Examples of Funded Grants in Implementation Science

Overview
The National Cancer Institute (NCI) frequently receives requests for examples of funded grant applications. Several investigators and their organizations agreed to let Implementation Science (IS) post excerpts of their dissemination and implementation (D&I) grant applications online.

About
We are grateful to the investigators and their institutions for allowing us to provide this important resource to the community. To maintain confidentiality, we have redacted some information from these documents (e.g., budgets, social security numbers, home addresses, introduction to revised application), where applicable. In addition, we only include a copy of SF 424 R&R Face Page, Project Summary/Abstract (Description), Project Narrative, Specific Aims, and Research Strategy; we do not include other SF 424 (R&R) forms or requisite information found in the full grant application (e.g., performance sites, key personnel, biographical sketches).

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424 R&R and PHS-398 Specific

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SF 424 R&R Face Page

PI: Agulnik, Asya

Grant Number: 1 R37 CA276215-01

Title: Sustainability determinants of an intervention to identify clinical deterioration and improve childhood cancer survival in low-resource hospitals

FOA: PAR-19-274

FOA Title: Dissemination and Implementation Research in Health (R01 Clinical Trial Optional)

Organization: ST. JUDE CHILDREN'S RESEARCH HOSPITAL

Department: GLOBAL PEDIATRIC MEDICINE

Senior/Key Personnel:	Organization:	Role Category:
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Project Summary/Abstract

Background and Goal. More than 90% of children with cancer live in low-resourced settings, where survival is only 20%. Sustainable evidence-based (EB) interventions yielding ongoing beneficial patient outcomes is critical to improve childhood cancer survival. A better understanding of factors promoting intervention sustainability in these settings is urgently needed. The goal of our project is to provide an empirical understanding of how clinical capacity, or the resources needed to sustain an intervention, impacts sustainment of a Pediatric Early Warning System (PEWS), EB interventions that improves pediatric oncology outcomes in low-resource hospitals by quickly detecting clinical deterioration in children with cancer, preventing the need for more intense treatment.

Aims and Methods: We will conduct a prospective, longitudinal study of 92 low-resource hospitals implementing and sustaining PEWS. This work will build on an ongoing St. Jude-Wash U Implementation Science Collaborative and Proyecto EVAT, a quality improvement collaborative of Latin American pediatric oncology centers. **Aim 1**: We will evaluate how clinical capacity for sustainability changes over time through 5 to 9 prospective measurements of capacity via survey of clinical staff using PEWS (n=13 per center) during the phases of PEWS adoption, implementation, and sustainability. **Aim 2**: We will determine the relationship between capacity and a) PEWS sustainment and b) clinical deterioration mortality among pediatric oncology patients at centers sustaining PEWS for 2 to 10 years using chart review and an existing patient outcomes registry. **Aim 3**: We will develop novel strategies to promote sustainability by gaining a deeper understanding of perceived challenges to building capacity and PEWS sustainment. In combination with quantitative outcomes, we will conduct 24 focus groups with hospital staff (doctors, nurses, and administrators) from hospitals with both high (n=4) and low capacity (n=4). We will then use implementation mapping to generate theoretically driven, empirically-supported strategies which promote sustainability. All aims will be informed by an External Advisory Board and the EVAT steering committee.

Innovation and Impact: Few EB sustainability strategies exist for low-resource settings. This study will advance implementation science by providing a theoretically-driven, foundational understanding of factors that predict sustainability among a large, diverse cohort of low-resource hospitals. We will then use this knowledge to develop sustainability strategies that optimize capacity and promote long- term sustainment of PEWS and improvements in patient outcomes in low-resource settings - ultimately promoting equity in childhood cancer care globally.

Project Narrative

A better understanding of factors contributing to sustainability of evidence-based interventions is urgently needed to improve childhood cancer survival in low-resource settings. This project studies the ability of low- resource hospitals in Latin American to sustain an evidence-based intervention, a Pediatric Early Warning System (PEWS), that improves outcomes among hospitalized children with cancer. Upon completion, this study will identify components of clinical capacity that contribute to long-term sustainability of interventions in low-resource hospitals and develop strategies to promote sustainability, thus advancing the science of implementation and improving survival for children with cancer globally.

Specific Aims

Failure to sustain effective clinical interventions results in detrimental outcomes, including waste of initial investments and loss of patient benefits. This is particularly problematic in low-resource hospitals where resources for intervention implementation are limited.[1-3] *Sustainability*, or the continued use of an intervention over time with associated positive health outcomes, is critical to maximize the long-term benefits of evidence- based interventions.[4-8] Our theoretical work suggests *clinical capacity for sustainability* is a primary determinant of intervention sustainability, consisting of engaged staff, leadership and stakeholders, organizational readiness, workflow integration, training, and monitoring and evaluation.[9,10] To date, studies examining determinants of sustainability include primarily high-resource hospitals and are largely theoretical.[11-13] The goal of this study is to move beyond conceptual frameworks to empirical testing; we seek to **understand the relationship between clinical capacity, intervention sustainment, and patient outcomes in low-resource hospitals over time.**

Pediatric cancer is an ideal context to examine sustainability. With modern treatment and supportive care, childhood cancer survival in high-resource settings is greater than 80%. However, more than 90% of children with cancer live in low-resource settings, where survival is only 20%.[14,15] Up to 50% of deaths in these settings are due to toxicity of cancer treatment,[16-19] representing preventable mortality that can be mitigated with appropriate supportive care interventions.

Pediatric Early Warning Systems (PEWS) are evidence-based supportive care interventions that aid in the early identification of clinical deterioration and improve patient outcomes in low-resource hospitals.[20-26] In 2017, Dr. Agulnik (PD/PI) at St. Jude Children's Research Hospital (St. Jude) established Proyecto EVAT, a collaborative of Latin American pediatric oncology centers to improve survival of children with cancer through PEWS implementation.[27,28] Proyecto EVAT mentors hospitals through a standardized implementation process to adopt and maintain PEWS. Currently, Proyecto EVAT encompasses 72 low-resource hospitals in 18 countries, with 10 new hospitals joining annually and impacting over 42,000 pediatric oncology admissions a year.[29] Preliminary work demonstrates PEWS implementation is feasible and reduces clinical deterioration mortality;[30-34] however, our ongoing evaluation indicates hospitals face various challenges *sustaining* PEWS.

Building on prior work between our teams at St. Jude and Washington University in St. Louis,[35,36] we will prospectively observe 92 Proyecto EVAT hospitals at various phases of PEWS adoption, implementation, and sustainability to accomplish the following specific aims:

- **Aim 1**: Evaluate change in capacity for PEWS sustainability over time. We will evaluate how overall capacity and its individual components change over time through 5 to 9 prospective measurements of capacity per hospital during the phases of PEWS adoption, implementation, and sustainability. We hypothesize that capacity develops during early implementation and increases over time.
- **Aim 2**: Determine the influence of capacity on PEWS sustainability. We will determine the long-term relationship between overall capacity and its individual components on: a) PEWS sustainment or abandonment and b) clinical deterioration mortality among pediatric oncology patients at hospitals sustaining PEWS for 2 to 10 years. We hypothesize that higher capacity will make long-term PEWS sustainment and ongoing positive patient outcomes more likely.
- **Aim 3**: Develop strategies to target clinical capacity and sustainability challenges in low-resource hospitals. Using a sequential mixed-method design, we will conduct focus groups of hospital staff (doctors, nurses, and administrators) to gain a deeper understanding of perceived challenges to and potential strategies for strengthening capacity. We will then use implementation mapping[37] to integrate our outcomes and develop novel strategies which promote clinical intervention sustainability and continued impact on patient outcomes.

