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Effectiveness and Implementation of an Early Childhood School-Based Mental Health Intervention in Low-Resource Communities

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Statement of Compliance

This study will be conducted in accordance with the Code of Federal Regulations on the Protection of Human Subjects (45 CFR Part 46), any other applicable US government research regulations, and institutional research policies and procedures. The Principal Investigator will assure that no deviation from, or changes to the protocol will take place without prior agreement from the sponsor and documented approval from the Institutional Review Board (IRB), except where necessary to eliminate an immediate hazard(s) to the trial participants. All personnel involved in the conduct of this study have completed Human Subjects Protection Training.

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List of Abbreviations

AE	Adverse Event/Adverse Experience
CFR	Code of Federal Regulations
CRF	Case Report Form
CSOC	Clinical Study Oversight Committee
DCC	Data Coordinating Center
DHHS	Department of Health and Human Services
DSMB	Data and Safety Monitoring Board
FFR	Federal Financial Report
FWA	Federalwide Assurance
GCP	Good Clinical Practice
HIPAA	Health Insurance Portability and Accountability Act
ICF	Informed Consent Form
IRB	Institutional Review Board
ISM	Independent Safety Monitor
MOP	Manual of Procedures
N	Number (typically refers to participants)
NIH	National Institutes of Health
OHRP	Office for Human Research Protections
OHSR	Office of Human Subjects Research
PI	Principal Investigator
QA	Quality Assurance
QC	Quality Control
SAE	Serious Adverse Event/Serious Adverse Experience
SOP	Standard Operating Procedure
US	United States

Protocol Summary

Title	Effectiveness and Implementation of an Early Childhood School-Based Mental Health Intervention in Low-Resource Communities
Short Title	School-Based Mental Health Effectiveness Study
Brief Summary	Promoting child mental health in low-resource or low-income country settings faces numerous challenges in global health research. Although efforts have been made to improve mental health interventions and services for young children, evidence-based interventions (EBIs) for children in low-and middle-income countries (LMICs) are limited. Most mental health EBIs in LMICs have not been scaled widely, and do not focus on early childhood. Mechanisms of action and effectiveness are not well understood. Additionally, most EBIs in LMICs rely on community health workers (CHWs) or a task-shifting approach of implementation because of resource barriers and shortage of mental health professionals (MHPs). However, challenges related to task-shifting (e.g., CHW stress and job burnout) have rarely been studied. For task-shifting to be successful, strategies to overcome challenges faced by CHWs and understanding mechanisms to conduct effective task-shifting are paramount. The overall goal of this study is to address these EBI effectiveness and implementation knowledge gaps by providing a preventive EBI (ParentCorps-Professional Development; PD) that utilizes a task-shifting and a scalable implementation model to promote early childhood students' mental health in a LMIC—Uganda. *PD* is a school-based EBI and preventive mental health service provision model that supports teachers and school personnel to apply EBI strategies to promote young children's mental health. The *PD* approach represents a task-shifting model of mental healthcare by shifting mental health preventive duties from professionals to teachers to optimize school children's mental health. Therefore, teachers are considered as CHWs. This study examines impacts and cost-effectiveness of the EBI/*PD* on teachers and students, as well as examines underlying mechanisms (or theories of change) that contribute to intervention effect. In addition, considering most Ugandan teachers (or CHWs) experience occupational stress that threatens *PD* uptake, effectiveness, and sustainment, this study will also test a teacher stress management package (T-Wellness, adapted from EBIs) as an enhancement to *PD.* This study will investigate whether *PD* + T-Wellness (*PDT*) is more effective for CHWs/teachers than PD alone.
Phase	Phase II/III
Objectives	This study include three specific aims: **Aim 1**. To evaluate the short- and longer-term effectiveness of, PD alone (**PD**), PD + T-Wellness (**PDT**), and control (C, provision of child mental health and referral information). Hypotheses: (a) PD is more effective than control; and (b) PD with T-Wellness (PDT) is more effective for CHWs/teachers than PD alone; and (c) PDT has a more favorable cost-effectiveness ratio than PD alone; **Aim 2.** To examine effectiveness mechanisms and theory of change underlying the EBIs. Hypotheses: the mediational mechanisms of PD (teacher EBI strategy use as a mediator between intervention and child outcomes) and PDT (teacher stress management and EBI strategy use as mediators) will be supported; **Aim 3**. To examine implementation contextual factors and mechanisms that contribute to CHWs' (teachers') uptake and sustainment of EBI strategies within PD and PDT schools. Hypotheses: better fidelity, teacher mental health and more supportive contexts will be associated with better teacher uptake and sustainment of EBI strategies and more effective task-shifting.

