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McMaster HEALTH FORUM

ADVANCING THE DEVELOPMENT OF NATIONAL CHILDHOOD CANCER-CARE STRATEGIES IN LATIN AMERICA

EVIDENCE >> INSIGHT >> ACTION

Evidence Brief:
Advancing the Development of National Childhood Cancer-care Strategies in Latin America

8 June 2015

McMaster Health Forum

For concerned citizens and influential thinkers and doers, the McMaster Health Forum strives to be a leading hub for improving health outcomes through collective problem solving. Operating at regional/provincial levels and at national levels, the Forum harnesses information, convenes stakeholders, and prepares action-oriented leaders to meet pressing health issues creatively. The Forum acts as an agent of change by empowering stakeholders to set agendas, take well-considered actions, and communicate the rationale for actions effectively.

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Merit review

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KEY MESSAGES

What's the problem?

- Latin America faces a heavy (but inconsistently measured) burden of childhood cancer morbidity and mortality.
- Access to childhood cancer care is inconsistent and limited, with significant differences in outcomes within and between countries in Latin America, as a result of inequities in access to diagnosis and treatment.
- There is a need for more coordinated system-wide practices and policies to strengthen childhood cancer control in Latin America as part of broader efforts to improve child health and strengthen health systems.
- Childhood cancer receives limited attention from policymakers despite its importance for reducing childhood mortality and improving health over the life course.

What do we know (from systematic reviews) about three viable options to address the problem?

- Element 1 – Convene a multi-stakeholder, pan-regional task force with national working groups to develop and oversee the implementation of national childhood cancer strategies to support cancer care in Latin American countries
  - This element might include activities to: 1) identify a clear picture of the challenges across Latin American countries related to addressing childhood cancer; and 2) engage in priority-setting processes to develop priorities as well as meaningful and achievable targets.
  - A framework highlighted the importance of identifying the causes of a policy challenge at different levels (individual motivation, team-level tasks, professional roles, organizational rules and system-level strategies), and a review focused on deliberative dialogues as a mechanism that can be used to further understand the challenge.
  - None of the four reviews we identified about priority-setting processes included an explicit assessment of benefits, harms and costs, but they did provide information related to key elements of such processes (e.g., use of formal or informal processes and the use of quantitative, qualitative and mixed techniques that can be used to elicit preferences from stakeholders).
- Element 2 – Develop health-system guidance to support the implementation of childhood cancer-care strategies based on national contexts, as well as integration with national cancer care control programs
  - Activities to develop health-system guidance might include: 1) creating a continuously updated knowledge 'hub'; 2) engaging the full spectrum of child and adolescent health stakeholders, as well as consumers to develop and refine guidance; and 3) developing 'workbooks' to support the implementation of the guidance in specific Latin American contexts.
  - Several systematic reviews point to benefits of stakeholder- and consumer-engagement processes, which include: ensuring that evidence is interpreted with the end user in mind, and developing final products that are readable and accessible; facilitating wider dissemination and uptake of the research findings; and supporting knowledge acquisition among stakeholders and consumers.
- Element 3 – Build capacity for monitoring and evaluation to support efforts to continuously refine the implementation of national childhood cancer-care strategies
  - This element could include activities to: 1) build system capacities for systematic monitoring and evaluation (especially through cancer registries); 2) identify relevant indicators and outcomes that can be tracked between countries; and 3) monitor and evaluate the extent of implementation, and adjust country-specific plans accordingly.
  - We did not identify any systematic reviews that were directly relevant to this element, but an essential component will be the development and implementation of robust national cancer registries with data specifically related to childhood cancer.

What implementation considerations need to be kept in mind?

- Implementing these elements will hinge crucially on: 1) making the case that addressing childhood cancer is not a competing policy priority, but rather one that is important for reducing childhood mortality, improving health over the life course and strengthening health systems; 2) building regional and national buy-in for the objectives and design of a multi-stakeholder taskforce; 3) engaging international and national organizations (e.g. child and adolescent health, non-communicable diseases, and cancer-specific networks) to encourage recognition of and joint action on childhood cancer policies; and 4) building capacity to develop health-system guidance as well as monitoring and evaluation.

REPORT

The burden of cancer morbidity and mortality will fall most heavily on low- and middle-income countries (LMICs).(1) The recent UN Political Declaration on non-communicable diseases (NCDs) calls on each Member State to incorporate NCDs – principally, diabetes, cardiovascular disease, lung disease and cancer – into their health plans and development agendas.(2) Taking action on childhood cancer is also a key component to addressing several global strategic objectives, including the Millennium Development Goal (MDG) 4 (which calls for a two-thirds reduction in global child mortality by 2015), the UN Secretary-General's Global Strategy for Women's and Children's Health, and the WHO-led Partnership for Maternal, Newborn and Child Health.

Children with cancer in high-income countries (HICs) have benefited from significant advances over the past several decades, and now enjoy overall cure rates above 80%.(3) Survival rates in LMICs, however, are estimated to be 5-60%.(4) Adjusting for incidence, approximately 186,000 children are known to develop cancer annually, of which only 22,000 live in HICs.(5) Further improvements in the global burden of pediatric cancer therefore require action in LMICs.

Considerable knowledge and effort exists on addressing the childhood cancer burden in LMICs. Several Latin American countries are developing local services and improving survival rates. However, in most places these advances have not translated into national strategies for childhood cancer care. Moreover, significant variation in levels of policy development, health-system capacity and political engagement persist within and across the countries in the region.

It is therefore timely to ask what can be done to advance the development of national childhood cancer-care strategies in Latin America. The Union For International Cancer Control, in commissioning this evidence brief (and the stakeholder dialogue it was prepared to inform), is seeking to advance these discussions to strengthen childhood cancer care in Latin American countries.

Therefore, the full range of system-level resources for addressing childhood cancer is in scope for the brief (and dialogue). This refers to detection, diagnosis and treatment. The brief therefore includes reference to cancer registration and outcomes data, supportive and

Box 1: Background to the evidence brief

This evidence brief mobilizes both global and local research evidence about a problem, three options for addressing the problem, and key implementation considerations. Whenever possible, the evidence brief summarizes research evidence drawn from systematic reviews of the research literature and occasionally from single research studies. A systematic review is a summary of studies addressing a clearly formulated question that uses systematic and explicit methods to identify, select and appraise research studies and to synthesize data from the included studies. The evidence brief does not contain recommendations, which would have required the authors of the brief to make judgments based on their personal values and preferences, and which could pre-empt important deliberations about whose values and preferences matter in making such judgments.

The preparation of the evidence brief involved five steps:

1) convening a Steering Committee comprised of representatives from the partner organizations (and/or key stakeholder groups) and the McMaster Health Forum;
2) developing and refining the terms of reference for an evidence brief, particularly the framing of the problem and three viable elements of a comprehensive approach for addressing it, in consultation with the Steering Committee and a number of key informants, and with the aid of several conceptual frameworks that organize thinking about ways to approach the issue;
3) identifying, selecting, appraising and synthesizing relevant research evidence about the problem, options and implementation considerations;
4) drafting the evidence brief in such a way as to present concisely and in accessible language the global and local research evidence; and
5) finalizing the evidence brief based on the input of several merit reviewers.

The three elements of a comprehensive approach for addressing the problem were not designed to be mutually exclusive. They could be pursued simultaneously or in a sequenced way, and each element could be given greater or lesser attention relative to the others.

The evidence brief was prepared to inform a stakeholder dialogue at which research evidence is one of many considerations. Participants' views and experiences and the tacit knowledge they bring to the issues at hand are also important inputs to the dialogue. One goal of the stakeholder dialogue is to spark insights – insights that can only come about when all of those who will be involved in or affected by future decisions about the issue can work through it together. A second goal of the stakeholder dialogue is to generate action by those who participate in the dialogue, and by those who review the dialogue summary and the video interviews with dialogue participants.

palliative care, prevention of treatment abandonment and non-adherence, and principles for adapting treatment regimens to local conditions. This brief does not, however, address clinical treatment details, long-term health effects (except in terms of potential resource considerations this has for long-term planning) and childhood cancer prevention (given that most childhood cancers are not thought to be preventable). Additional background about the process of preparing the brief is provided in Box 1.

The evidence brief gives particular attention to people of low socioeconomic status (SES), and people living in areas that are geographically remote from cancer treatment, and/or in rural/remote areas (see Box 2).

This evidence brief refers to a number of key concepts which we define below.

- *Childhood cancer*: malignant diseases affecting children (ages 0-14) and adolescents (ages 15-19), recognizing that in some countries, the upper age limit for childhood cancer funding and services varies (with many Latin American governments limiting the definition to ages 0-14 years).
- *Cancer care*: includes all cancer-directed diagnosis and treatment (medicine, surgery and radiation), and both medical and psychosocial supportive care (see below) involved in the care of children with cancer.
- *Palliative care*: An essential component of cancer care and an approach that aims to improve the quality of life of patients and their families facing life-threatening illness, through the prevention and relief of suffering. This is done through early identification and treatment of pain and distress .(6)
- *Supportive care:* a core component of cancer care necessary to support the safe delivery of cytotoxic therapy, and to manage complications of therapy, in children with cancer.
- *Cancer control:* policies and programs aimed at the prevention, detection, diagnosis and treatment of cancer in a population. Most childhood cancers are not thought to be preventable.
- *National cancer care plan/strategy*: a public health program designed to reduce the incidence and mortality of cancer and improve the quality of life of cancer patients in a particular country. This is done through the systematic and equitable implementation of evidence-based strategies for prevention, early detection, treatment and palliation, making the best use of existing health services and available resources.(7)
- *Cancer registry:* an organization for the systematic collection, storage, analysis, interpretation and reporting of data on subjects with cancer. To guide national childhood cancer strategies, registries should be population-based.(8)

Box 2: Equity considerations

A problem may disproportionately affect some groups in society. The benefits, harms and costs of elements of a comprehensive approach to address the problem may vary across groups. Implementation considerations may also vary across groups.

One way to identify groups warranting particular attention is to use "PROGRESS," which is an acronym formed by the first letters of the following eight ways that can be used to describe groups†:

- place of residence (e.g., rural and remote populations);
- race/ethnicity/culture (e.g., First Nations and Inuit populations, immigrant populations and linguistic minority populations);
- occupation or labour-market experiences more generally (e.g., those in "precarious work" arrangements);
- gender;
- religion;
- educational level (e.g., health literacy);
- socio-economic status (e.g., economically disadvantaged populations); and
- social capital/social exclusion.

The evidence brief strives to address the issue of those in Latin American countries, but (where possible) it also gives particular attention to two groups:

- people of low socioeconomic status; and
- people living in areas that are geographically remote from cancer treatment, and/or in rural/remote areas.

Many other groups warrant serious consideration as well, and a similar approach could be adopted for any of them.

† The PROGRESS framework was developed by Tim Evans and Hilary Brown (Evans T, Brown H. Road traffic crashes: operationalizing equity in the context of health sector reform. *Injury Control and Safety Promotion* 2003;10(1-2): 11–12). It is being tested by the Cochrane Collaboration Health Equity Field as a means of evaluating the impact of interventions on health equity.

THE PROBLEM

The problem can be understood using the following four themes:

1) Latin America faces a heavy (but inconsistently measured) burden of childhood cancer morbidity and mortality;
2) access to childhood cancer care is inconsistent and limited, with significant differences in outcomes within and between countries in Latin America, as a result of inequities in access to diagnosis and treatment;
3) there is a need for more coordinated system-wide practices and policies to strengthen childhood cancer control in Latin America as part of broader efforts to improve child health and strengthen health systems; and
4) childhood cancer receives limited attention from policymakers despite its importance for reducing childhood mortality and improving health over the life course.