A better understanding of how to sustain evidence-based interventions like PEWS is urgently needed to increase global survival of childhood cancer, particularly in low-resource settings, but there are few sustainability strategies appropriate for these settings. Upon completing the proposed work, we will **establish how capacity changes over time, determine its impact on intervention sustainment and patient outcomes, and use staff perspectives on capacity building to develop novel sustainability strategies**. This work is *significant* by providing a theoretically-driven, longitudinal understanding of factors that predict sustainability in a large cohort of low-resource hospitals delivering the same intervention in a variety of settings. It is *innovative* by moving beyond a cross-sectional exploration towards empirical, longitudinal evidence supporting the dynamic relationships between capacity and intervention sustainability. Furthermore, we will leverage this knowledge to address a widely identified need to develop sustainability strategies that optimize capacity, promote intervention sustainability, and encourage health equity in childhood cancer outcomes in low-resource settings.[38,39]

Research Strategy

A. Significance. The global burden of pediatric cancer is disproportionately shifted to low- and middle-income countries, which bear over 90% of childhood cancer cases,[14] with a dismal survival rate of approximately 20%.[15] To reduce these disparities, the WHO Global Initiative for Childhood Cancer[40] and other initiatives[28] emphasize the need to improve access to and outcomes of childhood cancer treatment globally. However, hospitals in low-resource settings frequently lack adequate infrastructure and staffing to deliver needed supportive care during cancer treatment,[41-43] resulting in late identification of clinical deterioration events (CDEs) and high rates of preventable deaths.[44,45] Our prior work in Latin America demonstrated high rates of CDEs among hospitalized children with cancer and a 30% mortality rate in patients with deterioration.[46] This illustrates an urgent need for effective, low-cost, and sustainable supportive care interventions, including strategies for timely identification of CDEs, to improve global childhood cancer survival. *Two key challenges persist in addressing this imperative: (1) successful implementation of evidence-based interventions and (2) long-term sustainability of implemented interventions. The latter is the focus of this proposed study.*

A.1 Promoting sustainable implementation of evidence-based interventions ensures long-term patient benefits, yet few theoretically-informed, evidence-based sustainability strategies apply to low-resource settings. While much of implementation science focuses on adopting and implementing evidence-based interventions, sustainability is the least studied phase of the implementation continuum.[39,47] Ideally, interventions should be sustained unless they are no longer effective or more effective interventions become available.[7,48,49] Many interventions are abandoned when they should be continued, often when external support, such as grant funding or collaborative assistance, is removed.[13,50-52] Implementing interventions is costly, and if interventions are not sustained, then initial investments are lost.[53,54] Most importantly, evidence-based interventions that are not sustained cannot provide continued health benefits to patients.

The current body of scientific literature focuses primarily on conceptualizing and theorizing sustainability in health.[11,54] A general consensus within the literature establishes the relationship between the immediate context where interventions are implemented and the likelihood of intervention sustainability.[11] Work by Drs. McKay (PD/PI) and Luke at Washington University in St. Louis (Wash U), suggests that *clinical capacity for sustainability*, or the resources necessary to sustain an intervention including engaged staff, leadership and stakeholders, organizational readiness, workflow integration, implementation and training, and monitoring and evaluation, are the most proximal contextual determinants influencing intervention sustainment.[9,10,53] While there are several conceptual frameworks identifying sustainability determinants, few have driven empirical examinations of sustainability determinants. A recent review of determinants of hospital interventions sustainability did not include a single study from a low-income country, and two-thirds of the studies were qualitative.[12] Another notable gap is a lack of theoretically informed, empirically driven sustainability strategies to modify determinants and promote intervention sustainability. A recent review of 62 sustainability strategies for health interventions noted the majority were strictly conceptual frameworks and only 2 were active strategies to either plan for sustainability or promote sustainability after implementation in acute care settings.[54] This existing work highlights *a lack of comprehensive evaluation of factors and strategies that promote sustainability in low-resource settings, a meaningful knowledge gap that will be addressed in the current study*.

A.2 Pediatric Early Warning Systems (PEWS) are evidence-based interventions that improve outcomes in hospitalized children with cancer and are feasible in low-resource settings. To more rapidly identify CDEs, many hospitals use PEWS: nursing-administered bedside clinical acuity scoring tools associated with escalation algorithms. PEWS accurately predict the need for pediatric intensive care unit (PICU) transfer in pediatric oncology patients in high-resource hospitals.[55,56] Escala de Valoración de Alerta Temprana (EVAT) is a Spanish-language PEWS adapted by Dr. Agulnik (PD/PI) at St. Jude Children's Research Hospital (St. Jude) for low-resource settings. EVAT includes a 5-component scoring tool (neurologic, cardiovascular, respiratory, staff and family concern) based on vital signs, physical examination findings, and treatment requirements.[20] Hospitalized patients are scored 0 to 11 using the tool by a bedside nurse during routine vital sign assessments. Higher scores indicate potential clinical deterioration and are addressed following an action algorithm that guides the clinical team in appropriate escalation of care. In 2014, Dr. Agulnik worked with local stakeholders to implement and validate this PEWS at a low-resource pediatric oncology hospital in Guatemala,[20,21,57] resulting in a 27% reduction in CDEs, optimized PICU utilization,[21] improved interdisciplinary communication, provider

empowerment and perceived quality of care,[23-25] and an annual cost-savings of over US$350,000.[22]

These results compelled Dr. Agulnik to establish *Proyecto EVAT*, a quality improvement collaborative to improve survival in hospitalized children with cancer in Latin America.[27,28] Since 2017, 41 hospitals of varying resource-levels have implemented PEWS through Proyecto EVAT,[29] with over 11,000 clinicians trained, more than 42,000 pediatric hospital admissions benefiting from PEWS use, and results showing improvements in patient outcomes.[30-34] Due to this work, regional enthusiasm for Proyecto EVAT has grown, with 10-15 new hospitals enrolling in the program annually and more expressing interest. In ongoing evaluation of PEWS at participating hospitals, we found that local implementation leadership teams successfully overcame implementation barriers and initially achieved excellent PEWS fidelity. Recognizing the importance of sustainability, we recently evaluated 36 hospitals using PEWS for up to 24 months and found approximately 30% had challenges with PEWS sustainment. Hospital staff identified multiple specific barriers to sustainability, including staff turnover resulting in insufficient training, difficulty obtaining leadership buy-in, and lack of internal systems for ongoing PEWS monitoring. These results suggest that while clinical capacity may improve during initial implementation of PEWS, not all hospitals have sufficient capacity for sustainability. *This proposal leverages the experience of Proyecto EVAT to longitudinally examine capacity and understand its impact on PEWS sustainability*.

A.3 The proposed study will provide a foundational understanding of capacity factors that predict sustainability. Sustainability of evidence-based interventions is perhaps the *most important aspect* of the implementation continuum, yet has not been rigorously examined, particularly in low-resource settings.[53] In this study, we will address a significant scientific gap by identifying aspects of clinical capacity that contribute to PEWS sustainability (Aim 1 and 2) and describe challenges faced in building capacity and sustaining PEWS (Aim 3). By identifying factors that contribute to intervention sustainability, we will then develop novel strategies that promote sustainability (Aim 3). Ultimately, these results will launch a trajectory of research that improves childhood cancer survival by effectively sustaining evidence-based interventions like PEWS and promotes equity by focusing on low-resource hospitals where preventable mortality remains high.

B. Innovation. The proposed work will advance the study of intervention sustainability in implementation science and equity of pediatric oncology care in low-resource settings, and is innovative in the following three ways:

(1) It is focused on dynamic intervention sustainability. Current scientific debate has led to a more dynamic conceptualization of context, intervention sustainability, and intervention adaptation.[7,54] However, empiric examination of this interplay requires the large-scale adoption and implementation of an intervention by multiple centers for years after external support has been withdrawn, with data collection consistently over time. As a well-established collaborative that has focused on implementing one intervention, PEWS, in over 70 diverse hospitals at various stages of implementation—many who have sustained PEWS for nearly a decade—Proyecto EVAT presents an exceptional opportunity to overcome this scientific barrier. In Proyecto EVAT hospitals, the setting and intervention are mature enough to allow us to move beyond cross-sectional exploration to prospectively observe the dynamic interplay among context, sustainability, and patient outcomes.

