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## ADDRESSING REGIONAL DISPARITIES IN PEDIATRIC ONCOLOGY: RESULTS OF A COLLABORATIVE INITIATIVE ACROSS THE MEXICAN-NORTH AMERICAN BORDER

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### Abstract

**Background**—Cancer is emerging as a major cause of childhood mortality in low-income and middle-income countries. In Mexico, cancer is the number one cause of death in children aged 5–14. Until recently, many children with cancer from Baja California, Mexico went untreated. We reasoned that an initiative inspired by the St. Jude Children's Research Hospital (SJCRH) “twinning” model could successfully be applied to the San Diego–Tijuana border region. In 2008, a twinning project was initiated by Rady Children's Hospital, SJCRH and the General Hospital Tijuana (GHT). Our aim was to establish a pediatric oncology unit in a culturally sensitive manner, adapted to the local health care system.

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#### Conflict of Interest Statement

The authors report no conflict of interest.

**Procedure**—An initial assessment revealed that despite existence of basic hospital infrastructure at the GHT, the essential elements of a pediatric cancer unit were lacking, including dedicated space, trained staff, and uniform treatment. A 5-year action plan was designed to offer training, support the staff financially, and improve the infrastructure.

**Results**—After seven years, accomplishments include the opening of a new inpatient unit with updated technology, fully-trained staff and a dedicated, interdisciplinary team. Over 700 children have benefited from accurate diagnosis and treatment.

**Conclusions**—Initiatives that implement long-term partnerships between institutions along the Mexican-North American border can be highly effective in establishing successful pediatric cancer control programs. The geographic proximity facilitated accelerated training and close monitoring of project development. Similar initiatives across other disciplines may benefit additional patients and synergize with pediatric oncology programs to reduce health disparities in underserved areas.

### Keywords

Pediatric Oncology; Global Health; International Oncology; Pediatric Cancer Disparities; International Collaboration; U.S-Mexico border

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### Introduction

Worldwide, close to 200,000 children are diagnosed with cancer each year and 80% reside in low-income and middle-income countries (LMIC). [1] Effective management of pediatric cancer is complex, expensive and requires an interdisciplinary approach, thus it is often out of reach in LMIC. A significant survival gap exists between cancer patients in high-income countries (HIC) and LMIC, where 5-year overall survival rates are 5–35% compared to 80–85% in HIC. [2–4]

The disease burden of pediatric cancer in Mexico—one of the most populated countries in the world—makes the need for providing adequate care for Mexican children an imperative, as cancer is the number one cause of death in children 5–14 years old. [5–7] Five-year overall survival for all childhood cancers in Mexico is estimated to be between 30–40%, [7,8] whereas across the border in the United States (U.S.) it is often above 80%. [9,10] In the Mexican state of Baja California as early as ten years ago, pediatric cancer outcomes were among the worst in the country. [8,11] Poor survival rates in several Mexican states, such as Baja California, are likely related to geographic barriers in accessing healthcare coupled with vast disparities in the quality of pediatric cancer care that stemmed from long-standing regional infrastructure differences similar to those reported in other countries. [2]

Twinning programs are dynamic and unique collaborative models of long-term engagement whereby a state-of-the-art center in a HIC establishes a long-term partnership with an emerging center in a LMIC. Their main purpose is to improve overall care for children with cancer and narrow the survival gap. [2,12–14] The impact of twinning programs on improving pediatric cancer outcomes in resource-strained settings is well documented. [15–18] However, twinning partnerships between institutions located in close proximity but separated by national borders and with profound cultural, economic and geopolitical differences are scarce. We hypothesized that developing a twinning initiative based on

principles of those implemented elsewhere [15–18] would rapidly improve pediatric cancer care in our particular setting.

Here we describe the implementation successes and challenges of a twinning program between Rady Children’s Hospital San Diego (RCHSD), California and the General Hospital Tijuana (GHT), Baja California, Mexico aimed at addressing pediatric cancer disparities along the Mexican-North American border.

