

IMPROVING PAEDIATRIC CANCER CARE IN LOW- AND MIDDLE-INCOME COUNTRIES: THE EXPERIENCE OF THE ST JUDE INTERNATIONAL OUTREACH PROGRAM

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This article describes the outreach programme devised by the St Jude Children's Research Hospital in the United States to help children suffering from cancer in low- and middle-income countries. It considers the essential components required for successful twinning and introduces the nine "Critical Cs" which need to be considered before embarking on a twinning partnership.

Survival of children with cancer has increased dramatically in high-income nations, from essentially zero in the early 1950s to rates approaching 80% today. This success is due in part to disease-adapted multimodality treatment, including surgery, chemotherapy and radiation, that has been refined through a series of multi-institutional clinical trials. Although new medications and procedures, such as Gleevec and haematopoietic cell transplantation, have contributed to survival, the optimization of conventional drugs has accounted for most of the treatment successes. Parallel gains in supportive care, particularly in the management of infectious complications, have made it possible to escalate the intensity and thus the efficacy of these therapies. However, an estimated 80% of about 200,000 children diagnosed with cancer each year lack access to modern treatment and thus have dismal outcomes. In a recent survey conducted in 10 countries, postulated survival rates varied from less than 10% to 60%, depending on the country. In four of the 10 countries surveyed, only about 15–40% of expected cases would have ever been seen by health care providers.

In 1994, the St Jude International Outreach Program (IOP)

was created with the mission of improving the survival of children with cancer in low- and middle-income countries by sharing knowledge and organizational skills and supporting the implementation of paediatric oncology units in public paediatric hospitals in selected countries. These "twinning" programmes were envisioned as culturally sensitive demonstration projects that would be integrated with and adapted to the local health care systems.

We define our twinning programmes as long-term, close relationships with centres in low- and middle-income countries. These programmes have several essential components. Strong local leadership of different programme components is essential. Local institutional, medical and community leaders create a sense of purpose by encouraging team building and sharing the ownership of the process among participants ranging from administrative staff and health professionals involved in family support to those directly involved in the treatment of children with cancer. This consistent mutual recognition of the efforts made by different team members and their inclusion in the decision-making process enables commitment, active participation and mission-oriented pursuits. Strong leaders are necessary

among health care providers (physicians, nurses, psychologists, nutritionists, social workers), institutions (hospital directors, university deans) and non-governmental foundation members (community and patient advocates). These individuals must understand the needs of children with cancer including physical, emotional, economic, social and spiritual as integral components of the chain of care and twinning relationships are not established unless or until all pieces are in place. Moreover, these activities have to take into account social and cultural values, required needs and available resources. Treatment plans must be based on medical evidence and integrated with other programmes existent in the health care system. The vision is that by implementing a paediatric cancer unit within a hospital, not only will children with cancer benefit but so will other sick children and the hospital itself. The goals include improving cure rates and access to care for children with cancer, producing generalizable knowledge that has global benefits, and demonstrating to the local community that progress in paediatric cancer care is both necessary and feasible. Although the benefits of twinning are almost always bidirectional, twinning programmes must be distinguished from contractual or commercial partnerships for mutual gain and from research collaborations that focus on a specific project. The St Jude twinning model emphasizes a horizontal distribution of resources dedicated to improving survival rates in childhood cancer overall and developing local support for children undergoing therapy. It also assists in the creation of fund-raising efforts (e.g., parents' associations) and the building of relationships with local foundations willing to provide financial support that ensures the sustainability of each project in the long term, rather than restricting the activities to single diseases that answer specific questions within a defined time-frame. St Jude staff integrate outreach activities into their daily schedules and maintain close contact with their peers through e-mails, phone calls and on-line meetings. Each country has assigned directors within the IOP and make site visits every one or two years – sometimes in association with educational meetings.