Box 3: Mobilizing research evidence about the problem

The available research evidence about the problem was sought from a range of published and "grey" research literature sources. Published literature that provided a comparative dimension to an understanding of the problem was sought using three health services research "hedges" in MedLine, namely those for appropriateness, processes and outcomes of care (which increase the chances of us identifying administrative database studies and community surveys). Published literature that provided insights into alternative ways of framing the problem was sought using a fourth hedge in MedLine, namely the one for qualitative research. Grey literature was sought by reviewing the websites of a number of organizations, such as Cure4Kids, International Agency for Research on Cancer, International Network for Cancer Treatment and Research, International Society of Paediatric Oncology, Pan American Health Organization, NCD Alliance, UNICEF, Union for International Cancer Control, World Child Cancer and World Health Organization.

Priority was given to research evidence that was published more recently, that was locally applicable (in the sense of having been conducted in Latin American countries), and that took equity considerations into account.

Latin America faces a heavy (but inconsistently measured) burden of childhood cancer morbidity and mortality

Reliable data on the incidence of and mortality from childhood cancers in most Latin American countries is rare. This is mainly because of the limited number of countries with population-based cancer registries, and the challenges with collecting high-quality, health-related data in the region. Some countries have reasonably comprehensive registration of cancer cases. For example, in Brazil, efforts to improve cancer registration have resulted in reasonable-quality data on the burden of childhood cancer.(9) Colombia has a number of long-established regional population-based cancer registries, though data quality varies considerably, from global under-coverage in registration at Bucaramanga and Manizales to disease- and location-specific gaps in registration at Cali and Pasto.(10) In Argentina, hospital-based childhood cancer registries were successfully expanded to cover whole populations.(11) Similar efforts are underway in Guatemala City and San Salvador. However, in many Latin American regions, no high-quality cancer registries exist. Reliable data on the incidence of childhood cancers are therefore still rare.

Leukemia and lymphoma

Exact estimates of, for example, the burden of childhood leukemia in Latin American countries is constrained by under-diagnosis, inconsistent reporting, and lack of comprehensive registry coverage.(12) Substantial variation in leukemia incidence rates has been reported by the International Agency for Research on Cancer (IARC) across Latin American countries ranging from:

- low rates in Brazil (27.8/million/year) and Peru (35.6/million/year);
- mid-range rates in Colombia (41.7/million/year) and Uruguay (43.2/million/year); to
- higher rates in Ecuador (55.4/million/year), Costa Rica (56.5/million/year) and Mexico (75.3/million/year).(13-16)

In contrast, registry studies in Canada and the U.S. document age-standardized leukemia incidence rates of 44.4/million/year and 47.6/million/year, respectively.(17;18) Variation between Latin American countries is likely

mainly because of limited local registry infrastructure coupled with difficulties in diagnosis and referral. It is possible that unique host and leukemia genetic characteristics in specific subpopulations of children (e.g. indigenous groups) may account for some of the variation in incidence and even outcomes.(12;19) However, without high-quality cancer registries, this remains speculative.

We do know that leukemia survival rates in Latin America are worse than in HICs, but with wide variability across countries. For example, recent data on children with acute lymphoblastic leukemia (ALL) in El Salvador have a five-year event-free survival (EFS) of 56% for those with standard-risk ALL, and 49% for those with high-risk ALL, as compared with 85% overall for both standard- and high-risk ALL in Canada.(17;20) Outcomes for acute myeloid leukemia (AML) between LMIC and HIC countries are also very different. LMIC children with AML experience much higher complications of treatment, often leading to death.(21) However, it is possible for LMIC to achieve HIC-like cure rates, as shown in a recent randomized trial for children with low-risk ALL in Brazil where children experienced excellent overall and event-free survival rates of 92.5% and 83.6%.(22) Given that rates of treatment complications leading to death depend on treatment intensity, as well as on local resources, institutional experience, and supportive-care infrastructure, one response has been to adapt treatment regimens to make them appropriate for settings with different resource levels.(23)

Solid and central nervous system (CNS) tumours

Little is known about the epidemiology and burden of childhood solid tumours in most Latin American contexts.(24-26) Available data again show differences across the region. For example, a study of 14 regional population-based cancer registries in Brazil found age-standardized incidence rates of retinoblastoma as high as 15 to 27/million/year among 0-4 year-olds in some states. In contrast, while still high, the age-standardized incidence of retinoblastoma in Mexico (5.8/million/year in 2010) and Argentina (5.0/million/year in 2010) are much lower.(16;27-29) Data from Mexico also suggest a low incidence of neuroblastoma (2.3/million/year in 2010), and an incidence of CNS tumours of 14.2/million/year in 2010.(16;28;29) While Brazil has a similar country-level rate, there is large intra-country variability with CNS tumour incidence ranging from 9.6 to 39 million/year.(9) Again, the relative contribution of inadequate cancer registration versus biologic variation in incidence is unknown.

Predictably, the treatment and outcomes of solid tumours in Latin American countries also vary between the type of tumour and health-system contexts. Pediatric sarcomas are characterized by high rates of metastasis at presentation, treatment abandonment and poor survival. Data from Central America show 30% event-free survival and 40% overall survival at four years.(30) In contrast, five-year event-free survival of 63% for malignant bone tumours and 72% for soft tissue sarcomas have been found in HIC settings.(17) In addition, a recent study of retinoblastoma in Central America reported a five-year overall survival rate of 48%, with 22% of families refusing or abandoning treatment.(26)

Access to childhood cancer care is inconsistent and limited, with significant differences in outcomes within and between countries in Latin America, as a result of inequities in access to diagnosis and treatment

Effective systems of childhood cancer care depend on the broader health system at several important points in the care journey: from initial symptom assessment and recognition, to referral and formal diagnosis, to treatment planning and delivery, to long-term follow-up. This involves education and engagement of both public and health-system stakeholders at the community level;(31) integration of primary health professionals and allied health workers into formal systems of referral to specialized cancer services at accredited centres; and mechanisms for sustained contact and collaboration between tiers of care for ongoing symptom management and disease surveillance. At present, many challenges exist when trying to deliver high-quality cancer care to children in most Latin American countries. These include:

- low overall investments in health, with corresponding limitations in health-system capacity;
- competing public health and health care priorities;(32)
- rural/urban divides and regional inequities in access to care;(16)
- weak systems for childhood cancer detection and registration, resulting in delayed and sometimes missed diagnosis;(13;33)

- unreliable supplies of chemotherapeutics;(32;34) and
- limited access to pediatric formulations of new cancer treatments as well as medical devices that support cancer care and treatment in childhood (e.g., because of policies that unnecessarily delay the inclusion of these formulations and devices on formularies).(35;36)

The multi-modality therapy required for many childhood malignancies (including chemotherapies, radiation, surgery and intensive supportive care) presents significant health-system challenges in many Latin American countries, including:

- insufficient human, infrastructural and technological resources for radiation therapy and oncologic surgery, relative to need;(16)
- geographic challenges related to coordination and delivery of services, with the vast majority of cancer care centralized;(30)
- lack of supportive care infrastructure, including infection control programs, blood products for transfusion, and resources to manage treatment complications, pain and symptoms;(12)
- lack of optimal tools for accurate and timely diagnosis and risk stratification of pediatric malignancies;
- inadequate numbers of nurses who may also have too narrow a scope of practice;
- limited availability of pediatric oncology-specific nursing education; and
- professional cultural barriers to multidisciplinary team-based care.(37-39)

Even when national childhood cancer policy and standards exist, they may not be based on the best available evidence. In addition, they may not be accompanied by systems to ensure adherence to such standards. Significant barriers also exist for effective palliative care, including cultural stigma associated with the use of opioids, leading to limited drug access, inconsistent government support, lack of trained personnel, and lack of palliative care education.(40-42)

Refusal/abandonment of therapy is one of the principal causes of cancer-associated mortality in LMICs, affecting up to 60% of children with cancer. Early abandonment is common, and often follows intensive phases of therapy (e.g. leukemia induction remission), or precedes radical surgery for solid tumours.(43;44) Factors leading to abandonment include difficulties in accessing care because of low SES or geographic distance; poor healthcare worker communication with families; and poor supportive care leading to decreased quality of life. Decreasing abandonment may be accomplished by decreasing logistical and financial burdens on families (e.g., transportation and accommodation) and by using dedicated psychosocial teams in treatment centres. One powerful, albeit partial, means of reducing financial barriers to treatment compliance is the extension of financial coverage to children with cancer. Evidence from Mexico suggests a steady decline in abandonment rates for childhood leukemia treatment from roughly 25% to 4% in the years following the introduction of state-financed health coverage for childhood leukemia under *Seguro Popular*.(16) However, given the many and varied drivers of abandonment, attention to issues beyond the costs of care alone are needed.

There is a need for more coordinated system-wide practices and policies to strengthen childhood cancer control in Latin America as part of broader efforts to improve child health and strengthen health systems

Many different health-system approaches to childhood cancers exist in Latin America, with different models of financing (including amount of coverage for needed care), care delivery, and governance between countries. Some countries have little to no organized pediatric oncology services, while others have institution-specific programming with minimal to no government involvement. A small number of countries have a national policy on childhood cancer.

Over the last two decades, pediatric oncologists in both HICs and LMICs have begun to address the limited access to childhood cancer care. The predominant model has been that of 'twinning partnerships', in which HIC and LMIC institutions collaborate to improve outcomes for children with cancer. Twinning programs have successfully improved infrastructure, enhanced access to drugs and diagnostic tests, provided access to HIC experts, and trained local healthcare providers. These programs can differ considerably in their design, implementation and capacity to finance twinning activities. Clinical research to optimize treatment in LMICs has been a key tool for

progress, and has allowed results from certain LMICs to be applied in others where research infrastructure is lacking.(45-48)

A number of Latin American countries continue to rely on these ad hoc 'twinning partnerships' with HIC institutions for capacity development in the delivery of treatment for childhood cancers. Financing for such programs typically comes from a mix of governmental, HIC institutional and private philanthropic sources, the latter often obtained by local foundations.(36) Seven Central American countries have jointly collaborated across 'twinning' sites through the Asociacio'n de Hemato-Oncología Pediátrica de Centro América (AHOPCA), though levels of government involvement and policy still vary between these countries.(49)

Mexico and Chile represent notable advances toward national policy on childhood cancer in the region, each with major reforms in health system financing, governance and delivery related to pediatric cancer.(50;51) The extension of financial coverage to families of children with all types of cancer through the *Seguro Popular* program of the System of Social Protection in Health (SSPH), beginning in 2005, has expanded access to care for previously uninsured segments of the population. Consequently, the percentage of childhood cancer cases covered by public financing in Mexico increased from 3.3% to 55.3% between 2006 and 2008.(52) *Seguro Popular* allocates childhood cancer funding to drug access, regional centres of excellence, and training in pediatric oncology.(53) In Chile, considerable discrepancies in access to and outcomes of cancer treatment persist at the population level, with geographical and socioeconomic inequities. Parallel public and private systems of cancer-care financing and delivery lie at the root of discrepant outcomes between rich and poor, and concentration of oncologists and cancer treatment centres in the country's capital, Santiago, contribute to geographic disparities in outcomes. Even so, Chile has declared cancer a public health priority, established a National Cancer Program, and begun to prioritize specific diagnoses and programs for funding.(54) Childhood cancer has been afforded unique focus in the Chilean context. In recognition of the proportionate burden of childhood mortality represented by pediatric cancer, Chile established the National Program for Antineoplastic Drugs for Children (PINDA) in 1987, which has facilitated improved access to and delivery of care for children with a variety of malignancies. There are currently 11 accredited pediatric oncology centres in the country, the majority of which are located in Santiago.(51)

Efforts to move from ad hoc partnerships to integrated, system-wide practices and policies remain a priority in many Latin American countries. Comprehensive national efforts at cancer control, including systems of financing for poor and underserved communities, have already demonstrated successes in select middle-income countries.(16;50;51;55-57) However, sustained and equitable gains in survival will require policy uptake at local, national and regional levels throughout Latin American countries.