(2) It will advance theory, measurement, and inform rigorous development of sustainability strategies. We will leverage both a conceptual model and measurement tool, the Clinical Sustainability Assessment Tool (CSAT), developed in our prior work.[58,59] The results from the proposed study will lend support to and further refine our conceptual framework. To our knowledge, the CSAT is the only reliable sustainability assessment tool designed for use in clinical settings, and the proposed work will continue to build validity for the CSAT. In addition, this is the only measure that can be applied in different linguistic settings; another notable scientific barrier in this field.[51,60] Even fewer models underpin sustainability strategies within implementation science. Our work will provide essential knowledge about contextual factors (i.e., capacity for sustainability) that drive intervention sustainability and identify potential sustainability strategies to modify these contextual factors and make sustainability more likely. We expect the results of this work to advance implementation science by establishing a rigorous approach for developing theoretically-driven, empirically-informed, novel strategies to support sustainable implementation of evidence-based interventions in a range of clinical settings and resource-levels.

(3) It targets improving equity in pediatric cancer treatment outcomes. A recent study of funding by the National Cancer Institutes noted that approximately 90% of cancer-related implementation science studies focused on prevention and screening, and only 4% focused on treatment.[61] Pediatric oncology patients represent

a critical population whose physiology, potential for comorbidities, and disease processes differ substantially from adults, who are the subjects of most prior studies. Because prevention and screening play a limited role in improving childhood cancer survival, our focus on cancer treatment will fill a vacant scientific niche. Most children with cancer live in low-resource settings where childhood cancer survival is significantly lower. However, most pediatric cancer research is conducted in high-income countries.[62] This study's focus on low-resource pediatric oncology centers addresses this disparity and promotes equity in childhood cancer care. Results of this work will thus fulfill an urgent need for implementation science research at this stage in childhood cancer care and reduce global disparities in childhood cancer survival.[6]

C. Approach. We propose a longitudinal observational study of a cohort of pediatric oncology centers over five years. The rigor of the proposed design is based on a long prospective observation period, a large and diverse set of hospitals, and multiple data sources. Guided by a sustainability conceptual framework, we will achieve our goal of understanding PEWS sustainability in low-resource hospitals through three distinct yet interrelated aims (Table 1), according to the proposed timeline (Section 2.7 Study Timeline). Upon completing this study, we will establish how clinical capacity changes over time (Aims 1), determine the influence of capacity on sustainment and patient outcomes (Aim 2), and use a mixed-method approach to understand staff perspectives on challenges to capacity building and sustainability and develop novel strategies to promote sustainability (Aim 3).

Table 1. Overview of Study Aims		
Question: What are the relevant components of capacity that determine PEWS sustainability in low-resource hospitals?		
Study Design: Prospective, longitudinal observational study of 92 pediatric oncology centers implementing PEWS		
Aim 1: Changes in Capacity Over Time	Question	How does capacity for sustainability and its components change over time through the phases of PEWS adoption, implementation, and sustainability?
	Hypothesis	Capacity develops during early implementation and increases over time
Aim 2: Sustainment & Patient Outcomes	Questions	How do changes in overall capacity and its components predict a) PEWS sustainment or abandonment and b) improvement in patient outcomes?
	Hypothesis	Capacity and its components predict PEWS sustainment and continued reduction in clinical deterioration event mortality over time.
Aim 3: Develop Sustainability Strategies	Questions	What are staff perceptions of challenges to capacity development and their impact on PEWS sustainability in low-resource hospitals? What are potential strategies that promote sustainability in these settings?

C.1 Research Team. We have assembled a diverse interdisciplinary team from two world-class institutions, St. Jude and Wash U, known for their influential work in pediatric oncology and implementation science, respectively. This study will be led by Drs. Agulnik and McKay as an extension of their prior collaborative work. The team includes researchers with complementary expertise in pediatric oncology, outcomes research in low-resource settings, implementation science, and intervention sustainability (Table 2) who have successfully worked together for over two years through the St. Jude-Wash U Implementation Science Collaborative.

Table 2. Study Team Experience and Roles. (See the Multi-PI plan and Biographical Sketches for more details.)			
Name	Role	Relevant Experience	Contribution to Study
Agulnik (St.Jude)	PD/PI	• Early-stage investigator with clinical expertise in pediatric onco-critical care. • Extensive experience conducting research to improve hospital outcomes for children with cancer in low-resource settings. • Principal Investigator of Proyecto EVAT. • Led pilot of the CSAT with Proyecto EVAT.	• Primary responsibility: Coordinating the St. Jude team across all study aims and provide clinical expertise. • Oversee PEWS implementation and integration of data collection with Proyecto EVAT. • Facilitate communication between study team and NIH and providing fiscal oversight.
McKay (Wash U)	PD/PI	• Early-stage investigator with expertise in implementation science, particularly sustainability and de-implementation. • Expertise in intervention mapping and strategy development. • Experience with mixed-methods and qualitative study design and analysis. • Helped test CSAT reliability with Proyecto EVAT.	• Primary responsibility: Coordinating the Wash U team across all study aims and provide implementation science expertise. • Oversee aspects of research related to implementation science including data collection, measurement, and analysis. • Support sustainability strategy development.
Luke (Wash U)	Co-I	• Extensive expertise in implementation science, particularly sustainability, with emphasis on cancer-related research. • Skilled in research design, quantitative methods, psychometrics, multilevel & longitudinal modeling. • Developed the CSAT measure.	• Oversee use of CSAT, including reliability and validity aspects. • Provide input into multilevel and longitudinal modeling (Aims 1 and 2)
Devidas (St.Jude)	Co-I	• Senior faculty biostatistician with extensive experience in pediatric oncology research and patient outcomes analysis.	• Oversee data analysis of implementation outcomes and integration with patient outcomes (Aims 1 and 2).
Graetz (St.Jude)	Co-I	• Extensive expertise conducting qualitative research in low-resource clinical settings.	• Will support qualitative research design, data collection, and analysis for Aim 3.

External Advisory Board (EAB): We have established a scientific EAB consisting of 3 senior investigators with a mix of clinical and implementation science expertise in global health: Drs. Carlos Rodriguez-Galindo, Christopher Dandoy, and Rachel Shelton (see letters of support). Together, the EAB has diverse expertise in pediatric oncology, quality improvement science, implementation science (implementation, adaptation, sustainability, and sustainability strategies), health equity, and research in low-resource settings to lend insights and supervise the proposed study. The EAB will convene twice annually by videoconference to review the project's overall progress, provide scientific oversight, and offer feedback at each stage of the proposed work.

Proyecto EVAT Steering Committee: The Proyecto EVAT Steering Committee (EVAT SC) is an existing 27-member multidisciplinary team of nurses and physicians from 10 hospitals in 8 Latin American countries. EVAT SC members are experts in PEWS implementation and are selected from regional PEWS training centers. The EVAT SC reviewed the CSAT for conceptual appropriateness, was involved in the translation and piloting of the CSAT (C3. Prior Work), and approved this proposed study as feasible, important, and regionally acceptable. For the duration of the proposed work, the EVAT SC will be updated on project progress twice annually to provide oversight and feedback and to ensure regional appropriateness and applicability (see letter of support).

C. Setting. The proposed work will be conducted with low-resource pediatric oncology hospitals participating in Proyecto EVAT. Currently, this includes 72 hospitals in 18 Spanish- and Portuguese-speaking countries in Latin America, representing over 8,000 new annual pediatric cancer diagnoses and more than 42,000 hospital admissions per year (Figure 1 and Table 3). Although 2 Proyecto EVAT hospitals are located in World Bank–designated high-income countries in South America, all hospitals self-identify as low-resource due to a broad range of limitations, including inadequate nursing and physician staffing to identify and manage CDEs, limited PICU space to accommodate children with cancer, and patients with low socioeconomic, educational, and nutritional indicators.[63-66] These broad challenges result in an increased frequency of CDE with worse outcomes than in high-resource hospitals,[46] and their inclusion enriches our study of sustainability across a range of

resource limitations. We expect that additional hospitals will be incorporated as we enroll new Proyecto EVAT cohorts during years 1 and 2 of the study period.