Our twinning programmes have been fully established in Amman, Beijing, Shanghai, Beirut, Casablanca, Rabat, Caracas, Maracaibo, Culiacán, Guadalajara, Tijuana, Davao, Guatemala City, Quito, Recife, San Jose, San Salvador, Santiago and Tegucigalpa. The St Jude IOP also enters into agreements with institutions in developed countries that have specific training needs or wish to actively participate in the development of twinning sites. These include the Hospital Infantil Manuel de Jesus Rivera in Managua, the Russian Children's Clinical Hospital in Moscow, the National

University Hospital in Singapore, the Ospedale Nuovo S Gerardo and Università di Milano-Bicocca in Monza, Italy, and Rady Children's Hospital in San Diego, United States. We have also facilitated other medical organizations to form their own twinning programmes. These include the Keira Grace Foundation with the Hospital Infantil, Dr Robert Reid Cabral (Santo Domingo, Dominican Republic); the American Society of Hematology International Consortium on Acute Promyelocytic Leukemia with institutions in Brazil, Mexico, Uruguay and Chile; and the Dana Farber Cancer Institute with the National Cancer Institute in Bogotá, Colombia. The latter project is supported by a grant from the World Child Cancer Foundation. Finally, the St Jude IOP has worked in collaboration with global health agencies such the International Agency for Atomic Energy to develop specific paediatric cancer control projects in member states and has collaborated with the Union for International Cancer Control (UICC) and the Sanofi-Esper Foundation to develop the My Child Matters programme, which funds specific paediatric cancer programmes in low- and middle-income countries.

Optimally, patients are cared for in a dedicated paediatric cancer unit that combines the necessary professionals, expertise and infrastructure. Agreements are only made when senior medical staff are able to devote themselves to the project on a full-time basis and to accept the St Jude philosophy of integrating the programme into the community and to provide holistic, multidisciplinary care to the children regardless of the ability of the family to pay for treatment. We found that medical competence in conjunction with compassionate care is the most crucial programmatic component. Ideally, the paediatric cancer unit becomes the focus of intense education for direct caregivers, including paediatric haematologists/oncologists, nurses, surgeons, pathologists, radiotherapists, infectious disease specialists, acute care physicians, family members and communities.

In many low- and middle-income countries, the paediatric cancer units must also be the focus of intense educational efforts to reduce death from infection and abandonment of therapy. Death from infection is a greater risk in low- and middle-income countries, partly because of a delay in starting antibiotics and other supportive measures.

We adopt a stepwise approach to implementing interventions. This takes into consideration local resources and needs. At most of the partner sites, acute lymphoblastic leukemia (ALL) is the initial disease to be addressed, as it is a common childhood malignancy and is highly curable with relatively accessible drugs and evidence-based treatment guidelines. However, successful management of ALL requires the integration of several components of care, including

Table 1: The St Jude Twinning Program's "Critical Cs" for childhood cancer care in low- and middle-income countries