Such efforts will need to take into account several important issues, especially financial and governance implications of addressing many of the access and delivery issues outlined above. For example, the extension of financial coverage to children with cancer in LMICs is a crucial component of sustainable national cancer programming.(58) However, budget expenditure on childhood cancer care and control in most Latin American countries is limited. Competing health-system priorities and the costs of resource allocation to childhood cancer control programming will create difficult decisions for many Latin American policymakers. Consistent and structured processes to guide priority setting for resource allocation decisions will be important,(32) as the potential repercussions of these decisions for other health-system priorities and programs should be anticipated and assessed. Constraints on resource allocation to cancer care and control may also result from international donor funding priorities. These need to be identified and considered in processes for national policy generation on childhood cancer.

In addition to coverage decisions, there are challenges in how to structure coverage in order to achieve desired outcomes.(52;59) For example, though Mexico achieved cross-country increases in public coverage for childhood cancer cases in the last decade, treatment outcomes vary across regions, with sub-optimal survival and high rates of toxic death in a number of areas. However, there are many possible causes of such variation other than health-financing policies. For example, one possible contributing factor is a fixed-rate capitation model that provides payment to organizations for pediatric cancer services, but provides little incentive to address disease complexity or treatment complications as they develop.(52;58) In Argentina, while a mixed model of healthcare financing involving public health, social security and private insurance sectors provides coverage for a broad swath of the population, poor integration across these systems permit gaps that result in

inadequate coverage for many. To address issues of system governance and integration related to cancer financing, coverage, and delivery of care, the Argentinian government established a National Cancer Institute in 2012.(54)

Many governance issues will also need to be addressed when integrating national childhood cancer-care strategies into existing Latin American health systems. These range from how to create evidence-informed policy and fairly allocate resources, to evaluating the effects of national policies. Incorporating scientific knowledge into health policy decisions could lead to improved health outcomes in Latin America.(60-63) but one of the most significant challenges is the lack of locally adapted, evidence-informed knowledge in this area.(64-66) More specifically, policymaking about national childhood cancer strategies (including difficult decisions about resource allocation and modes of financing) must: 1) consider the effectiveness and cost of diagnostic and treatment protocols developed in HICs when applied in specific LMIC settings; 2) make use of existing evidence on pediatric cancer care in Latin American contexts to inform clinical programming and priority setting; and 3) include structured opportunities for input from a variety of stakeholders and perspectives.

Policymakers must also consider possible differences between 'vertical' and 'horizontal' approaches to health system development.(67) The tension between 'vertical' (disease-specific) and 'horizontal' (primary healthcare) approaches to health system reform has dominated the health systems literature to date.(68-70) Recently, novel proposals for 'diagonal' design have argued that disease-specific models of care, properly implemented, can create system-wide benefits.(71-73) Nevertheless, every decision about how and where to allocate limited health-system funds involves trade-offs and opportunity costs. Consequently, the development and implementation of national childhood cancer strategies will require health-system leaders to pay careful attention to the potential for both positive and negative spill-over effects of childhood cancer policies and programs, and in particular, to the processes that govern priority-setting decisions. From a policy process perspective, relevant issues include: the role of the public in setting health priorities; accountability and transparency in policy decision-making; and mechanisms of program accreditation, evaluation and monitoring. Attempts to develop and implement ethically sound, evidenced-based policy on pediatric cancer care in LMICs will depend on processes that privilege consideration of these issues, and that engage relevant stakeholders in their examination.

Childhood cancer receives limited attention from policymakers despite its importance for reducing childhood mortality and improving health over the life course

Despite its responsibility for a growing percentage of overall global childhood mortality, childhood cancer has rarely made it onto the global child health agenda. This relative neglect is because of a lack of awareness of the importance of childhood cancer (e.g., because of significant attention given to the high burden of adult cancer worldwide), misinformation about the existence of cost-effective solutions, and competing priorities in already resource-limited health systems.(58) This neglect applies to stakeholders in both the NCD and global child health communities. Global institutions and networks concerned with improved NCD outcomes have largely excluded childhood cancer from their policy discussions and advocacy efforts.(74) This could, at least partially, be driven by the global NCD agenda being focused principally on primary prevention, and because addressing childhood cancer requires investments and actions to strengthen health-system capacity. Indeed, international calls for improved systems of cancer care and control in LMICs have rarely paid attention to children. The inclusion of child-specific cancer strategies in national cancer plans is therefore rare. At the same time, the global child health agenda – as seen in the MDGs, UNICEF priorities, and other high-level initiatives – has rarely recognized childhood cancer as a problem in need of organized policy response. As a result, national child and adolescent health programs have also largely ignored the issue of childhood cancer.

Grassroots mobilization and advocacy by patient groups and foundations will be crucial for spurring strengthened infrastructure, service delivery and financing of childhood cancer care in Latin American countries. Efforts that seek to develop sustainable and system-wide strategies for childhood cancer care in the region will need to engage with such stakeholders to ensure the relevance and acceptability of services to local contexts and populations. Though grassroots projects exist in many LMICs, the transition to a health-systems approach to childhood cancer has been slow, and childhood cancer services are poorly integrated with existing primary and secondary care. Perhaps most crucially, the recognition and framing of policy on childhood cancer care as an opportunity for

diagonal health-system strengthening is relatively recent, and stakeholders in both the global child health and NCD arenas are only beginning to appreciate its promise.(32)

Sustained and effective responses to the problem of childhood cancer will therefore require greater attention at both national and international levels, from governmental and civil society sectors alike. This could include national governments and policymakers engaging with existing child and adolescent health-service programs and providers, including patient groups and civil society leaders in childhood cancer advocacy, to build on established health-system capacities to childhood cancer strategies, especially for earlier diagnosis and improved access to treatment.(75) At the international level, institutions separately dedicated to improving NCD and child health outcomes could enhance collaboration on the global burden of NCDs in children, of which cancer represents a particularly pressing instance. Growing recognition of the need for such focus and collaboration – as represented in the life-course approach to NCD policy recently adopted by the NCD Alliance – yields promise for political momentum toward this end.(76)

Additional equity-related observations about the problem

A key equity issue in the Latin American context is the pronounced urban/rural divide in many countries and health-system infrastructure that characterizes much of the region, but which varies in proportion and impact from country to country. Though figures vary, greater than half of the population of the region live in urban settings, where health-system resources tend to be concentrated. Limitations in access to cancer care for those living in rural areas is compounded by higher rates of poverty (50% in rural regions, as compared with 24% in urban ones).(54) The health burden and system implications of childhood cancer affect those of low SES and people living in areas that are geographically remote from cancer treatment, and/or in rural/remote areas, in several ways. First, low levels of education, particularly in rural settings, may limit the ability to seek care, which limits efforts at timely cancer detection. Poverty represents another major barrier to access. The cost of treatment, much of which is borne by families, is often prohibitive, and can throw families of affected children into poverty. Even where treatment costs are covered, the cost of accessing care – including travel, accommodation, and lost wages – can still be a major barrier to obtaining and sustaining treatment. This burden is worsened by geographic distance from treatment centres, which are often located in urban centres. Abandonment of treatment frequently results.(43;44) These geographic challenges are difficult to resolve given the importance of centralized, accredited centres for childhood cancer care to the delivery of high-quality services.(77) Stigma surrounding both cancer diagnosis and the use of opiates for pain control can also hinder access to appropriate treatment and supportive/palliative care for children with cancer.

Considerable evidence also suggests that SES (as manifested by household income, parental level of education, and place of residence) plays a crucial role in determining outcomes in standard risk ALL, which is likely a reflection of its influence on timing of presentation, abandonment of therapy, and risk of treatment complications.(20;21;43;78) Furthermore, malnutrition among children with cancer in LMICs can reach 50-70%,(79) and the poor nutritional status of patients living in poverty may render them more susceptible to treatment-related morbidity and mortality.(80;81) Nutritional interventions for children with cancer are therefore an important adjunct to care.(82) Programs of food supplementation for children, such as those including the use of peanut butter in Malawi and food bags with incaparina in Guatemala, may therefore have significant impacts on the outcomes of treatment for childhood cancers.(83;84)

THREE ELEMENTS OF A COMPREHENSIVE APPROACH FOR ADDRESSING THE PROBLEM

Many approaches could be selected as a starting point for deliberations about advancing the development of national childhood cancer-care strategies in Latin American countries. To promote discussion about the pros and cons of potentially viable approaches, we have selected three elements of a larger, more comprehensive approach to develop such strategies. The three elements were developed and refined through consultation with the Steering Committee and key informants who we interviewed during the development of this evidence brief. The elements are:

1) Convene a multi-stakeholder, pan-regional task force with national working groups to develop and oversee the implementation of national childhood cancer strategies to support cancer care in Latin American countries;
2) Develop health-system guidance to support the implementation of childhood cancer-care strategies based on national contexts, as well as integration with national cancer care control programs; and
3) Build capacity for monitoring and evaluation to support efforts to continuously refine the implementation of national childhood cancer-care strategies.

The elements could be pursued separately or simultaneously, or components could be drawn from each element to create a new (fourth) element. They are presented separately to foster deliberations about their respective components, the relative importance or priority of each, their interconnectedness and potential of or need for sequencing, and their feasibility.

The principal focus in this section is on what is known about these elements based on findings from systematic reviews. We found few systematic reviews relevant to the elements and those identified are not necessarily specific to childhood cancer. However, the elements are designed to provide an outline for what actions could be taken. To help identify important components of the elements and how they might be operationalized, we have supplemented findings from systematic reviews with supporting frameworks wherever possible. For the included systematic reviews, we present key findings with an appraisal of whether their methodological quality (using the AMSTAR tool) (85) is high (scores of 8 or higher out of a possible 11), medium (scores of 4-7) or low (scores less than 4) (see the appendix for more details about the quality-appraisal process). We also highlight whether they were conducted recently, which we define as the search being conducted within the last five years. In the next section, the focus turns to the barriers to adopting and implementing these elements, and to possible implementation strategies to address the barriers.

Box 4: Mobilizing research evidence about elements of a comprehensive approach for addressing the problem

The available research evidence about elements of a comprehensive approach for addressing the problem was sought primarily from Health Systems Evidence (www.healthsystemsevidence.org), which is a continuously updated database containing more than 4,300 systematic reviews and more than 2,300 economic evaluations of delivery, financial and governance arrangements within health systems. The reviews and economic evaluations were identified by searching the database for reviews addressing features of each of the approach elements. This included searching the following categories: networks/multi-institutional arrangements, consumer & stakeholder involvement (all categories); quality monitoring and improvement systems, and organization-targeted implementation strategies.

The authors' conclusions were extracted from the reviews whenever possible. Some reviews contained no studies despite an exhaustive search (i.e., they were "empty" reviews), while others concluded that there was substantial uncertainty about the element based on the identified studies. Where relevant, caveats were introduced about these authors' conclusions based on assessments of the reviews' quality, the local applicability of the reviews' findings, equity considerations, and relevance to the issue. (See the appendices for a complete description of these assessments.)

Being aware of what is not known can be as important as being aware of what is known. When faced with an empty review, substantial uncertainty, or concerns about quality and local applicability, or lack of attention to equity considerations, primary research could be commissioned, or an element could be pursued and a monitoring and evaluation plan designed as part of its implementation. When faced with a review that was published many years ago, an updating of the review could be commissioned if time allows.

No additional research evidence was sought beyond what was included in the systematic review. Those interested in pursuing a particular element may want to search for a more detailed description of the element, or for additional research evidence about the element.