## Methods

### Program Development and Operational Plan

**Setting and Needs Assessment**—Collaboration between St. Jude Children’s Research Hospital (SJCRH) and RCHSD began in 2007 when we formed an alliance to combine resources and expertise to pursue clinical and translational research. In 2008, this alliance evolved into a partnership between RCHSD, SJCRH and the GHT in Mexico to initiate a twinning program in pediatric oncology.

Before the partnership was initiated with the GHT, there was no pediatric oncology unit in Baja California. First steps involved an assessment visit to the GHT in 2008. A modified SJCRH needs assessment tool was developed and carried out. [19]

The assessment revealed that, although the basic hospital infrastructure and services were available at the GHT, including anatomic pathology, laboratory and blood bank, the essential elements of a pediatric cancer unit, such as dedicated space; trained pediatric oncologists, nurses and allied staff; uniform treatment; and standardized supportive care guidelines were lacking. Patients were treated by an adult hematologist and admitted to the general pediatric ward without isolation measures or intensive care unit support. Even though some chemotherapy medications were available through local philanthropy, standard operational procedures for preparation, administration and record keeping were lacking. Psychosocial, palliative care and nutritional programs were not available. Medical records were incomplete and a hospital-based cancer registry did not exist. Based on Baja California’s population (Table 1), 150 new cancer cases per year were expected. [20]

**Action Plan and Implementation**—In response to the identified needs, an initial 5-year action plan was designed in adherence to the implementation guidelines of other twinning partnerships. [16,21–25]

Main goals of the of the RCHSD-SJCRH-GHT partnership were established based on the core components of a successful twinning program: 1) Infrastructure development and enhancement of care, including the establishment of a pediatric oncology unit at the GHT and case discussions with experts at RCHSD; 2) Establishment and training of a dedicated team of physicians, nurses and allied staff to provide high-quality care and designation of a local pediatric oncologist as program leader; 3) Development of a hospital-based cancer registry for data collection to document improvement in clinical outcomes; and 4) Development of capacity building and financial sustainability. To ensure long-term sustainability, most of the financial obligations were assumed by the GHT (e.g. personnel

salaries, equipment, supplies and medications), and a partnership with a local grassroots foundation was forged. A Hispanic, native Spanish-speaking pediatric hematologist/oncologist (PA) from RCHSD, who completed training in leadership and administration, was appointed to supervise the project and visited the partner site weekly for the first 1.5 years of the program. Adherence to the principles of good clinical practice was undertaken to ensure protection of data. The Institutional Review Board at the GHT approved this study.

## Results

### Infrastructure and Enhancement of Care

Infrastructure improvements began immediately, including the construction of a temporary, dedicated 5-bed unit that was completed in 2008; a permanent, modern facility was completed in 2011. This pediatric cancer unit—in use today—has 10 rooms with negative pressure capabilities, two dedicated intensive care beds within the oncology unit, a procedure room, outpatient clinic rooms, an outpatient infusion center, adequate bathrooms, meeting rooms for the staff and a school for the children.

Several workflow improvement strategies were also undertaken. These included adjustments to the process for blood sample collection, reorganization of the outpatient clinic space, provision of computers and telephones, internet access, development of policy and procedures for preparing and administering medications (including chemotherapy), medical record documentation and the development of a hospital-based cancer registry and data management program.