Figure 1. Proyecto EVAT: 72 Hospitals in 18 Countries

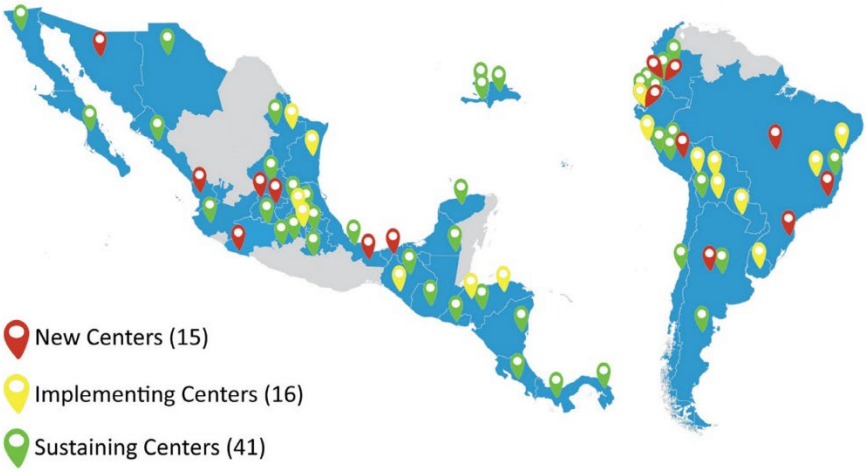


Table 3. Proyecto EVAT Hospitals (n=72)	
Characteristic	**n (%)**
Hospital type	
General (Adult and pediatric)	32 (44.5)
Pediatric multidisciplinary	28 (39)
Oncology (Adult and pediatric)	8 (11)
Pediatric oncology	4 (5.5)
Annual new pediatric cancer cases	
1–40	18 (25)
41–80	18 (25)
81–120	15 (21)
121+	21 (29)
Total clinical staff using PEWS	
1–25	16 (22.2)
26–50	26 (36.2)
51–75	11 (15.3)
76+	19 (26.3)

C.3 Prior Work & Study Feasibility. Our team has a proven track record of successful clinical and implementation science research, and our extensive prior work ensures the current study is well conceived and feasible within the proposed time frame.

Advancing the science of sustainable interventions. Drs. McKay (PD/PI) and Luke (Co-I) have set a research agenda focusing on sustainability research in implementation science,[39] introduced one of the first conceptual frameworks for understanding organizational capacity for program sustainability,[9] and created measurement tools to assess sustainability in public health.[67] Dr. McKay also has ongoing research testing implementation strategies in pediatric clinical settings.[68] To address the lack of sustainability measures for use in clinical settings, the team developed the CSAT to assess the sustainability of clinical practices across 7 domains specific to health care and clinical settings (see C.4 Conceptual Framework).[58] Initial testing of the CSAT showed excellent internal consistency and preliminary evidence for discriminant validity (i.e., differences in CSAT scores by academic vs. nonacademic organizations and by inpatient vs. outpatient settings).[58,59]

Promoting PEWS implementation in low-resource hospitals. Proyecto EVAT supports PEWS implementation in pediatric oncology hospitals in Latin America.[27] Hospitals that care for children with cancer are recruited to Proyecto EVAT through collaboration with the St. Jude Global Alliance[28] or via learning about the program from others. Hospitals apply to an annual cohort, obtain institutional approval to participate, and are assigned to one of nine mentor training centers. Each hospital assembles a local PEWS implementation leadership team, including at minimum a pediatric oncology nurse, pediatric oncology ward physician, and intensivist, adjusting the size to local needs. Approximately 10-15 hospitals enroll annually**.**

Proyecto EVAT hospitals are guided through a 3-phase implementation process via bimonthly virtual mentorship meetings. During the *planning phase*, hospitals implement a de-identified prospective registry of CDEs in pediatric oncology patients, collecting 6-12 months of baseline data. PEWS implementation leaders are educated on the PEWS protocol as follows: the PEWS score (0-11) is calculated by using the PEWS tool with every set of routine vital signs. The PEWS action algorithm then guides the medical response, with yellow scores (PEWS≥3) requiring increased monitoring and medical assessment and red scores (PEWS≥5) requiring ICU consultation.[21] To maintain effectiveness, fidelity with no changes is recommended to the validated components of the PEWS tool or how it is used in patient care.[20,69] Hospitals, however, are encouraged to adapt other elements of PEWS to their setting, including adjusting the wording of the PEWS tool and details of the PEWS algorithm to better fit with local medical language, available resources, and processes for care escalation in hospitalized children.[70]

After completing these activities, hospitals move to the *implementation phase*. Experts from St. Jude and the

mentor centers teach local implementation teams PEWS implementation strategies using a standardized curriculum. Implementation teams then conduct local training with clinicians, pilot PEWS, and assess its effectiveness. From the start of the pilot, local leaders track PEWS use and fidelity (measured by the three types of PEWS errors described in Table 4) and patient outcomes (CDE registry), which are sent to St. Jude monthly. Implementation is considered complete (i.e., implementation completion) when a hospital achieves sufficient PEWS use and fidelity, defined as <15% PEWS errors for two consecutive months. Hospitals then move to the *sustainability phase*, with the expectation of indefinite PEWS sustainment through continued PEWS use and fidelity, resulting an ongoing positive impact on patient outcomes. During this phase, hospitals continue collaborating with Proyecto EVAT through monthly virtual meetings and/or as mentor centers.

To date, **43 hospitals have successfully implemented PEWS through Proyecto EVAT**, requiring 3–13 months from pilot start to implementation completion, and 29 additional hospitals are currently implementing PEWS. Analysis from 17 hospitals demonstrates that patients experiencing CDEs post-implementation were less likely to require mechanical ventilation or suffer a cardiac arrest on the ward, had shorter ICU lengths of stay, and a 28% reduction in CDE mortality (38.8 vs. 28.7%, p=0.0012). Proyecto EVAT's 5-year experience supporting PEWS implementation in these diverse, low-resource settings establishes the feasibility of this study. This prior work has informed our data collection structure (Table 4) and serves as a means to operationalize both implementation phases and sustainability outcomes.

Preliminary data from Proyecto EVAT demonstrates hospitals improve clinical capacity during implementation but may struggle to sustain PEWS. A qualitative study of barriers and enablers to PEWS implementation at Proyecto EVAT 5 hospitals sustaining PEWS demonstrated several capacity-related barriers to implementation, including staff resistance to change, inadequate material and human resources, and perceived complexity of PEWS. To address these barriers and facilitate PEWS implementation, hospitals frequently developed capacity, including changing nursing documentation, frequency of vital sign assessments, and training staff.[70] Study participants, however, identified several specific barriers to PEWS sustainability, including the COVID-19 pandemic, fluctuations in human and material resources needed for PEWS, staff turnover resulting in insufficient training, difficulty obtaining leadership buy-in, and lack of internal systems for ongoing PEWS monitoring. In a preliminary analysis of hospitals using PEWS for up to 24 months, approximately 30% reported PEWS error rates above the 15% threshold for one or more months, indicating a lack of PEWS sustainment. These results suggest that while capacity may improve during initial PEWS implementation, not all hospitals have sufficient capacity for sustainability and a notable portion do not sustain PEWS. *This proposal will build on this prior work by examining clinical capacity beyond implementation to understand its impact on PEWS sustainability*.