Element 1 – Convene a multi-stakeholder, pan-regional task force with national working groups to develop and oversee the implementation of national childhood cancer strategies to support cancer care in Latin American countries

Sub-elements of this element might include activities to:

- identify a clear picture of the challenges across Latin American countries related to addressing childhood cancer by:
  - using high-quality data and evidence; and
  - systematically eliciting tacit knowledge, views and experiences of key stakeholders (e.g., policymakers, patients and families/caregivers, NGOs and the private sector);
- engage in priority-setting processes to develop:
  - short-, medium- and long-term priorities both within and across Latin American countries; and
  - meaningful and achievable targets that can be met and sustained in the long-term.

We identified one review (86) and a framework (87) with information relevant to the first sub-element (identifying a clear picture of the challenges faced), and four reviews (88-91) relevant to the second sub-element (priority-setting processes).

For the first sub-element, a recent review developed a model to describe key features and intended effects of deliberative dialogues.(86) Dialogues, such as the one this brief was prepared to inform, could be periodically convened by a multi-stakeholder taskforce to systematically elicit tacit knowledge, views and experiences of stakeholders, not only to identify a clear picture of the challenges faced in specific countries, but also to contribute to a broader stakeholder-engagement process to identify priorities and targets. The model developed in the review outlines three key features of deliberative dialogues, which include ensuring an:

1) appropriate meeting environment (e.g., by ensuring adequate resources, commitment from participants, transparency, timeliness of the issue, appropriate group size, clear meeting rules, pre- and post-meeting tasks and effective facilitation);
2) appropriate mix of participants (e.g., by ensuring fair and balanced representation of those with an interest in the issue, and that participants are motivated and provided with the resources they need to meaningfully engage in the issue); and
3) appropriate use of research evidence (e.g., fostering a clear understanding of the policy issue among all participants by presenting what is currently known about it based on the best available research evidence).

The model further outlines several intended effects of deliberative dialogues, including short-term (e.g., strengthened capacity of participants to address the policy issue), medium-term (e.g., strengthened community or organizational capacity) and long-term effects (e.g., strengthened system capacity to make evidence-informed decisions).(86) In addition, a recent evaluation of deliberative dialogues in six African countries found that they were viewed positively regardless of the country, health system issue addressed and the group actors investigated.(92)

The framework we identified (developed through a realist synthesis) outlines that the causes of a problem or policy challenge could be at one or more of the following levels:

1) motivation at the individual level (e.g., how knowledge, beliefs about capabilities and consequences, skills, memory, emotion and goals exert influence);
2) tasks at the individual or team level (e.g., how work routines and procedures function);
3) roles at the professional level (e.g., how responsibilities are assigned);
4) rules at the organizational level (e.g., how authority is allocated); and
5) strategies (e.g., allocating resources to provide universal coverage) at the system level (e.g., governance, financial and delivery arrangements).(93)

This framework could provide a helpful starting point for a multi-stakeholder, pan-regional taskforce and national working groups to organize relevant evidence, as well as tacit knowledge, views and experiences of key stakeholders, to iteratively develop a clear picture of the challenges faced in different contexts.

The four reviews related to priority setting that we identified are all older and of medium (88;90) or low quality.(89;91) While none provided an explicit assessment of the benefits, harms and costs of priority setting, they

did provide information related to key elements of such processes. In general, the reviews point to the importance of using a mix of quantitative (e.g., to solicit general feedback and guidance) and qualitative (e.g., where decisions are needed to identify priorities) techniques with different groups of stakeholders (e.g., policymakers, funders, patients and families/caregivers) for priority setting. One of the medium-quality reviews outlined that either formal (e.g., assembling a government-appointed committee with specific principles or factors to be considered during the process) or informal (e.g., informal debates, discussions or consensus-building meetings) priority-setting processes can be used.(91) The same review emphasized the importance of identifying principles and factors to be considered during priority-setting processes (e.g., equity, solidarity, equality, and effectiveness and efficacy of healthcare services under review). The other reviews found that these types of processes have been operationalized using a range of quantitative, qualitative and mixed techniques designed to elicit preferences from stakeholders.(88-91) For example, reviews of priority setting in developing countries (89) and for health technology assessments (90) indicate that several processes have used interdisciplinary panels or committees of funders, health professionals and researchers to provide advice. In addition, one of the reviews focused on public engagement in priority setting for resource allocation and found that engaging the public is most common at the visioning or goal-setting stages.(88)

A summary of the key findings from the synthesized research evidence is provided in Table 1. For those who want to know more about the systematic reviews contained in Table 1 (or obtain citations for the reviews), a fuller description of the systematic reviews is provided in Appendix 1.

Table 1: Summary of key findings from systematic reviews relevant to Element 1 – Convene a multi-stakeholder, pan-regional task force with national working groups to develop and oversee the implementation of national childhood cancer strategies to support cancer care in Latin American countries

Category of finding	Summary of key findings
Benefits	• **Identify a clear picture of the challenges across Latin American countries related to addressing childhood cancer** o Neither of the reviews relevant to this sub-element included an evaluation of benefits, but one outlined a model for deliberative dialogues and identified possible intended effects of deliberative dialogues, including short-term (e.g., strengthened capacity of participants to address the policy issue), medium-term (e.g., strengthened community or organizational capacity) and long-term effects (e.g., strengthened system capacity to make evidence-informed decisions).(86)
Potential harms	• **Engage in priority-setting processes to develop short-, medium- and long-term priorities to address childhood cancer both within and across Latin American countries** o An older low-quality review about priority for health interventions in developing countries noted important limitations in some of the priority-setting processes studies, including: ▪ using a limited number of criteria to inform priority-setting when a broader set of policy-relevant information could have been included; and ▪ relying exclusively on one technique (e.g., quantitative techniques such as discrete-choice experiments or qualitative techniques such as deliberative processes) to identify respondent preferences when not all criteria relevant to priority-setting are amenable to use in a single approach.(89)
Costs and/or cost-effectiveness in relation to the status quo	• **Engage in priority-setting processes to develop short-, medium- and long-term priorities to address childhood cancer both within and across Latin American countries** o An older, low-quality review found that costs related to public engagement activities are rarely reported, but noted that well-structured processes range from tens of thousands of dollars to $1 million or more.(88)
Uncertainty regarding benefits and potential harms (so monitoring and evaluation could be warranted if the option were pursued)	• Uncertainty because no systematic reviews were identified o Not applicable • Uncertainty because no studies were identified despite an exhaustive search as part of a systematic review o Not applicable (no 'empty' reviews were found) • No clear message from studies included in a systematic review o **Identify a clear picture of the challenges across Latin American countries related to addressing childhood cancer** ▪ The two recent reviews identified for this sub-element did not include information about benefits, harms and costs, but did include information related to key components of the elements (see below)

	○ **Engage in priority-setting processes to develop short-, medium- and long-term priorities to address childhood cancer both within and across Latin American countries** ▪ Most of the studies included in an older, low-quality review about priority for health interventions in developing countries were small pilot studies, which did not include evaluations of the priority-setting processes that were described.(89) ▪ One older, medium-quality review identified and compared priority-setting approaches for health technology assessment,(94) and another older but low-quality review described priority-setting processes for healthcare,(91) but neither evaluated the benefits, harms and costs of these processes given that both were focused on key characteristics of models that have been used (see the section below about key elements of the policy option for more information). ▪ An older, low-quality review noted that public engagement exercises are typically not formally evaluated, but that, despite the lack of evaluation, results of engagement processes are typically viewed as a success and claimed to have led to a direct impact on decisions.(88)
Key components of the policy element if it was tried elsewhere	• **Identify a clear picture of the challenges across Latin American countries related to addressing childhood cancer** ○ A recent review outlined a model for deliberative dialogues (as one possible component for identifying a clear picture of challenges related to addressing childhood cancer), which included three key features: ▪ ensuring an appropriate meeting environment (e.g., by ensuring adequate resources, commitment from participants, transparency, timeliness of the issue, appropriate group size, clear meeting rules, pre- and post-meeting tasks and effective facilitation); ▪ ensuring an appropriate mix of participants (e.g., by ensuring fair and balanced representation of those with an interest in the issue, and that participants are motivated and provided with the resources they need to meaningfully engage in the issue); and ▪ ensuring appropriate use of research evidence (e.g., fostering a clear understanding of the policy issue among all participants by presenting what is currently known about it based on the best available research evidence).(86) • **Engage in priority-setting processes to develop short-, medium- and long-term priorities to address childhood cancer both within and across Latin American countries** ○ An older, low-quality review about priority for health interventions in developing countries indicated that: ▪ most involved policymakers, health workers and general population in their priority-setting process; ▪ quantitative techniques (e.g., discrete-choice experiments) are most appropriate where general guidance on priority setting is needed; ▪ qualitative techniques (e.g., deliberative processes) may be best used in situations where decisions are required. ○ An older, medium-quality review found that: the majority of priority-setting frameworks (seven of the 12 that were identified) used a panel or committee to provide advice with all committees engaging representatives from funders, health professionals and researchers; some drew on advice from a board of directors (often in conjunction with a separate committee); one-third used a rating system to inform priorities (all of these were used along with a committee); and only two models explicitly considered the balance of costs and benefits in the assessments made.(90) ○ An older, medium-quality review of priority setting for healthcare identified formal and informal priority-setting processes.(91) ▪ Formal processes – assemble a government-appointment committee, identify principles and factors to be considered during the priority-setting process (e.g., equity, solidarity, equality, and effectiveness and efficacy of healthcare services under review). ▪ Informal processes – informal debates, discussions among policymakers and one-off consensus development meetings. ○ The same review indicated that tools for generating lists of priorities based on data were often found to be impractical or conceptually difficult to understand.(91)
Stakeholders' views and experience	• None identified

Element 2 – Develop health-system guidance to support the implementation of childhood cancer-care strategies based on national contexts, as well as integration with national cancer care control programs

Sub-elements of this element might include activities to:

- create a continuously updated knowledge 'hub' with evidence on childhood cancer epidemiology, treatment approaches, and health-system arrangements that can be used in the development of guidance;
- engage the full spectrum of health-system stakeholders involved in cancer, child and adolescent health, and non-communicable diseases (e.g., global health governance institutions such as the WHO, non-governmental organizations, a cross-section of select national policymakers, stakeholders and researchers) and consumers to develop and refine guidance; and
- develop 'workbooks' to support the implementation of the guidance in specific Latin American contexts through subsequent national-level deliberative processes.

Overview of health-systems guidance

Health-systems guidance is defined as "systematically developed statements created at the global or national level to assist decisions about options for addressing a health system problem in a range of settings and to assist with implementation and with monitoring and evaluation."(95) As summarized in a recent series of articles published about guidance for evidence-informed policies about health systems,(95-97) guidance addresses health-system problems by:

1) framing health-system problems;
2) identifying, translating and packaging the best-available evidence related to health-system and implementation issues;
3) using a deliberative process to recommend and formulate options to address the problem and to identify where action is needed; and
4) providing insights about strategies that can be used to implement and evaluate a policy.(96)

Health-systems guidance can therefore take many forms and could include a suggestion to pursue a particular option to address a problem faced in one or more countries given their specific health- and political-system features.(95) In contrast, for countries facing a somewhat different problem and that have different health- and political-system features, guidance may suggest a different option (or what monitoring and evaluation might be needed when insufficient evidence exists).

Given this, a continuously updated knowledge 'hub', stakeholder and consumer engagement, and 'workbooks' that provide a process to contextualize health-system guidance are essential. A 'hub' would collect and facilitate retrieval and synthesis of evidence related to the development of guidance about specific cancer-care strategies that could be used towards improving access and strengthening care (e.g., health promotion, treatment, supports needed to sustain treatment, etc.). Stakeholder and consumer engagement will then be essential for using deliberative processes to recommend and formulate options given the unique problems and the health- and political-system features in different countries. Throughout this process, workbooks can provide ongoing support for undertaking the series of steps needed to develop guidance. For example, the WHO recommendations for optimizing health-worker roles for maternal and newborn health(98) drew on a workbook, and the overall process is outlined in Figure 1. As can be seen, in addition to assessing the available research evidence, developing guidance also requires an analysis of health-system arrangements for countries that it is meant to support, as well as an analysis of the political-system context. These are then used to refine the understanding of the problem, options available to address it and implementation considerations.

