
- ✓ Developing evidence-based clinical practice guidelines stratified according to available resources (human, diagnostic, and therapeutic) to ensure rational use of resources and achieve the best possible care.
- ✓ Developing administrative databases to understand aggregated expenses associated with cancer care, by disease stage and site, to promote more efficient use of resources.
- ✓ Promoting well-trained teams of biostatisticians and health economists for evaluating the quality of the data collected and useful analysis.
- ✓ Supporting innovation and the development of translational academic research.
- ✓ Developing strategic operational plans for phased reintroduction of activities for early detection of cancer with the aim of reducing the risk of late diagnoses without overwhelming the capacity of oncology services

Main recommendations

Personal: Maintain prevention and monitoring. Avoid stopping cancer treatment. Ask your doctor.

Medical: Medical response to patients about what can be delayed, what decision they have options, and what to do, even during the crisis.

Health Systems: Maintain functional and operational health systems for cancer patients. To develop strategic operational plans for phased reintroduction of activities for early detection of cancer. Avoid excessive focus only on the COVID epidemic. Resilient health systems.

Public Policies: Preserve operational and funded National Cancer Plans.

Challenges

The control of cancer and NCDs in general in the post-pandemic setting

How governments and health systems will cope with the largest number of patients with delays, along with the usual volume, in the post-pandemic.

The highest estimated number of patients with late diagnosis and more advanced stages of the disease.

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