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Improving childhood cancer care in Latin America and the Caribbean: a PAHO Childhood Cancer Working Group position statement

Most children with cancer live and die in low-income and middle-income countries (LMICs). Medical and health system advances have brought cure to more than 80% of children with cancer in high-income countries (HICs),[1] but such advances have eluded children in most LMICs, where inequities can yield cure percentages anywhere from 5% to 60%.[2] Multiple factors contribute to the inadequate care of childhood cancers in LMICs, including resource scarcity, health system fragility, limited provider awareness, and absence of political attention.[3] These conditions are abetted by a lack of sustained political attention to childhood cancer at the international level. Despite a growing global burden of non-communicable diseases (NCDs), calls by global health governance institutions to address NCDs have largely failed to address the plight of children with cancer in LMICs.

A longstanding commitment by childhood cancer professionals and advocates in Latin America and the Caribbean has contributed to substantial, if variable, progress towards understanding the burden of childhood cancer and improving childhood cancer services in the region.[4] Past and present *Lancet Oncology* Commissions have underscored the challenges and opportunities that cancer presents in the context of strengthening health systems in Latin America.[5] Recent work[6] suggests opportunities to bring such efforts to scale through a strengthening of the policy and system dimensions of childhood cancer care. The Union for International Cancer Control (UICC) convened an international policy dialogue on childhood cancer in Latin America, identifying integrated elements necessary to improve childhood cancer outcomes in the region. The need for pan-regional leadership and collaboration on childhood cancer care was principal among these goals.[6]

As a follow-up to that policy dialogue, the Pan-American Health Organization (PAHO) recently convened a Childhood Cancer Working Group (PAHO-CCWG) to advance the development of health system-level policies and programmes to reduce

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	Challenges	Lessons
Governance	Insufficient governance capacity: absence of national childhood cancer plans, accreditation processes and treatment protocols Competing agendas in context of multiple needs divert attention from childhood cancer	International collaboration as facilitator of knowledge translation for context-sensitive programmes and standards Broad stakeholder engagement is key to increase political visibility of childhood cancer agenda
Access to medicines	Erratic supply of EML medicines for children with cancer: decentralised purchasing, weak procurement and supply management processes, and poor pharmacovigilance	Role of PAHO Strategic Fund to facilitate pooled procurement, improved supply management, and quality assurance to overcome existing market failures
Health workforce	Limited resources invested in human and infrastructural bases of childhood cancer care	Potential to regionalise health workforce training and translate successful models across jurisdictions
Financing	Constrained public resources in the context of competing health system priorities, perceived opportunity costs of resource allocation	Opportunities for innovative financing through cross-sector models, including private sector and civil society in public–private partnerships
Service delivery	Coordination and continuity of care: treatment delay and abandonment due to insufficient diagnostic or therapeutic capacities and sociodemographic barriers	Centralised referral of high complexity care and carefully distributed follow-up as a feasible model to increase coordination across the care continuum
Health information systems	Absence of reliable epidemiological and outcome evidence on which to adjudicate system performance	Opportunities for cross-country diffusion and scale-up of childhood cancer registry structures and processes

EML=WHO essential medicines list.

Table: **Major challenges and lessons for childhood cancer system strengthening in Latin America and the Caribbean**

inequities and improve cancer care of children in the region. The PAHO-CCWG represents a collaboration between domestic governments, international institutions, civil society, and academic partners, aimed at improving systems of childhood cancer care throughout Latin America and the Caribbean. Its inaugural meeting was held at the PAHO headquarters in Washington, DC, USA on Feb 2–3, 2017, with Ministry of Health-nominated representatives from 20 countries in attendance, all of whom had a deep understanding of the realities and complexities of providing childhood cancer care in their respective jurisdictions. The meeting was prefigured by a detailed regional mapping exercise, which drew on the results of interviews and surveys with a range of cancer system stakeholders in participating countries, to discern the major challenges and lessons needed to strengthen childhood cancer systems in the region (table). This exercise delineated both common and differentiating features of childhood cancer policies and programmes, and framed the Working Group's deliberation about potential solutions to address this growing concern. Although PAHO-CCWG members focused on areas that could benefit from supranational collaboration, they recognised the need for individual country context and experience in advancing childhood cancer care that would preclude a one-size-fits-all approach to the region.