Overview of evidence related to the sub-elements

We identified one review relevant to creating a knowledge 'hub' and 10 reviews relevant to engaging stakeholders and/or citizens and consumers to refine guidance. While we did not identify systematic reviews relevant to developing 'workbooks', Figure 1 outlines the overall process included in a recently developed workbook (as outlined above). Related to creating a knowledge 'hub', an older, medium-quality review assessed the available literature about collaborations between the primary care and public health sectors, and found such collaborations

to have beneficial outcomes at the level of health systems (e.g., improvements in the delivery of health services) and health professionals (e.g., improved partnerships and team functioning).(99)

Figure 1: Evidence-based health systems guidance for policymaking framework (reproduced with permission from Lavis and Alvarez)(100)

We identified two systematic reviews focused on stakeholder engagement,(101;102) and eight reviews that focused on public- and consumer-engagement processes.(103-110) For stakeholder engagement, one recent, medium-quality review focused on the benefits and challenges of engaging stakeholders in a process of developing and conducting systematic reviews.(101) Stakeholder engagement was found to be most beneficial for identifying and prioritizing topics for research, and providing pragmatic feedback on the research protocol. Other key benefits include ensuring that findings are interpreted with the end user in mind, developing final products that are readable and accessible, and facilitating wider dissemination and uptake of the research findings. The second review focused on stakeholder engagement in program evaluation and found limited research evidence, but did find considerable overlap in the key features of stakeholder-engagement processes in the literature.(102) Specifically, the review indicated that the methodological centrepiece of these processes is entering into collaboration with a collective willingness to participate, and placing emphasis on the need to draw on the strengths of each member while respecting their unique positions and expertise.(102)

Of the eight reviews about public and consumer engagement, all indicated that the available evidence is limited and that it is difficult to draw firm conclusions about the benefits of particular public- and consumer-engagement process.(103-110) One recent medium-quality review outlined that consumer engagement in healthcare aims to engage consumers, community members and the public in general as well as specific sub-groups that are involved in or affected by a particular issue (e.g., people from culturally and linguistically diverse backgrounds).(109) In addition, an older, medium-quality review found that those who participate in well-designed interactive public-engagement processes report high levels of satisfaction across different components of the process, as well as increased levels of topic-specific learning.(107) Another older, medium-quality review also found that case studies of project administrators' views about the impact of patient engagement indicate that it has contributed to changes in services.(105) The reviews also noted that:

- the underlying goal of public deliberations is to obtain public opinion (including from under-represented individuals and groups) to provide insight into social values and ethical principles for consideration in public decisions;(103)
- when adapting public deliberation processes (e.g., citizen juries) for specific aims, special attention should be paid to recruitment, independent oversight by a steering committee, duration of the jury, moderation, and respect for volunteer participants;(110)

- common tasks in public deliberation include developing policy directions, recommendations and tools, and priority setting for resource allocation;(103;110)
- strategies that can be used for public- and consumer-engagement vary in their goals, scope of activities and methods used,(109) and processes need to be adapted to the context of the policy issue;(107)
- public and consumer engagement can be helpful for improving dissemination of information and processes for developing interventions, as well as for enhancing awareness and understanding among citizens;(104;106) and
- training of patients and their families, as well as healthcare professionals is an important component for successfully involving cancer patients and their families in research, policy, planning and practice.(108)

A summary of the key findings from the synthesized research evidence is provided in Table 2. For those who want to know more about the systematic reviews contained in Table 2 (or obtain citations for the reviews), a fuller description of the systematic reviews is provided in Appendix 2.

Table 2: Summary of key findings from systematic reviews relevant to Element 2 – Develop health-system guidance to support the implementation of childhood cancer-care strategies based on national contexts, as well as integration with national cancer care control programs

Category of finding	Summary of key findings
Benefits	• **Create a knowledge 'hub' that is continuously updated with evidence on childhood cancer epidemiology, treatment approaches, outcomes and health system arrangements that can be used in the development of guidance** o One recent, medium-quality review of collaborations between primary care and public health found beneficial outcomes of such collaborations (as reported in primary studies, literature reviews and descriptive accounts) at the level of health systems (improved population health and public-health approaches, funding and resource enhancements, health service delivery improvements, improved health service delivery processes and new/innovative program development) and health professionals (improved partnerships and team functioning, professional development and improvements to education).(99) • **Engage stakeholders and consumers to develop and refine guidance** o An older high-quality review found some evidence that community engagement improves the dissemination of information and processes for developing interventions.(106) o A recent medium-quality review found that the main benefits of stakeholder engagement in developing and conducting systematic reviews include: identifying and prioritizing topics for research; providing pragmatic feedback on the research protocol; aiding in recruitment of research participants; helping the researchers understand the research subject's perspective; ensuring that findings are interpreted with the end user in mind and that final products are readable and accessible; and facilitating wider dissemination and uptake of research findings.(101) o The same review noted that stakeholder engagement in the topic refinement and research development phase of conducting a systematic review was identified as the point where stakeholder engagement yielded the greatest benefit.(101)
Potential harms	• **Engage stakeholders and consumers to develop and refine guidance** o A recent medium-quality review indicated that the biggest challenges of engaging stakeholders in the development and conduct of systematic reviews include time and resources, researcher skills for stakeholder engagement, finding the right people, balancing multiple inputs, and understanding the best/most appropriate time in the review process to engage different types of stakeholders.(101)
Costs and/or cost-effectiveness in relation to the status quo	• **Create a knowledge 'hub' that is continuously updated with evidence on childhood cancer epidemiology, treatment approaches, outcomes and health system arrangements that can be used in the development of guidance** o One recent, medium-quality review found that one of the possible risks of collaboration between primary care and public health was the added expense of supporting the collaboration.(99) • **Engage stakeholders and consumers to develop and refine guidance** o As noted for Element 1, an older, low-quality review found that costs related to public engagement activities are rarely reported, but noted that well-structured processes range from tens of thousands of dollars to $1 million or more.(88) o While not explicitly providing information about costs, an older, medium-quality review noted that, in general, effective patient involvement requires both personnel and financial commitments.(108)
Uncertainty regarding benefits and potential harms (so monitoring and evaluation could be	• Uncertainty because no systematic reviews were identified o **Develop 'workbooks' to support the implementation of the guidance in specific Latin American contexts through subsequent national-level deliberative processes** • Uncertainty because no studies were identified despite an exhaustive search as part of a systematic review

warranted if the option were pursued)	○ Not applicable • No clear message from studies included in a systematic review ○ **Engage stakeholders and consumers to develop and refine guidance** ▪ A recent, medium-quality review indicated that while there is some evidence to support the developmental role of public involvement (e.g., for enhancing awareness and understanding among citizens), no clear conclusions can be drawn due to lack of clarity about what success looks like.(104) ▪ Another medium-quality but older review similarly found few studies that described the effects of involving patients in the planning and development of healthcare.(105)
Key components of the policy element if it was tried elsewhere	• **Engage stakeholders and consumers to develop and refine guidance** ○ Eight reviews focused on public and consumer engagement. ▪ A recent, medium-quality review about public involvement in healthcare policy found that key features of public involvement are poorly defined and rarely detailed.(104) ▪ A recent, low-quality review outlined that having the potential to find common ground is a requirement for using public engagement to address issues, and that common goals include activities related to developing policy direction, recommendations and tools, priority setting, resource allocation and risk assessments.(103) ▪ The same review indicated that public-engagement processes include three broad characteristics: 1) a sponsor seeking input from the public; 2) participants considering an ethical- or values-based dilemma; and 3) provision of accurate and balanced information to participants about the dilemma.(103) ▪ A recent, medium-quality review indicated that when adapting public deliberation processes (e.g., citizen juries) for specific aims, special attention should be paid to recruitment, independent oversight by a steering committee, duration of the jury, moderation, and respect for volunteer participants.(110) ▪ Two medium-quality reviews (one recent and one older) outlined that the mechanisms used for public engagement need to be adapted according to the context of policy development around the issue (e.g., by forming the group in ways that are sensitive to the type of topic, history of the issue and possible power dynamics).(107;107) ▪ An older, medium-quality review found that training of patients and healthcare professionals is an important component for successfully involving cancer patients in research, policy, planning and practice.(108) ▪ An older, medium-quality review defined patient involvement as "the active participation in the planning, monitoring, and development of health services of patients, patient representatives, and wider public as potential patients."(105) ▪ An older, high-quality review indicated that community-engagement activities used a variety of approaches, including convening community groups, committees and workshops, and engaging educators, champions and volunteers.(106) ○ A recent medium-quality review indicated that there was considerable overlap in the key features of stakeholder-engagement processes in the literature, and found that the methodological centrepiece of stakeholder involvement is entering into collaboration with a collective willingness to participate and that draws on the strengths of each member while respecting their unique positions and expertise.(102)
Stakeholders' views and experience	• **Engage stakeholders and consumers to develop and refine guidance** ○ A recent, medium-quality review found that those who participate in well-designed interactive public engagement processes report high levels of satisfaction across different components of the process (e.g., communication of objectives, adequacy of the information materials provided to inform discussions, and the logistics and management of the deliberation), as well as increased levels of topic-specific learning.(107) ○ Case studies including project administrators' views about public engagement in the planning and development of healthcare in an older medium-quality review provided support to the view that patient engagement has contributed to changes in services.(105)

Element 3 – Build capacity for monitoring and evaluation to support efforts to continuously refine the implementation of national childhood cancer-care strategies

Sub-elements of this element might include activities to:

- build system capacities for systematic monitoring and evaluation (e.g., building high-quality cancer registries)
- identify relevant indicators and outcomes that can be tracked between countries to provide common benchmarks for analysis; and
- monitor and evaluate the extent of implementation using common benchmarks across countries, and adjust country-specific plans based on the results.

We did not identify any reviews that were directly relevant to this element. However, we outline below important considerations related to this element, including the key components of the RE-AIM (Reach, Effectiveness, Adoption, Implementation, and Maintenance) framework,(111) which has been used extensively to improve the sustainable adoption and implementation of effective, generalizable, evidence-based interventions.(112)

One important consideration, which figures prominently in objectives and recommendations from the Pan-American Health Organization for cancer control,(113;114) is that robust national cancer registries with data specifically related to childhood cancer will be an essential component of monitoring and evaluation. For example, robust national cancer registries will allow for consistent tracking of prevalence of childhood cancer, tumour markers, and other important indicators and outcomes that may be identified through stakeholder and consumer engagement processes. These indicators can then be used to monitor and evaluate progress towards targets, and to adjust country-specific plans as needed. In response to this need, the Global Initiative for Cancer Registry Development (as part of the IARC) has been created with the goal to ensure low- and middle-income countries have access to the data they need to inform policy designed to strengthen cancer control.(115) As part of this initiative, six regional hubs have been developed (including one each in El Salvador and Colombia), with 20 planned by 2020. The focus of these hubs is to empower countries to develop cancer control plans, provide localized training and tailored support, foster research, assist with advocacy, and develop networks.(115)

Another related consideration toward building capacity for monitoring and evaluation is the importance of drawing on strengths from complementary processes such as quality-improvement interventions. In general, quality-improvement interventions use formalized and systematic approaches to assess performance and make changes to improve health outcomes, system performance, and professional development.(116) While not directly applicable to this element, lessons can be drawn from factors that have been found to contribute to successful implementation of quality-improvement interventions, which include:

- leadership from top management;
- a supportive organizational culture (including support of board members);
- availability of data infrastructure and information systems (in this case cancer registries);
- experience with or years involved in quality improvement;
- physician involvement;
- motivation to change;
- sufficient resources;
- effective team leadership; and
- use of multifaceted interventions.(117;118)

As noted above, the RE-AIM framework offers an approach to build a robust monitoring and evaluation plan. The goal of the RE-AIM framework "is to encourage program planners, evaluators, readers of journal articles, funders, and policy-makers to pay more attention to essential program elements, including external validity, that can improve the sustainable adoption and implementation of effective, generalizable, evidence-based interventions."(119) RE-AIM provides a starting point for systematically assessing the impact of programs and policies by facilitating the assessment of their reach, effectiveness, adoption, implementation and maintenance. We provide in Table 3, the broad guidelines and questions to address when using the framework to assess the impact of interventions.(120) Collectively, these components can be used to assess impact at both the individual (i.e., end-

user) and organizational (i.e., delivery agent) level (112) as part of a monitoring and evaluation plan to ensure optimal impact of the selected and implemented approaches to optimizing clinical practices.