Critical "C"	Components	Content	Constraints
Commitment by HIC partner	<ol style="list-style-type: none"> 1. Leader in HIC (willing to devote time and effort to the programme) 2. Institutional commitment 	<p>A committed leader is necessary to define, develop, initiate, implement and maintain the programme. The leader facilitates intra- and inter-institutional communication and engages the hospital to mobilize resources (human, technical and financial)</p>	Lack of leadership in HIC makes a twinning programme unlikely to succeed
Commitment by LMIC partner	<ol style="list-style-type: none"> 1. Leader in LMIC (willing to devote time and effort to the programme) 2. Institutional commitment 	<p>A committed leader is necessary to define, develop, initiate, and implement the programme. The leader facilitates intra- and inter-institutional communication and must engage the hospital and community to mobilize resources (human, technical and financial)</p>	Lack of leadership in LMIC makes a twinning programme unlikely to succeed
Community advocacy and fundraising in LMIC	<ol style="list-style-type: none"> 1. Non-profit, non-governmental foundation to solely support childhood cancer care 2. One cancer foundation per geographic area 	<p>Members of the supporting foundation should include influential members of society, professionals and parents/relatives of patients The foundation works with both government and the medical team to effect change Credibility of foundations established yearly by independent auditing agencies</p>	If multiple foundations develop in a single region, their message is diluted and their ability to raise money and advocate are diminished
Collaborative spirit	<ol style="list-style-type: none"> 1. Respect 2. Trust 3. Humility 4. Collegiality 	<p>Twinning must be a culturally sensitive relationship of equals who are willing to learn from one another. In the best programmes, the association is beneficial and enjoyable on both sides</p>	A focus on individual accomplishments is less helpful than a focus on the shared mission to cure patients with cancer
Communication	<ol style="list-style-type: none"> 1. Effective 2. Comprehensive 3. Multimodal 	<ol style="list-style-type: none"> 1. Rapid, honest, in the same language 2. Addresses programmatic aspects (contracts, financial matters, documentation of activities), patient care (individual cases, supportive care, protocols), continuing education and hospital infrastructure 3. E-mail, on-line meetings, phone conversations, exchange visits of key personnel 	Absent or dishonest communication makes a twinning programme impossible
Core activities	<ol style="list-style-type: none"> 1. Based on the needs identified in the LMIC and the capacity of the HIC to address the needs 2. Data collection and analysis must always be included 	<ol style="list-style-type: none"> 1. Goals and specific activities must be very well defined in writing. Goals may change over time by mutual agreement. 2. Documentation of causes of treatment failure and death is essential to target interventions and measure progress. 	Improvements in cancer diagnosis, infection control, protocol design, education, nursing, and outcome evaluation are all important; these needs must be prioritized by the twinning partners
Capital and operational budget	<ol style="list-style-type: none"> 1. The HIC should seek funding to initiate and maintain the twinning relationship for at least 5 years 2. Increasing local fundraising capacity should be part of most twinning programmes 3. Ultimately, alliance with government is necessary to scale up the programme 	<p>Funding is needed to support key salaries in the LMIC (medical director, nurse educator, data manger), to provide some equipment and supplies, and to pay for exchange visits. Expenditures should be specifically tied to desired outcomes, with a focus on developing leaders and implementing simple, effective methods to improve cure rates. About US\$ 100,000 per year plus the time of the HIC participants is sufficient to develop a strong demonstration project in a public hospital managing about 200 annual new cases of childhood cancer</p>	Large expenditures on advanced technology or bench research should be deferred until basic cancer care is excellent
Continuity	A long-term relationship is essential, because the goal is to develop a self-sustaining programme	At least a 5-year plan should be developed at the very beginning so that both partners can agree on the goals of the twinning relationship and timing of the included activities	Short-term projects have some value, but a long-term relationship is necessary to gain the benefits of twinning

diagnostics, supportive care, delivery of multi-agent chemotherapy, adherence to treatment, and long-term follow-up. Hence, implementation of an effective treatment plan for ALL allows that many other chemotherapy-sensitive malignancies can be treated as well. We suggest treatment protocols be based on published evidence and developed with specific local conditions in mind, including the availability and affordability of the chemotherapy agents, the expected requirements for supportive care and the availability of support services needed to deliver the therapy. The goal is to quickly achieve a 60% event-free survival rate and then to target the most common causes of failure for improvement. For example, if abandonment of therapy and toxic deaths are the most common causes of failure, improved hospital supportive care and the social and economic help for the families are the logical priorities. The above points were elegantly demonstrated by our experience in Recife, Brazil, in which the rate of abandonment was reduced to less than 1% and the rate of toxic deaths to less than 10%. Toxic deaths were reduced through a combination of improved supportive care and individualization of the treatment protocol according to each patient's clinical condition. For example, patients with a large tumour burden and associated morbidity, such as infection and malnutrition, received gentle tumour reduction, treatment for infection, and nutritional support for several days before the intensity of anticancer therapy was escalated. Individualized protocol adaptation is facilitated by weekly case discussions between the local and St Jude physicians via the www.cure4kids.org web-conference tool.

The infrastructure created to treat ALL can support the successful management of lymphomas, promyelocytic leukemia, and other cancers that can be cured with chemotherapy alone. With the availability of trained paediatric surgeons and radiotherapists, Wilms tumour, favourable-prognosis rhabdomyosarcoma, neuroblastoma, Ewing sarcoma, osteosarcoma, and retinoblastoma can also be adequately treated. In some countries, chemotherapy-only protocols have been developed for childhood Wilms tumour and Hodgkin's lymphoma because of the unavailability of radiation therapy. Management of acute myeloid leukemia (AML) and brain tumors remains challenging at many partner sites.