Integrating clinical capacity assessment with Proyecto EVAT. A recent review of sustainability measures noted a lack of pragmatic, psychometrically sound tools to assess factors contributing to successful sustainability of evidence-based practices,[71] particularly in low-resource[51] or acute care settings.[72] We will overcome this scientific barrier by leveraging the CSAT, a reliable measure developed by our research team, to evaluate clinical capacity for sustainability among the Proyecto EVAT hospitals as part of the ongoing St. Jude–Wash U Implementation Science Collaborative (see Facilities & Other Resources). Drs. Agulnik, McKay, Luke, Graetz, and Devidas worked with the Proyecto EVAT SC to translate, regionally adapt, and validate a Spanish version of the CSAT measure and associated report for use in low-resource settings. The CSAT was reviewed with the EVAT SC for conceptual and cultural appropriateness, translated by bilingual St. Jude staff, iteratively edited for clarity and syntax, and back translated to confirm accuracy. An electronic version of the tool was piloted among 19 EVAT SC members to establish acceptability within the context of Proyecto EVAT, and feedback was used to create the final tool (see Appendix).[35] In this pilot, survey completion required 10–15 min. The Spanish CSAT was distributed to PEWS leadership teams at 29 hospitals in July 2020 (mean 7 participants per hospital, n=210). The pilot survey achieved an 80% response rate in 1 month, with an average CSAT score of 4.4 (out of 5; range 3.8–4.8). This Spanish CSAT had good reliability, with an average internal consistency of 0.77 (0.71–0.81), and confirmatory factor analyses supported the 7-domain structure. The CSAT score was associated with respondent perceptions of the evidence for PEWS, its use in patient care, and the hospital culture and implementation climate. The mean CSAT score was higher among respondents at hospitals with a longer history of using PEWS (p<0.001). Focus group participants noted the CSAT report helped them assess their hospital's capacity to sustain PEWS. This work confirms the CSAT is culturally and contextually appropriate and discriminates

between high- and low-capacity hospitals.

Based on positive participant feedback, the CSAT was integrated into the Proyecto EVAT timeline in 2021, with three standardized CSAT measurements during the PEWS implementation phase (1. after staff training to inform the PEWS pilot, 2. after PEWS pilot to inform full-scale PEWS implementation, and 3. at implementation completion). To date, CSAT assessment has been conducted per this schedule 15 times across 9 hospitals, resulting in a response rate of 65% (253/391 participants, mean 19/30 per hospital). As some Proyecto EVAT hospitals are predominantly Portuguese speaking, we also translated the CSAT and its report to Portuguese (see Appendix) and piloted this with 26 clinicians from one hospital in Brazil through a similar process.

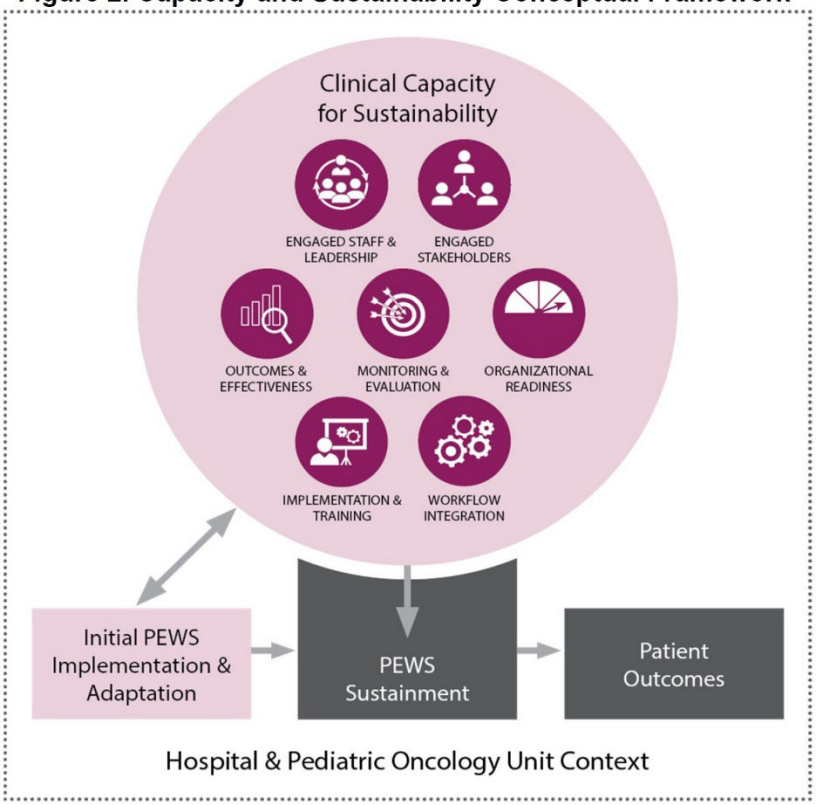
Prior work demonstrates the feasibility of the proposed study and need for deeper understanding of capacity and sustainability. Proyecto EVAT and ongoing collaboration through the St. Jude–Wash U Implementation Science Collaborative uniquely position us to examine sustainability of PEWS in low-resource pediatric oncology centers. Through Proyecto EVAT, we routinely collect process and outcomes measures at a growing number of collaborating hospitals, demonstrating the feasibility of the proposed research design and data collection methods. We have also successfully measured clinical capacity among these hospitals via the Spanish and Portuguese CSAT, an integral research innovation of the proposed work, and CSAT assessments are now fully integrated into Proyecto EVAT. Previously, we have successfully completed multiple research endeavors in these settings, including collection of quantitative, qualitative, implementation, and clinical outcomes data. We used these findings and experience to inform our proposed research design, methods, and analyses. Furthermore, our preliminary work suggests that while hospitals grow their capacity to implement PEWS, not all hospitals have sufficient capacity to sustain PEWS long term. *In the current proposal, we will extend this prior work by quantitatively evaluating capacity over the phases of PEWS adoption, implementation, and sustainment to determine its impact on PEWS sustainability and qualitatively exploring clinician perceptions on challenges to capacity development and sustaining PEWS to develop novel strategies that promote sustainability*.

C.4 Conceptual Framework. Our conceptual model (Figure 2) is guided by two frameworks: the dynamic sustainability framework[10] and the public health capacity for sustainability framework.[9] The dynamic sustainability framework posits that interventions are implemented within a clinical context nested in a broad ecological system with a complex interplay between sustainability determinants, intervention sustainment, and intervention outcomes. We use the term *sustainment* to refer to the continued use of evidence-based intervention elements after implementation, often without external support, and *sustainability* to more broadly include intervention sustainment, ongoing beneficial patient outcomes, and intervention adaptation to improve sustainment (both gray boxes).[7] We theorize that hospitals' *clinical capacity for sustainability,* which refers to the resources needed for an intervention, is the primary set of determinants of intervention sustainability. To promote sustainability, interventions may be adapted, or capacity may be changed to support ongoing intervention use, resulting in a feedback loop between the intervention and capacity over time. To conceptualize the clinical context in sufficient detail, we use the Clinical Capacity for Sustainability Model.[59] This model suggests that clinical capacity for sustainability falls within 7 domains: (1) engaged staff and leadership—frontline and administrative staff who are supportive of the intervention; (2) engaged stakeholders—other individuals, such as patients or parents, who are supportive of the intervention; (3) organizational readiness—organizational internal support and the resources needed to effectively manage the intervention; (4) workflow integration—how well the intervention fits into work that is done or will be done; (5) implementation and training—the process of implementing and training to deliver

and maintain an intervention; (6) monitoring and evaluation—a process to evaluate the intervention to determine its effectiveness; and (7) outcomes and effectiveness—using monitoring and evaluation to determine outcomes for clinicians or patients.

An organization's capacity may change during different implementation phases and influence the likelihood of sustaining the intervention long-term. We suggest that an organization's baseline capacity and capacity developed during initial implementation makes sustainability more likely.[54,73] If capacity decreases substantially, sustainability may be jeopardized, leading to premature intervention abandonment and loss of health benefits.[49] Alternatively, the intervention may be adapted to better suit available capacity, presuming that the intervention remains effective and positive health outcomes continue.