Note that we have not included a table summarizing findings from systematic reviews for this element, given that no relevant reviews were identified.

Table 3: RE-AIM elements and questions to ask (*reproduced with permission from Gaglio and Glasgow 2012) (120)

RE-AIM element	Questions to ask
Reach • Percent and representativeness of participants	• Can the program attract a large and representative percent of the target population? • Can the program reach those most in need and most often left out?
Effectiveness • Impact on key outcomes, quality of life, unanticipated outcomes and sub-groups	• Does the program produce robust effects across sub-populations? • Does the program produce minimal negative side effects and increase quality of life or broader outcomes?
Adoption • Percent and representativeness of settings and staff that participate	• Is the program feasible for the majority of real-world settings in terms of costs, expertise, resources, etc.? • Can it be adopted by low-resource settings and typical staff serving high-risk populations?
Implementation • Consistency and cost of delivering the program and any adaptation made	• Can the program be consistently implemented across program elements, different staff and over time? • Are the costs (e.g., personnel, upfront, marginal, scale up and equipment) reasonable and proportionate to effectiveness?
Maintenance • Long-term effects at individual and setting levels	• Does the program include principles to enhance long-term improvements (e.g., follow-up contact, community resources, peer support and ongoing feedback)? • Can the settings sustain the program over time without added resources and leadership?

Additional equity-related observations about the three elements

Several implications about the three elements can be drawn related to people of low SES, and people living in areas that are geographically remote from cancer treatment, and/or in rural/remote areas. Across all three elements, the main implication relates to meaningful engagement and recognition of these two groups. For example, in the first element (a multi-stakeholder task force on national childhood cancer strategies in Latin America), this means identifying the specific challenges faced by both groups. In addition, it also means that voices from these groups are heard in priority-setting processes to ensure that priorities developed are relevant at the country level, but also to those disproportionately affected by the issue. For the second element (developing health-system guidance), meaningful engagement and recognition means ensuring that stakeholder-engagement processes involve these two groups to ensure that health-system guidance is attuned to the specific challenges faced by them (and across different health-system contexts). Lastly, for the third element (monitor, evaluate and continuously refine the implementation of national childhood cancer control plans), this means ensuring that benchmarks include indicators that will allow for measurement of progress (e.g., improving access to needed services, retention in treatment and survival rates).

IMPLEMENTATION CONSIDERATIONS

Efforts to actualize the identified elements of a comprehensive approach to advancing childhood cancer strategies in Latin America need to take account of potential barriers to their implementation (Table 4), as well as consider potential windows of opportunity for pursuing any or all of the elements (Table 5). Such barriers differ according to element components and categories of involved stakeholders, and are likely to vary across health system contexts. The prospects for a multi-stakeholder, pan-regional task force and national working groups on national childhood cancer strategies will hinge crucially on buy-in from regional and national policymakers and stakeholders to its objectives and design. Such consensus may be difficult to come by, and will depend on the degree to which national governments can be assured of common interest, mutual benefit, and political palatability. If such supra-national coordination proves intractable, an alternative option could be to involve the coordination and conduct of separate national-level task forces on childhood cancer policy within interested jurisdictions. While such efforts would have the benefit of sustained and in-depth focus on internal health system dynamics and prospects for reform, they might forfeit opportunities for cross-national policy learning. A further complication may arise in efforts to involve international and national organizations with sometimes divergent mandates (e.g. child and adolescent health, NCD and cancer-specific networks) that have overlapping interest in, and bearing on, childhood cancer policies in Latin American countries.

Those planning to convene and steer the deliberations of such a task force could draw on the findings of a recent, medium-quality systematic review that identified the following factors for successful implementation: "1) the organization and staff have planned for the initiative; 2) there are enough people with necessary and synergistic skills to implement the initiative; 3) there are capabilities and a receptiveness for change; 4) the chosen implementation [approach] meets needs and is the best fit for the organization and stakeholders; 5) the necessary human and financial resources are available for implementation; 6) there is support and momentum throughout the implementation process; and 7) processes to support mid-to-long-term acceptance are established during preparation and anchored throughout the implementation process".(121)

The production of health-system guidance relevant to national childhood cancer-care strategies will depend on both legitimate bases of expertise and the capacity to produce guidance with context specificity and relevance. Again, potential tension may surface at the interface of global institutional production of health-system guidance and local fit. Legitimate bases and capacity for the development of health-system guidance exist at the international level, and such legitimacy often stems in part from national engagement of global institutions to produce guidance. Careful attention to adapt internationally developed guidance to national health system and political contexts is warranted.(122) Optimally, these efforts would include deliberative processes that situate such guidance within the local context, and engage a broad cross-section of relevant stakeholders in its assessment and adoption.(96)

Finally, efforts to build the requisite capacity for monitoring and evaluation of national childhood cancer strategies will depend on dedicated resources, the receptivity of politicians to transparent disclosure of policy outcomes, and the political will for continued policy and programmatic reform based on such evaluation. In health systems with heightened resource constraints, the allocation of human, material and financial resources to evaluative activities may meet political resistance. Similarly, competing policy priorities may curb the willingness and/or ability of policymakers to sustain political focus on childhood cancer, with attendant implications for the long-term viability of efforts to monitor, evaluate and reform existing systems of care.

Table 4: Potential barriers to implementing the identified elements

Levels	Element 1 – Convene a multi-stakeholder, pan-regional task force with national working groups to develop and oversee the implementation of national childhood cancer strategies to support cancer care in Latin American countries	Element 2 – Develop health-system guidance to support the implementation of childhood cancer-care strategies based on national contexts, as well as integration with national cancer care control programs	Element 3 – Build capacity for monitoring and evaluation to support efforts to continuously refine the implementation of national childhood cancer-care strategies
Patient/Individual	Important groups of patients (especially those marginalized by low SES, low education, minority status or geographic distance) may not feel equipped or empowered to contribute to such a task force or in priority-setting processes Principles and processes for selecting participants to such a task force may be challenged and their dispute could undermine its legitimacy	Important groups of patients (especially those marginalized by low SES, low education, minority status or geographic distance) may not feel equipped or empowered to contribute to a broader stakeholder engagement process for developing health-system guidance	None identified
Care provider	Some care providers may resist proposals for altered or expanded scopes of practice for other providers Some primary care providers may not feel childhood cancer is a priority, given competing time and resource constraints	Some care providers may resist the local application of internationally developed health-system guidance, stemming from the perceived misalignment of guidance with the realities of local care delivery	Some care providers may resist monitoring and evaluation, especially if public reporting is involved
Organization	Discrepant priorities and political commitments may hinder effective collaboration between international organizations with different mandates (e.g. global child health and global NCD), organizations at various intra-national tiers (e.g. ministries of health and grassroots advocacy organizations or patient groups), or between international and national-level institutions	Some organizations may not have the resources (e.g., human or financial) to contribute their perspectives to processes aimed at adapting guidance for specific institutional contexts	Some organizations may not have the key success factors for implementation in place (as described above) Some organizations may resist transparent reporting of program functioning and outcomes
System	System leaders may not want to invest in an exercise that involves voices and examples from different political contexts, given the risks to internal political capital this might entail System specificity might be lost in efforts to generalize beyond national jurisdictions and isolate policy lessons from a supra-national forum	Tensions between international and national perspectives on health-system priorities and capacities may hinder uptake of health-system guidance at the national level Some systems may not have the resources to commit to local refinement of health-system guidance through deliberative processes	Some policymakers may resist transparent disclosure of policy outcomes Some systems may not have the capacity to allocate human, material and financial resources to evaluative activities Efforts to monitor and evaluate existing services may meet public or political resistance in the context of health systems with resource constraints that preclude the implementation of other needed programs or services

Table 5: Potential windows of opportunity for implementing the elements

Type	Element 1 – Convene a multi-stakeholder, pan-regional task force with national working groups to develop and oversee the implementation of national childhood cancer strategies to support cancer care in Latin American countries	Element 2 – Develop health-system guidance to support the implementation of childhood cancer-care strategies based on national contexts, as well as integration with national cancer care control programs	Element 3 – Build capacity for monitoring and evaluation to support efforts to continuously refine the implementation of national childhood cancer-care strategies
General	The increasing prominence of NCDs on the global health agenda (e.g., as represented by the recent high-level UN summit on NCDs), and the allied institutional infrastructure to advance policy and advocacy on NCDs, represents an opportunity for the global childhood cancer community to make the case for national childhood cancer strategies in LMICs. Many international childhood cancer advocacy organizations can support the advancement of childhood cancer policies in global NCD discourse and in the development of the post-2015 MDG agenda. The International Cancer Control Planning Partnership, which is led by the UICC, is supporting the development of national cancer plans, and there could be an opportunity to include childhood cancer plans as part of these efforts. The Global Initiative for Cancer Registries led by the IARC plans to expand from six to 20 regional hubs by 2020 with the goal of empowering countries to develop cancer control plans. This initiative provides an opportunity both to include childhood cancer in these strategies and to ensure childhood cancer data are incorporated in the development of cancer registries.(115) PAHO-led efforts to include childhood cancers in the established regional program for Integrated Management of Childhood Illnesses could support the integration of national childhood cancer strategies with overarching child health programs in countries across the region.(123) This could both facilitate improved detection and referral at the primary care level, and enhance service integration across tiers of care. The existence of an extensive and well-connected network of institutional 'twinning' partnerships on childhood cancer care in Latin America (and beyond) has helped develop baseline infrastructure and programs for childhood cancer care on which national policies can build. Regional attention to and action on the issue of access to cancer medicines (e.g., through the PAHO Strategic Fund) have demonstrated both the political viability and mutual benefits of regional collaboration on issues related to the delivery of childhood cancer care. Robust and encouraging examples of national approaches to childhood cancer care policy (e.g., in Chile and Mexico) may provide political legitimacy and momentum to policy uptake in other Latin American settings.		
Element-specific	None identified	None identified	Efforts to build more robust childhood cancer registries in a number of Latin American countries will buttress attempts to monitor and evaluate the outcomes of national strategies for cancer care in children

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APPENDICES

The following tables provide detailed information about the systematic reviews identified for each option. Each row in a table corresponds to a particular systematic review and the reviews are organized by sub-element (first column). The focus of the review is described in the second column. Key findings from the review that relate to the option are listed in the third column, while the fourth column records the last year the literature was searched as part of the review.

The fifth column presents a rating of the overall quality of the review. The quality of each review has been assessed using AMSTAR (A MeaSurement Tool to Assess Reviews), which rates overall quality on a scale of 0 to 11, where 11/11 represents a review of the highest quality. It is important to note that the AMSTAR tool was developed to assess reviews focused on clinical interventions, so not all criteria apply to systematic reviews pertaining to delivery, financial, or governance arrangements within health systems. Where the denominator is not 11, an aspect of the tool was considered not relevant by the raters. In comparing ratings, it is therefore important to keep both parts of the score (i.e., the numerator and denominator) in mind. For example, a review that scores 8/8 is generally of comparable quality to a review scoring 11/11; both ratings are considered "high scores." A high score signals that readers of the review can have a high level of confidence in its findings. A low score, on the other hand, does not mean that the review should be discarded, merely that less confidence can be placed in its findings and that the review needs to be examined closely to identify its limitations. (Lewin S, Oxman AD, Lavis JN, Fretheim A. SUPPORT Tools for evidence-informed health Policymaking (STP): 8. Deciding how much confidence to place in a systematic review. *Health Research Policy and Systems* 2009; 7 (Suppl1):S8.