The purpose of the PAHO-CCWG is to support the development of equitable, responsive, and evidence-based systems of childhood cancer care through structured knowledge exchange, capacity building, and collaboration, to improve outcomes for all children with cancer in Latin America and the Caribbean. Core functions of the Working Group include: (1) health system evidence development; (2) knowledge exchange and capacity building among country-level stakeholders; (3) knowledge translation for policy development on issues with regional scope; and (4) regional interface with national governments.

Because of its collaboration between national Ministries of Health throughout the region, PAHO, the UICC, and North and South American academic partners, we believe that the Working Group is uniquely positioned to identify and promote effective strategies for policy reform and health system strengthening for children with cancer. We are committed to a belief in collective action to advance the development of childhood cancer care strategies in Latin America and the Caribbean, with a focus on generating and sharing data for public health use, shaping primary care for early detection and diagnosis, and improving access to affordable childhood cancer medicines aligned with the WHO model essential medicines list. We hope that such efforts will bear fruit for children living with cancer in the region. Furthermore, we note the potential for concerted efforts at improving childhood cancer services to strengthen the broader health systems in which they sit. To this end, we call on national governments and on the international community to ensure that childhood cancer remains on the political agenda as part of global efforts to reduce child mortality, to address NCDs, and to achieve universal health coverage. Our vision is for a world where the cure of childhood illness is bounded by the limits of our knowledge, not the vagaries of our political systems.

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Under-representation of peritoneal metastases in published clinical trials of metastatic colorectal cancer

The present landscape of clinical trials for metastatic colorectal cancer is dominated by visceral metastases, as was highlighted at the recent American Society of Clinical Oncology Gastrointestinal Cancers conference held in San Francisco, CA, USA, in 2017. Peritoneal metastases are difficult to image by cross-sectional imaging and this leads to a disproportionate under-representation of this site of metastases in clinical trials.

Peritoneal metastases differ in their presentation from visceral metastases, which are often incidentally detected. Peritoneal metastases tend to be more symptomatic, leading to bowel obstructions, hydro-ureter, and ascites, which rapidly lead to inanition and death. Additionally, peritoneal metastases tend to have a higher percentage of the worse prognosis *BRAF*-mutated tumours compared with other sites. This is seen in pooled analysis of NCCTG trials, which showed a median survival of 12·7 months compared with 17·6 months for other disease sites (hazard ratio 1·32, 95% CI 1·15–1·50, p=0·001).[1]

The true incidence of isolated peritoneal-only metastases is difficult to ascertain. The National Comprehensive Cancer Network guidelines quote an incidence of 2%, extrapolated from the pooled analysis of clinical trials. This might be disproportionately lower than the true incidence of isolated peritoneal disease, because of the systematic exclusion of such patients from the same clinical trials that were used to calculate incidence. In fact, autopsy series of 5817 autopsies revealed an incidence of 6% isolated peritoneal metastases in adenocarcinomas and 15% isolated peritoneal metastases in mucinous adenocarcinomas and signet-ring cell carcinomas.[2] The percentage of patients with any peritoneal metastases was 20% in adenocarcinomas, 48% in mucinous adenocarcinomas, and 51% in signet-ring cell carcinoma. Although it is possible that patients dying of peritoneal disease are over-represented in autopsy series, it is intriguing to

	Number of patients in treatment groups	Number of patients with peritoneal disease (%)
Ducreux, *Lancet Oncology* 2011[3]	410	63 (15·4%)
Hong, *Lancet Oncology* 2012[4]	340	73 (21·5%)
Jonker, *NEJM* 2007[5]	572	45 (7·9%)
Seymour, *Lancet* 2007[6]	2135	288 (13·5%)
Seymour, *Lancet Oncology* 2013[7]	460	99 (21·5%)
Tournigand, *Lancet Oncology* 2015[8]	700	83 (11·9%)
Yoshino, *Lancet Oncology* 2012[9]	169	28 (16·6%)

Table: **Clinical trials that included patients with peritoneal metastases from published clinical trials for metastatic colorectal cancer (72 clinical trials, 45 783 patients)**