### Patient Clinical Outcomes and Treatment Abandonment

The rate of new pediatric cancer cases per year since the establishment of the program increased from 10–20 per year to 60–70 per year, a three-fold increase, corresponding to 50% of the cases expected per year in the state of Baja California. This was anticipated, as several other publications have reported a similar increase in new pediatric cancer cases in LMIC, as the ability to diagnose and treat additional cases is improved when oncology centers are established. [1,2,4,26] The distribution of the diagnoses in the patient population by cancer type fairly matched the epidemiology data described in the rest of the world (Figure 1). The five-year overall survival and the five-year event-free survival rates for acute lymphoblastic leukemia at the GHT are currently at 55% and 49%, respectively, up from an estimated 10% in 2007. Principal causes of mortality included infection and disease relapse. Table 2 shows a summary of selected clinical outcome measures. Of note, the mortality rate during induction therapy for acute lymphoblastic leukemia at our center was higher when compared to institutions in HIC, but lower (5.3%) when compared to other LMIC (28%). [25,27]

Despite the usual risk factors for treatment abandonment in LMIC previously reported [28–31] such as poverty, lack of transportation and increased mean home-to-hospital travel time, we encountered factors particular to the diverse population in the state of Baja California. These include a floating immigrant population, single-parent household status, relying on informal activities for income, parent substance abuse and family violence. About 25% of

the patients treated at the GHT came from single-parent households, and the mean home-to-hospital travel time was 1.5 hours (range 0.5 to 8 hours).

To address the needs of this complex population, a psychosocial team was established. The team received training at the Guatemalan Pediatric Oncology Unit affiliated with SJCRH, where they had developed expertise in preventing abandonment in complex settings. [15] In partnership with the local grassroots foundation, the psychosocial team's ongoing initiatives have dramatically decreased treatment abandonment rates (Table 2).

### **Dedicated healthcare team**

As its importance was clearly identified in the literature, [3,4,23,28] establishing and training a dedicated interdisciplinary healthcare team was one of the most important aspects of the RCHSD-SJCRH-GHT twinning program action plan. Tailored “team building” training was provided to the team members upon establishment of the program. A local pediatric oncologist (RRG) was appointed as the local leader and currently oversees all the ongoing programmatic projects with the support of the program medical director at RCHSD (PA), who currently provides ongoing mentorship and visits the unit on a regular basis. This “team-based” approach has proved innovative and effective at the GHT.

To overcome the shortage of pediatric oncologists in the region, a “physician-extender” model was created. This model hinges on providing intensive targeted training to general pediatricians to cover the lack of trained subspecialists. Conducted over several years, this training has resulted in eight general pediatricians who have obtained greater expertise in supportive and intensive care at the GHT; they now provide 24-hour coverage for patient care in the dedicated oncology unit. Thus patients are seen—and often times admitted—directly to the oncology unit, avoiding delays and errors in the general emergency settings. Table 3 summarizes the growth and evolution of the healthcare team since 2007.

Targeted training for nurses, allied staff and families has been a priority since the inception of the program. More than 8,000 hours of in-person and online training have been provided to nurses within the oncology unit. Some of the training has also been provided at other twinning sites affiliated with SJCRH such as Guatemala and Chile [2,16,32] or at RCHSD for staff fluent in English. As a result, robust psychosocial, child life, nutritional, oral health and infection control programs have been established to support patients and their families. [33]

Pediatric cancer awareness efforts in the community have also been implemented locally and regionally, similar to other community education programs described elsewhere. [2] To date, this education initiative has reached nearly 3,000 healthcare providers, community leaders and school teachers in Baja California.

### **Local Capacity Building and Financial Sustainability**

The expansion of the government support for cancer care in Mexico [7,34,35] has been instrumental to the success of the RCHSD- SJCRH-GHT twinning program because 99% of families receiving care at the GHT live on incomes less than \$200 USD per month and lack private or public health insurance. At the initiation of the project, priority was given to assist

the GHT to improve the current infrastructure and apply for national accreditation from the Mexican Ministry of Health aiming to ensure permanent funding from the government to cover expenses associated with care for pediatric oncology patients. Approval as an accredited unit depended on having well-trained healthcare professionals and adequate resources to provide appropriate care. [7] Achieving full accreditation took several months and was completed in 2008.