The last three columns convey information about the utility of the review in terms of local applicability, applicability concerning prioritized groups, and issue applicability. The third-from-last column notes the proportion of studies that were conducted in Latin American countries, while the second-from-last column shows the proportion of studies included in the review that deal explicitly with one of the prioritized groups. The last column indicates the review's issue applicability in terms of the proportion of studies focused on childhood cancer. Similarly, for each economic evaluation and costing study, the last three columns note whether the country focus is Latin America, if it deals explicitly with one of the prioritized groups, and if it focuses on childhood cancer.

All of the information provided in the appendix tables was taken into account by the evidence brief's authors in compiling Tables 1-3 in the main text of the brief.

Appendix 1: Systematic reviews relevant to Element 1 - Convene a multi-stakeholder, pan-regional task force with national working groups to develop and oversee the implementation of national childhood cancer strategies to support cancer care in Latin American countries

Sub-element	Focus of systematic review	Key findings	Year of last search	AMSTAR (quality) rating	Proportion of studies that were conducted in Latin American Countries	Proportion of studies that deal explicitly with one of the prioritized groups	Proportion of studies that focused on childhood cancer
Identify a clear picture of the challenges across Latin American countries related to addressing childhood cancer	Deliberative dialogues as a mechanism for knowledge translation and exchange in health systems decision-making (86)	The model developed in the review outlines three key features of deliberative dialogues, which include ensuring an: 1) appropriate meeting environment (e.g., by ensuring adequate resources, commitment from participants, transparency, timeliness of the issue, appropriate group size, clear rules meeting rules, pre- and post-meeting tasks and effective facilitation); 2) appropriate mix of participants (e.g., by ensuring fair and balanced representation of those with an interest in the issue, and that participants are motivated and provided with the resources they need to meaningfully engage in the issue); and 3) appropriate use of research evidence (e.g., fostering a clear understanding of the policy issue among all participants by presenting what is currently known about it based on the best available research evidence). The model further outlines several intended effects of deliberative dialogues, including short-term (e.g., strengthened capacity of participants to address the policy issue), medium-term (e.g., strengthened community or organizational capacity) and long-term effects (e.g., strengthened system capacity to make evidence-informed decisions)	2009	No rating tool available for this type of synthesis	0/17	0/17	0/17
Engage in priority-setting processes to develop: short-, medium- and long-term priorities to address childhood cancer both within and	Public engagement in priority setting and resource allocation (88)	As the literature covers all levels of government, decision-makers are likely to find information relevant to their own setting and situation. The pressures that decision-makers face to satisfy demands for a greater public role in priority setting is indicative of their involvement in public-engagement processes. Most decision-makers use multiple methods to engage multiple publics, and according to the researcher's perspective, it provides a balance that may lead to a more rounded understanding of the public's desires. In addition, the willingness to seek public input in an ongoing,	2006	4/10 (AMSTAR rating from McMaster Health Forum)	Not reported in detail	27/190	Not reported in detail

Sub-element	Focus of systematic review	Key findings	Year of last search	AMSTAR (quality) rating	Proportion of studies that were conducted in Latin American Countries	Proportion of studies that deal explicitly with one of the prioritized groups	Proportion of studies that focused on childhood cancer
across Latin American countries; and meaningful and achievable targets that can be achieved and sustained in the long-term		sustainable fashion over time provides a promising way of obtaining public engagement in priority setting. Public engagement is most common at the visioning or goal-setting level, and in specific decisions about sites or programs, but is less common in monitoring and evaluation activities. Consultations are typically one-off rather than on-going, and not likely to involve the public in direct face-to-face interaction with decision-makers. Costs are seldom reported, but well-structured processes can range from tens of thousands of dollars to the million-plus range.					
	Setting priorities for health interventions in developing countries (89)	This study reviewed empirical studies on priority setting of health interventions in developing countries, classified their methodological approaches and defined methodological suggestions for future studies. The studies covered a wide range of priority-setting areas: 10 studies prioritized interventions across the healthcare system, four studies across several disease areas and four studies concentrated on particular disease areas. Most of the identified studies (14/18) focused on priority setting at the national level. Findings show that most of the included studies involved policymakers, health workers and the general population in their priority-setting process. This coincides with observations in the literature which emphasize the need to involve relevant stakeholders in these debates. Additionally, a number of studies involved only a limited number of quantitative criteria, whereas observations in the literature stress that many other criteria, including medical (e.g. effectiveness of interventions and severity of disease) and non-medical (e.g. economic efficiency, ethical reasons and political circumstances) criteria, may also be important to consider. Furthermore, some studies identified criteria through literature review, however the definitions of criteria are likely to be dependent on culture and perspective. As such, authors suggest identifying these criteria through focus group discussions with relevant	2008	2/10 (AMSTAR rating from McMaster Health Forum)	2/22	0/22	0/22

Sub-element	Focus of systematic review	Key findings	Year of last search	AMSTAR (quality) rating	Proportion of studies that were conducted in Latin American Countries	Proportion of studies that deal explicitly with one of the prioritized groups	Proportion of studies that focused on childhood cancer
		stakeholders as a better approach to obtain an appropriate set of criteria. It was also found that a number of studies relied solely on quantitative techniques to elicit preferences of respondents. Weighing the strengths and weaknesses of both approaches, authors suggest that quantitative techniques may be relevant to situations where general guidance on priority setting is required, whereas qualitative techniques may be more apt in situations where more specific decisions are required on, for example, implementation of certain interventions. Lastly, a number of studies presented their results in descriptive format such as identified criteria or respondents' preferences, and authors suggest that studies should also present the impact of their findings in this respect.					
	Priority setting for health technology assessments (90)	A majority (7 of 12) of priority-setting frameworks used a panel or committee to provide advice regarding priorities. In all cases, committees contained representatives from healthcare system funders, health professionals and researchers. Advice from a board of directors was used in four priority-setting systems and in conjunction with a committee in two of these. Four of the 12 frameworks identified used a rating system to inform priorities. In all cases, these were used in conjunction with a committee. Two systems explicitly considered the cost benefit of conducting the assessment in deciding priorities. Eleven categories were identified for priority-setting criteria (listed in descending order of prevalence): clinical impact, economic impact, disease burden, budget impact, evidence, expected level of interest, timeliness of review, variation in rates of use, controversial nature of proposed technology, ethical, legal, or psychosocial implications, and alternatives.	2007	4/10 (AMSTAR rating from McMaster Health Forum)	0/18	0/18	0/18

Sub-element	Focus of systematic review	Key findings	Year of last search	AMSTAR (quality) rating	Proportion of studies that were conducted in Latin American Countries	Proportion of studies that deal explicitly with one of the prioritized groups	Proportion of studies that focused on childhood cancer
	Describing priority-setting processes for healthcare that either exist or have been tried in different jurisdictions around the world (91)	Priority-setting processes were identified as both formal and informal at national/state and regional levels. Formal processes began with the assembly of a government-appointed committee and identified principles and factors to be considered during priority setting (values such as equity, solidarity, equality, effectiveness/benefit and efficacy of healthcare services under review). Informal approaches comprised informal debates, discussions among policymakers, and a one-off consensus development meeting. Tools for generating a list of priorities, which relied heavily on data, were found to be impractical and conceptually difficult to understand by decision-makers.	2005	3/10 (AMSTAR rating from McMaster Health Forum)	0/10	0/10	0/10

Appendix 2: Systematic reviews relevant to Element 2 – Develop health-system guidance to support the implementation of childhood cancer-care strategies based on national contexts, as well as integration with national cancer care control programs

Sub-element	Focus of systematic review	Key findings	Year of last search	AMSTAR (quality) rating	Proportion of studies that were conducted in Latin American countries	Proportion of studies that deal explicitly with one of the prioritized groups	Proportion of studies that focused on childhood cancer
Create a continuously updated knowledge 'hub' with evidence on childhood cancer epidemiology, treatment approaches, and health-system arrangements that can be used in the development of guidance	To determine what is known about: 1) structures and processes required to build successful collaborations between public health (PH) and primary care (PC); 2) outcomes of collaborations between PH and PC; and 3) markers of successful collaboration between PH and PC (99)	Findings highlighted the importance of collaboration between levels of government; coordination and priority setting to enhance PH and PC collaboration were stressed. Facilitators for collaboration: 1. Systemic level: fit between government and local needs, funding, education and training; 2. Organizational level: Leadership management and accountability, geographic proximity of partners, information sharing; 3. Interpersonal level: role clarity, shared purpose, philosophy and professional identity, developing and maintaining good relationships, effective communication and decision-making strategies. Barriers for collaboration: 1. Systems level: policy, funding, power and control issues, and information infrastructure; 2. Organizational level: lack of a common agenda, resource limitations, lack of knowledge and skills; 3. Interactional level: attitudes and beliefs, relationship challenges. Successful collaboration between PH and PC led to positive outcomes for the healthcare system and health professionals, and health benefits for individuals and populations.	2008	4/10 (AMSTAR rating from the McMaster Health Forum)	0/114	Not reported in detail	Not reported in detail
Engage the full spectrum of health-system stakeholders involved in cancer, child and	Effectiveness of community-engagement approaches and methods for health promotion interventions (106)	There is little evidence on the effects of specific interventions on health promotion. Varying qualities of evidence suggest that interventions that engage the community improve the dissemination of information and the development of interventions. The review	Not reported (published in 2008)	9/10 (AMSTAR rating from McMaster Health Forum)	0/21	9/21	0/21

Sub-element	Focus of systematic review	Key findings	Year of last search	AMSTAR (quality) rating	Proportion of studies that were conducted in Latin American countries	Proportion of studies that deal explicitly with one of the prioritized groups	Proportion of studies that focused on childhood cancer
adolescent health, and non-communicable diseases (e.g., global health governance institutions such as the WHO, non-governmental organizations, a cross-section of select national policymakers, stakeholders and researchers) and consumers to develop and refine guidance		includes no evidence regarding the effectiveness of community-engagement approaches and methods for health-promotion interventions with regards to optimizing clinical practice. The evidence from one study suggests that community champions used in planning/design or delivery of health-promotion interventions can increase their level of knowledge, skills and confidence following training, and feel that they make the greatest impact in areas in which they have ownership and a stronger voice within their communities. The community-engagement approaches reviewed included the use of community groups, committees, educators, volunteers, workshops and champions. In addition, the community-engagement methods and approaches focused on the planning, design and delivery of intervention(s) in areas of cardiovascular health, childhood immunization, injury prevention, sexual health, smoking, alcohol use, nutrition and physical activity.					
	Effective strategies for interactive public engagement in developing healthcare policy and program delivery at a provincial/regional level (107)	Interactive public engagement designed to contribute to decision-making can be successfully implemented in various situations. The relative success of implementation is influenced by a range of contextual variables, of which organizational commitment and issue characteristics play more important roles than other contextual variables. In well-designed interactive public engagement processes, participants generally report high levels of satisfaction with the communication of objectives, adequacy of the information materials, and the logistics of the deliberations. These public-engagement methods can influence participant views, but are less likely to alter	2009	4/9 (AMSTAR rating from McMaster Health Forum)	0/29	5/29	0/29