Figure 2. Capacity and Sustainability Conceptual Framework



For the current proposal, the clinical context includes both the hospital and pediatric oncology unit. Clinical capacity for sustainability is the primary predictor of PEWS sustainability including both PEWS sustainment and continued benefit to patient outcomes. Capacity growth, PEWS adaptation, and PEWS implementation will co-occur during the initial implementation process with support from Proyecto EVAT. As mentioned in Section C.3, hospitals are encouraged to adapt some elements of PEWS to suit local capacity but are expected to maintain fidelity to the PEWS tool and how it is used in patient care. Once implementation is complete, hospitals sustain PEWS, including both PEWS use and fidelity, independently of Proyecto EVAT. Hospitals may continue to build capacity or experience capacity declines. Generally, we hypothesize that a hospital's baseline capacity and ability to increase or maintain capacity (Aim 1) leads to a greater likelihood of PEWS sustainability (Aim 2). In pediatric oncology centers, we expect PEWS to be sustained indefinitely, specifically by continuing to use and maintain fidelity to the PEWS tool, despite minor fluctuations in overall capacity, its individual components, or appropriate PEWS adaptation. Through PEWS sustainability, we expect lower CDE mortality rates long-term (Aim 2). If capacity drops substantially or organizations cannot use PEWS with fidelity, PEWS may not be sustained (i.e., abandoned), resulting in increased CDE mortality rates. By identifying challenges to capacity, we expect to develop sustainability strategies targeting these challenges, which will subsequently improve PEWS sustainability (Aim 3).

C.5 Start-up activities. During a start-up period of 4 months, we will finalize the study protocol, hire and train staff, refine data collection instruments, and develop data management procedures. We will also enroll Proyecto EVAT hospitals to the study and secure local approvals. Of note, all current Proyecto EVAT hospitals already have local approval to participate in the collaborative, implement PEWS, and collect the de-identified process and patient outcomes measures needed in this study, and time for these is not included in start-up activities.

C.6 Overall Study Design and Data Collection. For Aims 1 and 2 we will use a longitudinal observational research design. This will allow us to follow the natural development of capacity and the impact of capacity on PEWS sustainability in a variety of natural contexts. Over the study period, we will capture hospitals at various points in the implementation and sustainment process, ranging from those newly adopting PEWS to ones sustaining PEWS for over 10 years. We anticipate having between 5 and 9 observations of clinical capacity per hospital, dependent where hospitals are in the PEWS implementation process. We have structured data collection to occur at three relevant milestones in Proyecto EVAT (See C.3) to capture potential capacity increase

during the adoption, initial implementation, and sustainment of PEWS. Once hospitals complete PEWS implementation and are sustaining PEWS, we will collect data every 6 months over the 4-year study data collection period (Figure 3). We selected this interval to allow us to capture major changes in capacity and sustainability while minimizing participant burden. Among hospitals that have completed PEWS implementation, the primary outcomes, PEWS sustainment and CDE mortality rate will be assessed in the two months prior to capacity assessments. This proposed study design will result in a large quantity of rich data which will allow us to examine our research questions flexibly and in depth. In particular, the large number of hospitals along with the high number of observed time points gives us very good power to detect the hypothesized relationships between clinical capacity and sustainability outcomes (see Section C.11) while minimizing data collection burden. For Aim 3, we will use a sequential mixed- method design by nesting qualitative data collection among hospitals who exhibit high and low capacity and have been using PEWS for at least 2 years (not pictured). We will use focus groups of implementation leaders, clinicians, and hospital administrators to understand staff perspectives of the influence of capacity on PEWS sustainability and identify strategies that may develop capacity and support sustainability. We will then use an intervention mapping approach to identify critical capacity components and develop novel sustainability strategies for low-resource hospitals.

C.7 Recruitment

Hospital Recruitment and Enrollment. All current Proyecto EVAT hospitals will be recruited for participation at the start of the project, and we expect to recruit two additional annual cohorts during the study period, resulting in approximately 92 study hospitals (72 current hospitals + 10 new hospitals per year × 2 years in subsequent cohorts). Each hospital's local PEWS implementation leadership team will be contacted for participation in the study and asked to identify a site lead. Site leads will be responsible for obtaining hospital approval for participation and guide data collection at their hospitals. All 72 current Proyecto EVAT hospitals have already obtained formal permission to participate in Proyecto EVAT, and to collect de-identified process and patient outcomes measures (see C3. Prior Work). If hospitals do not wish to participate, they will have the option to opt out of the study but remain in Proyecto EVAT.

Participant Recruitment: All PEWS implementation leadership team members (mean 7, range 4-15) and frontline clinical staff who routinely use PEWS (mean 20, range 9-61) will be eligible and invited to participate at each survey data collection time point (anticipated 27 participants per time point). Based on preliminary data, we conservatively expect at least a 50% response rate (currently 65%), resulting in at least 13 responses per time point (current mean is 19 per hospital, see Section C.3). St. Jude will work with local site leads to identify study participants, including all ward and ICU frontline staff (physicians and nurses) who use PEWS and can assess clinical capacity. Participation will be voluntary and anonymous. Based on preliminary data, we expect participants to be approximately 75% female, with 70% having ≥6 years of experience working in their profession. Further enrollment details are included in Recruitment and Retention and Protection of Human Subjects**.**

C.8 Study Measures. Study measures and collection methods are summarized in Table 4 which aligns with our conceptual model. In alignment with our concept of sustainability, our primary outcomes are PEWS sustainment (i.e., sustainment outcome) and CDE mortality rate (i.e., patient outcome). Our primary quantitative covariates and predictors include hospital characteristics, participant characteristics, and clinical capacity for sustainability, and PEWS adaptation.

We operationalize PEWS sustainment as 2 consecutive months of PEWS use and fidelity, defined as <15% PEWS errors (Table 4). Based on our prior work, we expect that some hospitals will have errors above this threshold and thereby be considered not sustaining. We will follow these hospitals to understand whether they resume PEWS sustainment or experience continued decline and PEWS abandonment. The primary patient outcome will be measured by the CDE mortality rate, calculated based the de-identified quality improvement CDE registry (Table 4). We selected this patient outcome because it is the most reliable, easily collected, and most reflective of the effects of PEWS on patient care. Implementation leaders will collect sustainment and CDE mortality data for 2 months before each data collection time point.

Table 4. Overview of Study Measures. See Appendix for data collection instruments.		
Data Domain	**Measures**	**Methods**
Hospital Characteristics	Hospital type, funding, bed capacity, pediatric oncology and ICU staffing, annual volume of new diagnoses, and dates of PEWS adoption, training, pilot, and implementation completion.	• Collected by St. Jude at entry into Proyecto EVAT, confirmed by local site lead at study enrollment.

Participant Demographics	6 demographic questions on profession, role in PEWS implementation, years working in profession, gender, age, and hospital of employment.	• Anonymous Spanish or Portuguese paper or electronic Qualtrics survey, requiring 10–15 min to complete.
		• Distributed to (estimated n=27 per hospital):
		  • PEWS implementation leadership team (nurses and physicians, mean n=7, range 4-15).
		  • Frontline clinical staff (all ward and ICU physicians and nurses using PEWS, mean n=20, range 9-61).
		• Participants allowed 3 weeks to complete survey with 3 reminders.

Clinical Capacity for Sustainability	CSAT: 7 domains with 5 questions (35 total), ranked on a 5-point Likert scale (1=low to 5=high agreement). Domain scores are the mean of domain items, and overall score is the mean of all domain scores; higher scores represent greater capacity.	
PEWS Adaptation	3 close-ended and 1 open-ended question on adaptations made to the PEWS scoring tool and algorithm.[74] Reported adaptations will be summed per respondent then averaged across all participants at each hospital.	
PEWS Sustainment	PEWS use and fidelity indicated by 3 types of errors (omission, scoring, and algorithm) in the 2 months before each CSAT data collection following implementation completion (sustainability phase). • Errors: (1) *omissions* (documented vital signs without using PEWS), (2) errors in PEWS *scoring*, and (3) PEWS *algorithm* nonadherence. • Dichotomous (yes/no <15% in all three error types) and continuous (% errors).	• Assess by the implementation team by reviewing nursing documentation of vital signs and PEWS in all hospitalized patients. • Assessed weekly during implementation until implementation completion. • Assessed for two-months prior to survey assessment during the sustainability phase. • Submitted electronically to St. Jude. • Data aggregated to calculate monthly error %
Patient Outcomes	• CDE: an unplanned transfer to a higher level of care (i.e., ICU), use of an ICU intervention on the ward (vasoactive infusion, invasive or noninvasive mechanical ventilation, or cardiopulmonary resuscitation), or a ward death in a patient without limitations on resuscitation.[46] • CDE mortality rate: percent of death occurring during event or within 24 h of event conclusion.[46] • Reported for 2 months before each CSAT data collection time point during sustainability phase	• Prospective de-identified registry of all CDEs in hospitalized pediatric oncology patients collected by the PEWS implementation team from start of participation in Proyecto EVAT. • For each CDE, a de-identified case report form is completed by local site leads and entered into a RedCAP database[75] by a clinical research associate at St. Jude. • Data analysis checks for missing and incorrect values assure data quality.
Challenges to Capacity and Sustainability	Perspectives from hospital staff on challenges to capacity development, PEWS adaptation, and PEWS sustainability, as well as possible interventions to support sustainability.	• Focus groups of 5–7 physicians, nurses, and hospital administrators (3 focus groups per hospital) at 4 high- and 4 low-capacity hospitals as assessed by the CSAT.