This consistent funding stream provided by the government has been essential to meet operating expenses, but it has not been enough. Local grassroots efforts have offered various services for patients and their families, including shelter for families who reside outside Tijuana (about 35%), transportation and food subsidies, and medications not covered by the government. Patronato Pro-Hospital General de Tijuana –*Patronato*—is a local, apolitical organization founded in 2000 to support all GHT patients. The close relationship between leadership of the twinning program and *Patronato* has led to effective community advocacy efforts and strengthening of partnerships with local authorities, which have been instrumental to the successful launching and sustaining of the program.

## Discussion

Modern therapy has dramatically increased survival rates for children with cancer, but still remains unavailable to close to 80% of pediatric cancer patients throughout the world. [36] This disparity is most acutely felt in countries with emerging economies, in which progress is asymmetric, such as along the Mexican- North American border.

While the twinning partnership has been vital in the San Diego-Tijuana region, major recent enhancements have occurred in the complex Mexican healthcare system to expand access to care and improve clinical outcomes nationwide. Founded in 2003, the *Popular Medical Insurance* is a government-sponsored fund to pay for basic healthcare for Mexico's uninsured citizens, which comprise approximately 50% of the population. This fund was expanded in 2008 to include coverage for pediatric cancer care. [5,7] This increased coverage, along with several public health efforts in recent years, [34,35] have led to improvements in childhood survival and other clinical outcomes. [36,37,38] One example is abandonment of cancer treatment, which several studies from other countries had linked to a high cost of care. [22,39,40]. In a clinical study of 3,821 Mexican pediatric cancer patients from 2006 to 2009, coverage of new cancer cases increased from 3.3% to 55.3% and treatment abandonment was reduced. [7]

Nevertheless, despite the *Popular Medical Insurance* expansion to finance pediatric cancer treatments, a reduction in pediatric cancer mortality was still not achieved as of 2010. [7] This is partly a result of underdeveloped interdisciplinary “team-based” approach models and regional shortages in pediatric oncologists—44% of them are concentrated in Mexico City, and 18% practice in the second and third largest cities of Guadalajara and Monterrey. [34,35] Some of the contributing demographic, economic and infrastructure factors to inequities between San Diego and Tijuana in the border region are described in Table 1. [41]



Despite the described geopolitical challenges, our results show the feasibility of establishing a twinning program involving two mentor institutions across such a landscape: SJCRH served as the primary “model” institution and RCHSD and the GHT acted as the “executor” institutions, located in close proximity. The benefits of such close vicinity between mentor and mentee sites are numerable, including feasibility for close supervision, implementation in record time and rapid outcome improvements (Tables 2 and 3).

In addition to proximity, input from the local community was a key factor to the program’s success. The establishment of a new pediatric oncology unit was a high priority. To navigate the developing Mexican health system, we partnered with both local government authorities and the grassroots foundation to develop the program from the ground up. Initiating relationships in this way builds local capacity, because the institution in the LMIC begins the partnership already “owning” the program and with the expectation to achieve self-sustainability.

The development of these relationships required an understanding of the great variation in cultures and local circumstances. Data related to challenges associated with cultural differences or language barriers within twinning programs is scarce. [42] The medical director (PA) from RCHSD, who was bi-lingual and bi-cultural, was able to effectively bridge communication and overcome some of the cultural barriers that arose during the program implementation.

This dynamic collaboration facilitated the establishment of a fully functional oncology unit, with a highly trained and cohesive interdisciplinary team. The new team at the GHT has successfully provided clinical care for more than 700 patients from 2008 to 2015. Infection-related complications [33] and survival outcomes, particularly for acute lymphoblastic leukemia, have dramatically improved and mortality rates have decreased significantly (Table 2), consistent with outcomes reported by others in twinning programs in LMIC. [3, 14, 15,16, 23, 43]

The significant decrease in infection-related mortality is partially attributed to the establishment of dedicated beds for critical patients requiring intensive care within the pediatric oncology unit, where care is provided by the “physician extenders” who have successfully applied the knowledge gained from targeted training. This model is similar to the U.S. Nurse Practitioner/Hospitalist model in pediatrics, [44,45] which is not currently available in Mexico.