To measure the progress of partner sites' cancer units, we established several quantitative and qualitative variables and individualized them for each programme. An increase in the number of children assisted and survival rates are the absolute indicators of success. Other outcome indicators are

the number of children who finish treatment, the number of children who remain in follow-up, the number of diseases managed with uniform guidelines (evidence-based), the number of children enrolled on protocols with uniform guidelines and the number of health care providers dedicated to paediatric oncology. Finally, an important consideration is to determine whether a partner country's fundraising organization and government are achieving self-sustainability. The amount of St Jude's direct financial contribution relative to the entire paediatric cancer unit is one of these indicators. For example, in many of our partner sites, at the start of our programme, the St Jude contribution represented the largest portion of the paediatric cancer unit's budget. As the programme develops and financial support from non-governmental and governmental sources becomes available, the relative St Jude contribution to the entire cancer unit budget traditionally decreases to about 3% to 4% of the total expenses. Careful documentation and analysis of the adverse events in children managed uniformly on treatment protocols is crucial to detect areas that need improvement. Weekly data manager training sessions are held via www.Cure4kids.org in both English and Spanish. A database specifically designed for paediatric oncology (Paediatric Oncology Networked Database [POND], www.Pond4kids.org) has been available for partner sites. St Jude IOP is improving POND to accommodate a tumour registry as well as cancer-specific, nutritional, psychosocial, and socioeconomic information. The data are stored on a dedicated server, which is encrypted, password protected, and backed up every 10 minutes. This server is located in the United States and we are modifying POND software to allow the data to be stored at the local user facilities. Treatment protocols can be shared via a global library so that other sites can use them.

The sustainability of the paediatric oncology units has been an important consideration since the inception of the twinning concept. The public sector is an unlikely funding source for these initiatives. In most countries in which St Jude's IOP establishes partnerships, government health budgets are barely adequate to fund the management of common communicable paediatric diseases. In addition, government officials in these countries often lack the experience base needed to implement a national paediatric cancer programme; hence, paediatric cancer care emerges as an individual or private-sector initiative. A local NGO has been developed at almost all St Jude IOP partner sites where paediatric cancer treatment is not fully government-funded, to complement the support needed for the diagnosis and

treatment of childhood cancer. The NGOs are also an important vehicle for community education and fundraising for additional services, such as bone marrow transplantation, clinical investigation, and continuing education of clinicians. The key leaders of the local NGOs are trained by ALSAC, the St Jude fundraising organization. Importantly, all funds raised in partner countries are used within that country.

Some key members of the partner-site multidisciplinary teams receive salary supplementation from the NGOs to allow them to work full-time in the paediatric oncology unit. Although the amount varies among the different partner sites, annual salary supplementation is commensurate to the salaries of the physicians working in paediatric haematology/oncology that combine academic and private activities. This strategy aims to retain these individuals in the public hospitals, which serve large patient populations and have insufficient personnel, medications, and infrastructure.

The St Jude IOP twinning programmes have demonstrated that it is feasible and affordable to rapidly improve the cure rates of children with cancer in countries with limited resources and to improve their access to care in public hospitals. The major challenge is to scale up the quantity and quality of care and services for partner sites and countries in the region. Recently, St Jude IOP has initiated an innovative

model in an effort to help partner sites expand their local programmes in a regionally oriented fashion. In this new model, a St Jude international partner site will be equipped to provide most of the services required in paediatric oncology including diagnosis, supportive care and training opportunities. After reaching this status, the centre (Hub) will be able to provide assistance to other centres that exist both within the country and regionally (Spokes). This Hub-Spoke model has not been tried before in health care. We hope to see paediatric international oncology become an academic discipline within paediatric and medical oncology, with the goal of creating models to implement existent knowledge in countries with limited resources to avoid unnecessary death and suffering caused by childhood cancer. ●

Acknowledgements

This work was supported in part by a Cancer Center Support Grant (CA21765) from the National Institutes of Health and by the American Lebanese Syrian Associated Charities (ALSAC).

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