C.9 Aim 1 Analyses. Changes in clinical capacity to sustain PEWS over time. We will investigate how overall capacity and its components change through the phases of PEWS adoption, implementation, and sustainment. We hypothesize that capacity will develop during early implementation and increase over time using PEWS. Primary data for Aim 1 will be hospital characteristics, participant demographics, and clinical capacity (Table 4). Data will be examined for missingness and outliers and tested for normality, linearity, and homoscedasticity. Corrective strategies will be used as appropriate but may not be necessary given the robustness of mixed-effects modeling to various assumption violations.[76,77] Data will be analyzed to generate descriptive statistics (e.g., frequencies, central tendencies, and variabilities) and diagnostic plots (e.g., bar charts and contingency tables) of capacity. Descriptive analyses will include variability of capacity across hospitals over time. All data management and analyses will be conducted using R (v4.1.2).

Given that our study design includes a large number of hospitals and a relatively high number of time points, we will be able to conduct multiple relevant analyses. The *primary* question for Aim 1 is to model change in clinical capacity for sustainability over time. Other secondary analyses will focus on related questions, including 1) change in specific *components* of capacity over time; 2) association between capacity and hospital

characteristics; 3) cross-sectional capacity at different implementation stages across hospitals; and 4) within-hospital agreement between implementation leaders and other clinical staff about capacity.

For the primary research question, we will use a mixed-effects modeling approach to build a series of growth curve models of capacity (CSAT scores) over time. The growth curve models will allow us to assess individual- and hospital-level associations with changes in capacity. Moreover, because capacity will be measured at many time points (5-9), the growth curve models will allow us to identify the linear and nonlinear change patterns of sustainability.[77] This rich description of changes in capacity is an important contribution of this study. The mixed-effects model template that will be used for these growth curve analyses is: $SustCap_{tij} = IC_{tij} + HC_{tj} = IC_{tij} * HC_{tj}$,where *SustCap* is capacity measured by the total or domain-specific CSAT scores; *IC* is the set of individual-level covariates (e.g., staff role); and *HC* is the set of hospital-level covariates (e.g., size). $Time_0$ defines the start of the data collection; observations will be collected at time *t* for each outcome variable and time-varying covariate. The interaction term between the individual and hospital-level covariates allows us to explore cross-level interactions between setting and clinical staff characteristics. Mixed-effects modeling has many advantages for this type of organizational-level observational study.[78] It will allow us to build multilevel models that can appropriately handle staff- and patient-level data clustering within hospitals, examine the effects of both individual and hospital characteristics on the dependent variables, and analyze patterns of change over time.

C.10 Aim 2 Analyses. Determine clinical capacity components that predict PEWS sustainability. We will identify capacity components that influence long-term sustainability. We hypothesize that greater overall capacity makes PEWS sustainment and continued benefits to patient outcomes more likely. Key variables include hospital characteristics, clinical capacity, PEWS adaptation, PEWS sustainment, and patient outcomes (Table 4).

We will follow a similar modeling strategy as described in Aim 1. We will build a series of mixed-effects growth curve models to assess changes in PEWS sustainment and patient outcomes over time, as a function of individual- and hospital-level, as well as capacity characteristics. As above, mixed-effects modeling has many advantages for this type of multi-level longitudinal study.[78] The first set of models will focus on PEWS sustainment as the primary outcome: $SustOutcome_{tj} = IC_{tij} + HC_{tj} + IC_{tij} * HC_{tj} = CSAT_{tij}$,where *SustOutcome* measured at time *t* for hospital *j* is one of the PEWS sustainment variables (Table 4); *IC* is the set of individual-level covariates (e.g., staff role); *HC* is the set of hospital-level covariates (e.g., size), and CSAT is the set of total and domain-specific CSAT scores. Sustainment outcomes are either binary or percentages, so generalized mixed- effects modeling will be used.[78] The second set of models will then look at patient outcomes: $PatientOutcome_{tj} = IC_{tij} + HC_{tj} + IC_{tij} * HC_{tj} + CSAT_{tij} + SustOutcome_{tj}$.The interpretation of this model is similar to the previous one, but here we can add the PEWS sustainment outcomes as an additional covariate. This will allow us to assess the extent to which success in PEWS sustainment is associated with downstream clinical outcomes. We will use either general or generalized mixed-effects modeling depending on the dependent variable (e.g., a *Poisson* model will be used for CDE mortality rates, Table 4).

For both models, we can examine additional interaction terms as our hypotheses and preliminary analyses suggest. For example, we anticipate exploring some interactions between hospital characteristics and capacity scores. Additional secondary analyses will focus on PEWS adaptation, which will be included as a time-varying moderating covariate, allowing us to examine how adaptation moderates the influence of capacity on outcomes.

C. 11 Power estimates (Aim 1 and 2). We used a simulation approach for power analysis in mixed-effects models according to the proposed analytic models.[79] We selected 2 prototypic models for estimating power: a *multilevel* model in which individual clinical staff are nested within hospitals (corresponding to secondary research questions that include cross-sectional multilevel analyses) and a *longitudinal* model in which hospital-level covariates and outcomes are

Table 5. Power Analyses for Proposed Models.

Effect Type	Effect Size	Power	95% CI
Multilevel (13 participants in 90 hospitals)			
L1–Staff	Small	100	99–100
L2–Hospital	Medium	91	82–96
CLI–Staff by hospital	Small	100	97–100
Longitudinal (7 time points in 90 hospitals)			
L1–Time	Small	94	88–98
L2–Hospital	Medium	83	75–89
CLI–Time by hospital	Small	95	89–99

measured over time (corresponding to the primary research questions in Aims 1 and 2). We obtained parameter estimates from study design decisions (e.g., number of hospitals) and analysis of the pilot data (e.g., means and variability of CSAT scores and hospital CDE mortality rates). We used conservative estimates of the number of participants, hospitals, time points, and intraclass correlation values. For the longitudinal models, we will have between 5 and 9 observations for each hospital (C.6). For power analyses, we assume 7 time points, which is a conservative estimate of the minimum number of observations we will have from most hospitals.

We conducted the power analyses with the SIMR package in R (Table 5).[80] For each prototypic model, we calculated the power for detecting small or medium effect sizes for level 1, level 2, and cross-level interactioneffects (L1, L2, CLI, respectively). Small and medium effect sizes are based on standardized estimates.[80,81] The estimated power for the study ranged from good to excellent. Although the L2 main effects had lower power due to the number of hospitals, the more important effects for both models were CLIs (e.g., how clinical outcomes vary over time for different types of hospitals), which were excellent (> 95%) for both analyses.

C.12 Aim 3. Develop strategies to target clinical capacity and sustainability challenges. We will evaluate perspectives of clinical staff and hospital administrators on capacity development, PEWS sustainment, and impact on patient outcomes in a subset of Proyecto EVAT hospitals exhibiting high- and low-capacity for sustainability. Using a sequential mixed-methods design, we will *qualitatively* determine staff perspectives on changes to capacity over time and how this relates to PEWS sustainment and patient outcomes. We will triangulate this with our *quantitative* assessment of capacity to provide a deeper understanding of how capacity relates to sustainability. We will then use an established implementation mapping process[37] to develop novel strategies to support PEWS sustainability in low-resource hospitals and address identified capacity challenges.