One challenge in training healthcare professionals in LMIC is that individuals may have a significant work load despite inappropriately low monetary compensation. As a result, motivation can suffer and fully adopting new procedures can be difficult. To address these issues, innovative incentive programs for the staff and alternative ways to provide added compensation were implemented at the GHT, including team building, empowerment, emotional intelligence and burnout prevention workshops. We are not aware of prior reports addressing this issue or showing this innovative approach. These initiatives have greatly contributed to the satisfaction and retention of the team members and the overall long-term success of the program.



Another challenge relates to the start-up shared budgets between RCHSD, SJCRH, and the GHT, which involve a blend of funding streams from these institutions, the Mexican government and *Patronato*. Thus, the program is not entirely sustainable alone at the current moment. However, the foundation for financial investment and sustainability on the part of the Mexican government has been laid, and the goal is that they, in partnership with *Patronato*, will take over full operational and fiscal control of the pediatric cancer unit within the GHT.

Throughout the tripartite collaboration, we learned several insightful lessons that may shed light on the systematic process required to establish a successful twinning program, which are included in Table 4.

## Conclusion

The RCHSD- SJCRH-GHT twinning program is a unique model of collaboration, involving institutions located directly across an international border in a region with profound economic and cultural disparities. The close proximity has allowed for rapid improvements in care for children with cancer in Baja California. As a result of this partnership, clinical outcomes, including overall survival rates- particularly for acute lymphoblastic leukemia- and morbidity for all cancers have improved, local healthcare infrastructure has been strengthened, and generalizable knowledge has been shared with the GHT for use in other areas of care. These accomplishments are also spreading to other centers in the region, such as the emerging pediatric oncology program in the neighboring state of Baja California Sur. The challenge going forward includes the continuation of local capacity development so all children with cancer in Baja California can be diagnosed and referred to the GHT promptly, a challenge common in LMIC. [14,25,26,29]

Future directions include continuing the education program for the staff and patients' families, building up a pediatric neurosurgery program, enhancing the palliative care efforts, maintaining the psychosocial support for families, and continuing to consolidate the newly established collaborative program in Baja California Sur, through the development of a "training hub" in Tijuana. If our efforts in these areas continue for five more years, we expect the five-year survival rate for acute lymphoblastic leukemia to reach 70%, similar to that in many HIC, and other programs in LMIC such as in Guatemala and Brazil. [30,46]

Bi-directional twinning partnerships pursued with the methods outlined above not only strengthen local healthcare system infrastructure and capacity in the LMIC in a positive, sustainable way; they have a dramatic impact on the HIC institution, where an immense body of experiential knowledge is gained and can be immediately applied to provide better care locally, contributing to reducing disparities in underserved children in HIC.