Sub-element	Focus of systematic review	Key findings	Year of last search	AMSTAR (quality) rating	Proportion of studies that were conducted in Latin American countries	Proportion of studies that deal explicitly with one of the prioritized groups	Proportion of studies that focused on childhood cancer
		dominant views, such as the highest priorities. Researchers note that continued ambiguity in the terminology, goals, theoretical properties and benefits of public engagement amongst Canadian health-system managers and policymakers will threaten potential meaningful progress towards informing practice and involving the public in the development of healthcare programs.					
	Examining the peer-reviewed empirical evidence on outcomes of public involvement in healthcare policy (124)	The outcome of public involvement in healthcare policies remains largely underdeveloped and poorly documented. There is little to no evidence for the longer-term impact demonstrated by public involvement. There is no clear conclusion on the effectiveness of policy development from involvement activities. The review includes no evidence regarding the effectiveness of public involvement with regards to optimizing clinical practice. There is some evidence for the developmental role of public involvement (e.g. enhancing awareness, understanding and competencies among lay participants), but the unclear definition of success impedes on forming a conclusion about public involvement. There is limited data available to address the primary research questions. The key features of public involvement remain poorly defined, and its objectives are rarely specified in the literature. Indicators used to determine outcomes of this form of intervention remain inconsistent and poorly specified.	2010	4/9 (AMSTAR rating from McMaster Health Forum)	0/19	0/19	0/19
	Examining the effects of involving patients in the planning and development of healthcare (125)	A review of 337 studies involving patients in the planning and development of healthcare found that few studies described the effects of involving	2000	5/9 (AMSTAR rating from	Not reported in detail	0/40	0/40

Sub-element	Focus of systematic review	Key findings	Year of last search	AMSTAR (quality) rating	Proportion of studies that were conducted in Latin American countries	Proportion of studies that deal explicitly with one of the prioritized groups	Proportion of studies that focused on childhood cancer
		patients in the planning and development of healthcare. The review defined patient involvement as "the active participation in the planning, monitoring, and development of health services of patients, patient representatives, and wider public as potential patients." Case studies reporting on project administrators' views about the impacts of patient engagement support the view that involving patients has contributed to changes to services. An evidence base does not exist for the effects on use of services, quality of care, satisfaction, or health of patients. The effects of patient involvement on accessibility and acceptability of services or impact on the satisfaction, health or quality of life of patients, has not been examined. The effect of patient contributions to the planning and development of services on the quality and effectiveness of these services across various settings is unknown.		McMaster Health Forum)			
	Stakeholder involvement in program evaluation (102)	A review of 41 studies on the involvement of stakeholders in program evaluation consisted of reports of original research on stakeholder involvement, independent of actual evaluations, or reports of actual evaluations or meta-evaluations. There is a small percentage of studies reporting original research. Nearly half of the reviewed studies were set in health or education. The dominance of these disciplines suggests that stakeholder involvement is emphasized to a greater extent within these disciplines. Considerable overlap was found between the component and component features that the studies addressed, reflecting a conceptive	2010	4/9 (AMSTAR rating from McMaster Health Forum)	Not Reported	Not reported in detail	Not reported in detail

Sub-element	Focus of systematic review	Key findings	Year of last search	AMSTAR (quality) rating	Proportion of studies that were conducted in Latin American countries	Proportion of studies that deal explicitly with one of the prioritized groups	Proportion of studies that focused on childhood cancer
		commonality among researchers of stakeholder involvement. The component, *Affective Aspects of Involvement and Collaboration, Communication, and Interaction*, where parties "enter into collaboration with the appropriate degree of willingness to participate …draw on the strengths of each while respecting the positions and expertise of each other", reflects the methodological centre of stakeholder involvement. The review found very little research on stakeholder involvement in evaluation. The limited number of studies reviewed should not be taken to imply that stakeholder involvement has received little attention in the broader literature.					
	Public deliberation as a method for increasing public input for health research (103)	Public deliberation is presented in the literature as a specific area of political science, and it encourages members of the public to engage in and be informed about issues that shape their public life. Evidence remains consistent in suggesting that public deliberation is a method of obtaining public input on decisions that are important to society. The goals of public deliberation are to obtain informed public opinion, to obtain input that includes under-represented individuals and groups, to bring insights into social values and ethical principles, and to promote the acceptance of public decisions. In addition, the effects of deliberation on participants improve understanding of the complexity of decisions and enhance civic-mindedness. Identified issues that are best suited for public deliberation involve ethical and social dilemmas. It is also important to note that the potential to find common ground is a requirement for issues addressed through public deliberation. Common deliberative tasks in healthcare include	2010	1/9 (AMSTAR rating from McMaster Health Forum)	Not reported	Not reported	Not reported

Sub-element	Focus of systematic review	Key findings	Year of last search	AMSTAR (quality) rating	Proportion of studies that were conducted in Latin American countries	Proportion of studies that deal explicitly with one of the prioritized groups	Proportion of studies that focused on childhood cancer
		the development of policy direction, recommendations and tools, priority setting and resource allocation, and risk assessments. The process of public engagement is facilitated through discussion and prompts the public to develop solutions to societal problems posed to them. It includes three broad characteristics: a sponsor seeking input from participants (i.e., the public); participants considering the ethical- or values-based dilemma; and an information phase in which participants are given accurate and balanced information about the relative positions involved by way of educational materials, experts, etc.					
	Effectiveness of the agenda of involvement of people affected by cancer in research, policy and planning, and practice (108)	Training of patients and healthcare professionals is necessary for successful involvement of cancer patients in research, policy and planning, and practice. Patient involvement requires personnel and financial support. The opposing ideologies of individualism and collectivism are the most common rationales as to why people affected by cancer should be involved in research, policy and planning, and practice. Some policy and planning, and research organizations have involved people affected by cancer at a strategic level, most notably in the U.K. and the U.S.A., but it is not clear how much power and influence they hold at a strategic level. 'One-off' involvement exercises to influence local policy and planning have taken place in the U.K. in the acute sector, and at a national level to develop guidelines and services, but no examples were found in social care or primary care. The	2004	4/9 (AMSTAR rating from McMaster Health Forum)	Not reported in detail	Not reported in detail	Not reported in detail

Sub-element	Focus of systematic review	Key findings	Year of last search	AMSTAR (quality) rating	Proportion of studies that were conducted in Latin American countries	Proportion of studies that deal explicitly with one of the prioritized groups	Proportion of studies that focused on childhood cancer
		biggest gap in literature about the involvement agenda is rigorous evidence of its impact on research, healthcare services, on those involved and on the agenda itself.					
	Defining the benefits of stakeholder engagement in systematic reviews (101)	This review sought to examine the benefits and challenges of engaging stakeholders in the process of developing and performing systematic reviews. Benefits cited include identifying and prioritizing topics for research; providing pragmatic feedback on the research protocol; aiding in recruitment of research participants; helping the researchers understand the research subject's perspective; ensuring that findings are interpreted with the end user in mind and that final products are readable and accessible; and facilitating wider dissemination and uptake of research findings. In particular, the topic refinement and research development phase of conducting a systematic review was identified as the point where stakeholder engagement yielded the greatest benefit. Challenges include time and resources, researcher skills for stakeholder engagement, finding the right people, balancing multiple inputs, and understanding the best/most appropriate time in the review process to engage different types of stakeholders. Additionally, it was found that very few studies directly measured the impact of or had quality standards for stakeholder engagement, with most relying heavily on observations and inferences.	2013	5/9 (AMSTAR rating from McMaster Health Forum)	0/24	0/24	0/24
	Strategies in consumer and community engagement in health care (109)	This review used the term CCE to encompass the involvement of consumers (patients and their carers) and community members (i.e., non-patient community members and the community more broadly). The authors note that there remains a paucity of evidence related to the effectiveness of CCE strategies, and participation of different groups of consumers in the CCE process.	Not reported	4/9 (AMSTAR rating from McMaster Health Forum)	Not reported	2/90	0/90

Sub-element	Focus of systematic review	Key findings	Year of last search	AMSTAR (quality) rating	Proportion of studies that were conducted in Latin American countries	Proportion of studies that deal explicitly with one of the prioritized groups	Proportion of studies that focused on childhood cancer
		CCE encompasses strategies that have been used to facilitate the improvement of the level of general service delivery and specific services within preventative care, technology, and related healthcare fields. Various tools and activities are utilized by CCE initiatives, including shared decision-making, decision aids, consumer representation, electronic and internet-based facility application, and peer support and community-based interventions. The review indicated that literature focusing on CCE strategies targeting children found that children and adolescents want to participate in their decision making, but that healthcare professionals require guidance to assist in their involvement. When reviewing literature focusing on populations from lower socioeconomic backgrounds, the authors noted that lowered costs, increased primary care physician involvement, and modification of communication to better meet individuals' needs were all strategies that facilitated enhanced cancer screening for women in one included study. The authors indicated that a key finding from the review is that CCE initiatives should be rigorously evaluated before their implementation, as they often require immediate resource mobilization and may have hidden costs associated with them (e.g., training healthcare professionals and consumers). Additionally, there are a number of context-related factors that play a role in the success of CCE strategies; the review outlines a model to facilitate assessment of these strategies (i.e., an					

Sub-element	Focus of systematic review	Key findings	Year of last search	AMSTAR (quality) rating	Proportion of studies that were conducted in Latin American countries	Proportion of studies that deal explicitly with one of the prioritized groups	Proportion of studies that focused on childhood cancer
		eight-step process identifying aim, type of activity, participants, preparedness for CCE, engagement methods, measurement, barriers and facilitators).					
	The use of citizens' juries in health policy decision-making (110)	The review describes citizen juries as a method allowing citizens to engage with evidence and deliberate and deliver recommendations surrounding a variety of complex topics. Steering committees and advisory groups involved in the citizens' jury method described in the reviewed studies included key stakeholders (e.g., policymakers) discipline experts, advocacy group representatives, clinical practitioners, deliberative methodologists, patients and caregivers. Studies described the role of the groups in a variety of ways, such as to: prevent bias in expert presentation; guide question development and evidence presentation; disseminate or implement findings; and engage stakeholder representatives. The authors found that among the study population, a large number of juries were shorter in duration than recommended, and few rulings were considered by decision-making bodies (which limited transfer into policy and practice). The authors indicate that when adapting a citizen jury for a particular aim, development of the jury should involve special attention toward recruitment, independent oversight by a steering committee, duration of the jury, moderation, and respect for volunteer participants.	2010	5/9 (AMSTAR rating from McMaster Health Forum)	1/35	0/35	0/35
Develop 'workbooks' to support the implementation of the guidance in specific Latin	No systematic reviews identified						

Sub-element	Focus of systematic review	Key findings	Year of last search	AMSTAR (quality) rating	Proportion of studies that were conducted in Latin American countries	Proportion of studies that deal explicitly with one of the prioritized groups	Proportion of studies that focused on childhood cancer
American contexts through subsequent national-level deliberative processes							

Appendix 3: Systematic reviews relevant to Element 3 – Build capacity for monitoring and evaluation to support efforts to continuously refine the implementation of national childhood cancer-care strategies

Option element	Focus of systematic review	Key findings	Year of last search	AMSTAR (quality) rating	Proportion of studies that were conducted in Latin American countries	Proportion of studies that deal explicitly with one of the prioritized groups	Proportion of studies that focused on childhood cancer
Building system capacities for systematic monitoring and evaluation (e.g., building high-quality cancer registries)	No systematic reviews identified						
Identify relevant indicators and outcomes that can be tracked between countries to provide common benchmarks for analysis	No systematic reviews identified						
Monitor and evaluate the extent of	No systematic reviews identified						

Option element	Focus of systematic review	Key findings	Year of last search	AMSTAR (quality) rating	Proportion of studies that were conducted in Latin American countries	Proportion of studies that deal explicitly with one of the prioritized groups	Proportion of studies that focused on childhood cancer
implementation using common benchmarks across countries, and adjust country-specific plans based on the results							

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