Recruitment and Enrollment. Three focus groups (physicians, nurses, and administrators, separately) will be conducted at each of 8 Proyecto EVAT hospitals that have been using PEWS for at least 2 years (24 focus groups). The hospitals will be sampled purposively with a modified positive and negative deviant approach[82] to include four high-capacity and four low-capacity hospitals (using upper and lower quartiles of CSAT scores to recruit two high- and low-capacity hospitals in years 2 and 3, see Section 2.7 Study Timeline). Based on our prior work indicating variation in capacity, this approach will allow us to explore how differences in capacity relate to sustainability and staff perspectives on identified capacity challenges. We will recruit participants using a purposive sampling approach[83] to include implementation leaders and clinical staff recruited for Aim 1 and 2, and hospital administrators identified by site leads, aiming to enroll 5–7 participants per focus group (total 120-168 participants). We will use homogenous grouping by participant roles to help ensure honest discussions.[84,85]

Data Collection. Similar to our prior work, focus groups will be conducted using the video conferencing platform WebEx in Spanish or Portuguese by two native-speaking facilitators from St. Jude unknown to participants, and audio-recorded.[35,86] The facilitation guide will be based on our conceptual framework (Figure 2) and assess perceived challenges to capacity in the 7 CSAT domains, PEWS adaptation, PEWS sustainment, impact on patient outcomes and potential strategies to promote sustainability (see Appendix).

Analysis Plan. As in our prior work, audio recordings will be translated into English and transcribed through a certified service.[23-25,86,87] English transcripts will be de-identified, segmented, and uploaded to MAXQDA for analysis. A qualitative analysis team (Drs. Agulnik, McKay, and Graetz) will develop an initial codebook with ***a priori*** codes informed by the CSAT domains and conceptual framework as well as inductive codes developed using a constant comparative approach with iterative memoing of transcripts to allow for emergent themes.[88] Transcripts will be coded independently by two coders. Interrater reliability will be monitored, and discrepancies resolved through consensus and a separate adjudicator. We expect to use two broad analytic approaches: categorical coding, which will group data conceptually according to the domains of our framework, and thematic coding, which will describe the relations among the concepts (e.g., the dynamic between capacity and PEWS sustainability).[89] Because our approach is guided by a structured framework and a previously employed method for inductive codes, we are confident that this strategy will achieve analytic saturation.[90]

Data Synthesis. The results from *quantitative* assessment of capacity using the CSAT will be triangulated with

qualitative participant perspectives on capacity development and PEWS sustainability to provide convergence (i.e., to assess how different data answer the same question).[91,92] We will further explicate primary quantitative findings through joint displays, facilitating comparisons of quantitative and qualitative results.[93] Specifically, qualitative results will be used to gain a deeper understanding of capacity strengths and challenges, as well as how capacity relates to PEWS sustainability.[94,95]

Strategy Development. In year 5, we will use results from the above analyses to develop sustainability strategies by leveraging implementation mapping, which applies intervention mapping to implementation strategy development.[37] This work will be supported by Wash U's Dissemination and Implementation Research Core (see letter of support). To date, sustainability strategies for clinical settings have been primarily developed based on literature review and without a systematic process.[54] Intervention mapping is widely used to design and adapt behavioral interventions and provides a systematic process to development interventions using five steps: 1) conduct a needs assessment; 2) identify sustainability outcomes, performance objectives, determinants, and create matrices of change; 3) choose theories of change and select strategies; 4) produce strategy protocols and materials; 5) evaluate outcomes.[96,97] Our activities and analyses from the three study aims will serve as the needs assessment and address step 1: identify capacity barriers and needs. To accomplish the second step, our research team we will use study results to identify performance objectives and create matrices of change. Performance objectives are actions that will accomplish the intended sustainability outcome. For instance, a simple performance objective to improve PEWS maintenance would be to have nurses use PEWS more often. Matrices of change are an analytic technique that help integrate determinants, theories of change, performance objectives, and sustainability outcomes to select strategies that directly address critical determinants in a theoretically-sound manner (third step). For instance, we may identify nurse turnover and lack of PEWS knowledge (determinants) as primary barriers to PEWS use among nurses (performance objective) impacting overall PEWS sustainment (outcome). To address this barrier, we may select an educational strategy, based on the theoretical assumption that knowledge leads to behavior change, such as booster PEWS training sessions for new nurses. We will present our strategy development progress to the EVAT SC for feedback. By the end of the study period, we will have developed materials and protocols needed for these strategies (fourth step) using recommendations for specifying strategies[98] and be positioned to evaluate these strategies (step 5) in future work using a design, such as a hybrid type III trial, appropriate for strategy evaluation. While we cannot anticipate the exact strateg(ies) that may be appropriate, we expect we will have sufficient time, expertise, and feedback from the EVAT SC to develop several different types of strategies (e.g., educational materials or workshops, tools, facilitation, or technical support) targeting different actors and relevant components of clinical capacity.

C.13 Potential pitfalls, alternative designs, and considerations.

COVID-19 pandemic. Proyecto EVAT responded to the pandemic by adapting its mentorship model to a fully virtual format in March 2020. Since that time, 14 hospitals successfully completed PEWS implementation and 14 new hospitals joined the 2021 Proyecto EVAT cohort. Despite the pandemic, our team also completed the CSAT pilot in August 2020. Based on this experience, we are confident that our program will continue adapting to the evolving challenges from the pandemic throughout the study period.

Research in low-resource settings. Conducting research in low-resource settings poses several challenges, including limited personnel to collect data, incomplete clinical documentation in paper charts, variable requirements for research approval, frequent staff turnover, poor participant recruitment, and political and environmental disruptions. Our research team has extensive experience overcoming these challenges to successfully completed multiple research studies at the proposed collaborating hospitals, achieving necessary research approvals, recruiting participants, and collecting high-quality data within set timelines.

Site and participant recruitment. Given the growth of and ongoing interest in Proyecto EVAT in Latin America, we are confident we can recruit at least 10 new hospitals per year during year 1 and 2 of the proposed study. In prior work, no hospital declined to participate or dropped out of a research study associated with Proyecto EVAT. Starting in 2021, measurement of the CSAT has been integrated with the Proyecto EVAT PEWS implementation strategy, with all eligible hospitals participating and a preliminary response rate of 65%. We expect the proposed study will be similar and are confident that we can achieve the anticipated hospital participation (at least 92 hospitals) and participant response rate (at least 50% at each data collection time point). Similarly, based on our

prior experience conducting qualitative research with both clinical staff and hospital administrators at Proyecto EVAT hospitals,[23-25,35,70] we are confident we can recruit participants to focus groups as proposed in Aim 3.

Observational study design. This study does not assess the effectiveness of PEWS, which we have done in prior work,[21-26] nor intervene in PEWS sustainability. Instead, it prospectively follows capacity and its impact on sustainability over time. By choosing this design, we accept loss of control over recruitment and measurement conditions. However, our design is strengthened by the diversity in location, size, and capacity of the participating hospitals, allowing us to longitudinally follow the natural course of PEWS sustainability over many years. A longitudinal observational study is the most appropriate design to provide empirical evidence for the interrelations between capacity, PEWS sustainment, and patient outcomes in *real-world* low-resource hospitals.

C.14 Consideration of Sex and other Relevant Biological Variables. Male and female clinical staff will be enrolled in all study aims. Age and sex will be included in all analyses as relevant biologic variables.

C.15 Dissemination Plan & Study Timeline. Our work will occur according to the study timeline (Section 2.7 Study Timeline). Our dissemination plan considers various audience, including researchers, hospital administrators, clinical staff, and funders. We will share our findings through conference presentations and open-access publications. All versions of the CSAT are publicly available at the *SustainTool.org* website,[99] which will be updated with study results and resources for study partners. We will also develop an interactive dashboard to share findings and developed strategy materials with study participants and the public (see Resource Sharing Plan). Making these tools freely available will expedite their use as common measures in future studies and by clinicians and other stakeholders looking to assess the clinical capacity of their organizations.

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