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## Abbreviations Table

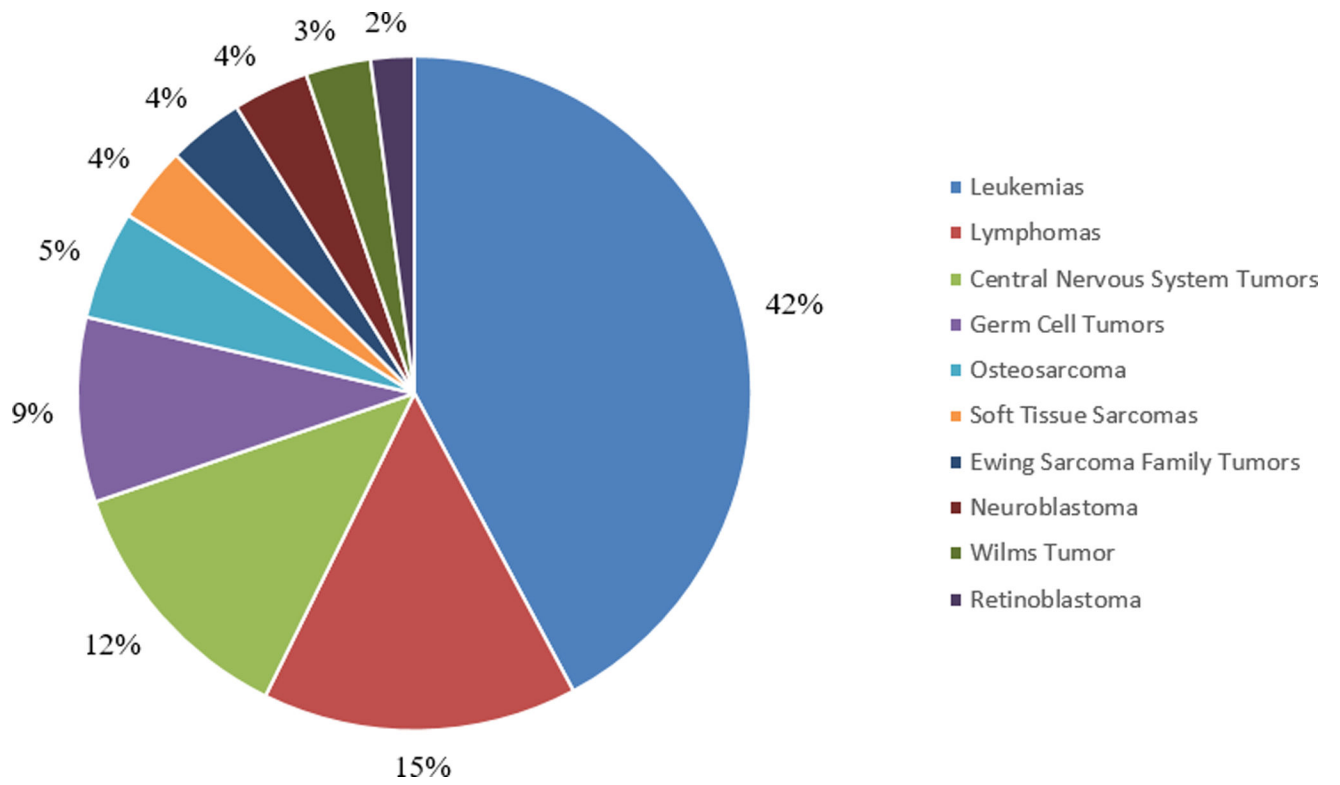
<b>SJCRH</b>	St. Jude Children's Research Hospital
<b>GHT</b>	General Hospital Tijuana
<b>LMIC</b>	Low-income and middle-income countries
<b>HIC</b>	High-income countries
<b>U.S.</b>	United States
<b>RCHSD</b>	Rady Children's Hospital San Diego
<b>Patronato</b>	Patronato Pro-Hospital General Tijuana

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**FIGURE 1.** Distribution of New Pediatric Cancer Diagnoses at the General Hospital Tijuana from 2008–2015 (N=285).

**TABLE 1**

Comparisons between Baja California and San Diego County, and Mexico and the United States of America

<b>Regional Data</b>	<b>Baja California</b>	<b>San Diego County</b>	<b>References</b>
Population	3,155,070	3,105,115	[20,47]
Percentage of population < 14 years old	29%	19%	[20,47,48]
New immigrants per year	130,000 <sup>a</sup>	159,502	[20,47]
Percentage of population below the effective poverty line	863,587 in Tijuana alone (66% of Tijuana's population)	22.7%	[49,50]
Estimated number of new pediatric cancer cases per year	200 <sup>a</sup>	300	[51]
<b>National Data</b>	<b>Mexico</b>	<b>United States of America</b>	<b>References</b>
Spending on healthcare per capita (in USD)	\$618	\$8,895	[48]
Ranking of healthcare spending per capita	#66 out of 189	#3 out of 189	[48]
Number of oncologists per 100,000 inhabitants	1.07	3.75	[13,34,45]
National Population-based Cancer Registry	Not Established	Established	[10,34,35]

<sup>a</sup>Estimate

**TABLE 2**

Comparison of selected clinical outcomes in 2008 and 2015

Category	2008	2015
New cancer cases per year	21	70
Relapse rate	Unknown	22%
Abandonment rate <sup>a</sup>	10%	2%
Mortality rate during induction therapy for acute lymphoblastic leukemia	Unknown	5.3%
Infection-related mortality rate	27%	0% <sup>b</sup>
CLABSIs rate <sup>c</sup>	5.72	3.22

<sup>a</sup>Treatment abandonment was defined as an unplanned delay in therapy of more than four weeks, not related to medical reasons or due to patient not returning for care.

<sup>b</sup>Data from 2013.

<sup>c</sup>Central line-associated bloodstream infections (per 1,000 central line days; device use ratio 0.94–0.97; 9,625 central line days analyzed over the study period).[33]



**TABLE 3**

Healthcare professional development progress at the General Hospital Tijuana, 2007–2015

Position	2007 (N=5)	2008 (N=27)	2015 (N=68)
Physicians <sup>a</sup>	3	11	17
Nurses <sup>b</sup>	1	10	33
Allied healthcare staff <sup>c</sup>	1	3	11
Administrative and other staff <sup>d</sup>	0	3	7
Number of staff membersexclusive to the GHT pediatric oncology unit	0	0	63

<sup>a</sup>Includes oncologists, hematologists, intensive care specialists, anesthesiologists, infectious diseases specialists, pathologists, and surgeons

<sup>b</sup>Includes general nurses, nurse educators and infection control nurses

<sup>c</sup>Includes infection preventionists, psychologists, social workers, child life specialists, pediatric dentists, dieticians, pharmacists, and lab technicians

<sup>d</sup>Includes school teachers, administrative assistants, runners, and data managers

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TABLE 4

Lessons learned during the establishment of a Twinning Program in the Mexico-US border region

Lesson learned	Insight
Relationships	Strong, long-term, and culturally-aware relationships with local authorities in LMIC <sup>a</sup> are essential to fulfilling the purpose of a sustainable twinning program.
Innovation	Program leaders must constantly innovate to implement strategies to motivate healthcare professionals in institutions in LMIC <sup>a</sup> and help them enjoy their work despite low compensation.
Empowerment	Twinning program empowerment centers around the interdisciplinary “team-based” approach. Through knowledge sharing, a newly-trained interdisciplinary team becomes capable of treating more patients effectively. This “team-based” dynamic strategy allows various members to become peers and recognize the critical importance of the “team” contribution to the overall mission of the program. As a result, team members’ feelings of appreciation and accomplishment increase.
Flexibility	Individuals involved in twinning programs need to be mindful and make adjustments to local culture and resources. Geographic proximity between partner institutions can greatly impact the number and quality of physical site visits to the developing site, which can significantly increase the team’s ability to adapt.
Leadership training	The leaders of twinning programs benefit immensely from acquiring administrative and leadership skills. These are vital tools when establishing sustainable programs with limited resources via small budgets and complex, changing financing mechanisms. Starting the partnership with realistic, accurate, and sustainable goals is vital to its long-term success.
Local sustainability development	To ensure long-term sustainability of the program, it is essential that the institution in the LMIC <sup>a</sup> becomes financially independent as quickly as possible. Start-up funds may be provided by grants, but the ultimate goal is to achieve sustainability because the processes are sufficiently hardwired through the enhancement of the local healthcare system with the support of a strong grassroots foundation, the local community and the local and national government in the LMIC <sup>a</sup> .

<sup>a</sup>LMIC: Low-income and middle-income countries.