Methodology	A cluster randomized controlled trial (cRCT), single blind and mixed-methods design will be applied. All study activities will be conducted in Uganda. Thirty-six public primary schools (18 urban and 18 rural), 540 teachers (~15 per school) and 1,980 parent-child pairs (~55 per school) will be recruited. Schools will be assigned to one of three conditions (PD, PDT, control). A stratified-block randomization procedure will be applied to ensure approximately similar characteristics across study regions and conditions.
Endpoint	Effectiveness outcomes will be assess 3 times (Time 1= before intervention; Time 2= immediate after PD/PDT intervention; Time 3= 12 months after Time 2). The *primary teacher effectiveness outcomes* (or intermediate effectiveness outcomes) are teachers' EBI strategy use and teacher stress management. The *primary child effectiveness outcomes are* child externalizing and internalizing problems (mental health outcomes). The secondary child effectiveness outcomes are emotion regulation, executive functioning (ability for cognitive processes that are foundation for the cognitive control of behavior), and social relationship (student-teacher relationship, peer relationship).
Study Duration	This is a four-year study. Year 1 will be focused on study preparation (including conducting user-centered testing for the T-Wellness package and finalizing the PDT contents), developing implementation partnership, and capacity building for the PD/PDT implementers (Trainers from Teacher Training Colleges/TTCs and mental health institutions). Years 2-4 are intervention implementation, evaluation data and cost-benefit data collection, and data analyses.
Participant Duration	Participation duration will be varied by types of participants. • The *intervention implementers* (TTC trainers and mental health professional trainers) will participate in study for 4 years. • *Teachers participants for the T-Wellness Package User-centered & Optimization testing* will participate in the study for 6 months (during Year 1 preparation only). • *Primary school teachers and selected school leadership staff* (Head teacher, PTA leaders) will participate in the evaluation study for 2 years. Teachers (i.e., pre-primary and primary 1st to 4th grade, serving students between the ages of 3 and 10 years) and PTA leaders are the primary targets of the PD/PDT. • *Children and caregivers* will participate in the evaluation study for 18 months. •
Duration of behavioral intervention	Intervention schools' teachers (pre-primary to 4th grade teachers) and representative PTA leaders will participate in PD (3 days) or PDT workshop (4 days) in their regional Teacher Training College (TTC) during their 1st year of participation and before the 1st school term. Following the workshop training, they will also receive 8 sessions (12 hours) of face-to-face group-based coaching during the 1st and 2nd terms. For the teachers in the PDT group, additional stress management group coaching activities will also be integrated (3 additional monthly 1-hr wellness sessions for teachers as a group in each school).
Population	The study populations include: (1) Teachers for the *T-Wellness User-centered & Optimization testing* (n=60; from 4 non-RCT schools in year 1); (2) Intervention implementers (n=8; 6 TTC trainers and 2 mental health professionals from urban/Kampala and rural/Hoima regions; (3) Primary school teachers/head teachers (n=540) from 36 schools and PTA leaders (n=24) from 24 intervention schools; and (4) Children and caregivers (n= 1980 parent-child pairs) form 36 study schools.
Study Sites	36 schools (12 receiving PD, 12 receive PDT, and 12 control).
Number of participants	2544 adults and 1980 children for Aims 1-3 (This is not including 60 teachers for the T-Wellness User-centered testing during Year 1 preparation year).

Description of Study Intervention/ Procedure	• Prior to the RCT study (or during Year 1), T-Wellness Package (a brief teacher stress management psychoeducation package, adapted from EBIs and including a half-day workshop for common stress management and a half-day for burnout management, and three follow-up group support sessions) will be tested to insure user-centeredness. we will recruit 4 study schools and applying factorial design to test the effect of each component (1 Common Stress management; 1 Burnout Stress management; 1 Combined Common and Burnout Stress management; 1 control; with ~15 teachers in each condition). Both groups' will also receive 3 post-workshop group support sessions. We will compare pre-post differences on teacher stress management and mental health using a mixed-methods data collection. • To implement PD/PDT using a scalable approach, we will formalize partnership with the Ugandan Ministry of Education (MOE), Ministry of Health (MOH), academic medical center, and Teacher Training Colleges (TTCs) stakeholders in Year 1. The partnership and intervention implementation team will receive training from NYU PD trainers, and implement PD/PDT in Years 2-4. • To study effectiveness-implementation aims (Aim 1-3), a cRCT will be conducted. Public primary schools from Kampala/urban and Hoima/ rural will be recruited. A stratified-block randomization procedure will be applied to ensure approximately similar characteristics across geographic regions and three intervention conditions (PD, PDT, and control). Teachers from the PD will receive a 3-day training, and teachers from the PDT will receive a 4-day training. Both intervention groups will receive 8 group-coaching sessions (with teachers from their own school). Teachers from the control schools will receive child mental health promotion materials. They will receive T-Wellness in Year 4 after the evaluation study is completed. Given the large numbers of students in schools, research staff will randomly select 10% of students and families from each school for participation in the evaluation study. A total of 1,980 families (parent-child pairs) from 36 schools (averaging 55 families/per school) will participate in the evaluation study. Effectiveness outcomes will be assessed at 3 time points over 18 months (baseline/T1, post-PD or PDT, 5-6 month/T2, and 16-18-month follow-up/T3). Objective observation, implementers, school staff, parent, and child report data (quantitative and qualitative) will be gathered. • To study underlying mechanisms, we will use the evaluation data describe above to examine whether intervention effects on children's mental health outcomes is *mediated* through improvement on teachers' EBI practices (primary) and teacher stress coping. To study *moderation* mechanisms, geographic region, fidelity (including adherence, quality of program implementation, engagement, exposure) and other implementation contextual factors (i.e., EBI fidelity, school climate), guided by the Consolidated Framework for Implementation Research, will be studied. • Identifiers will be removed from the identifiable survey and field notes. Data may be used for future research studies or shared with other researchers and we will not request additional informed consent from you to use these specimens as we have noted here.
Reference Therapy	Multi-level Mixed Effect Model and Structural Equation Model are the statistical analysis approaches planned for this study.
Key Procedures	36 schools (12 receiving PD, 12 receive PDT, and 12 control).
Statistical Analysis	2544 adults and 1980 children for Aims 1-3 (This is not including 60 teachers for the T-Wellness User-centered testing during Year 1 preparation year).

Schematic of Study Design

Figure 1. Diagram of Enrollment and Randomization

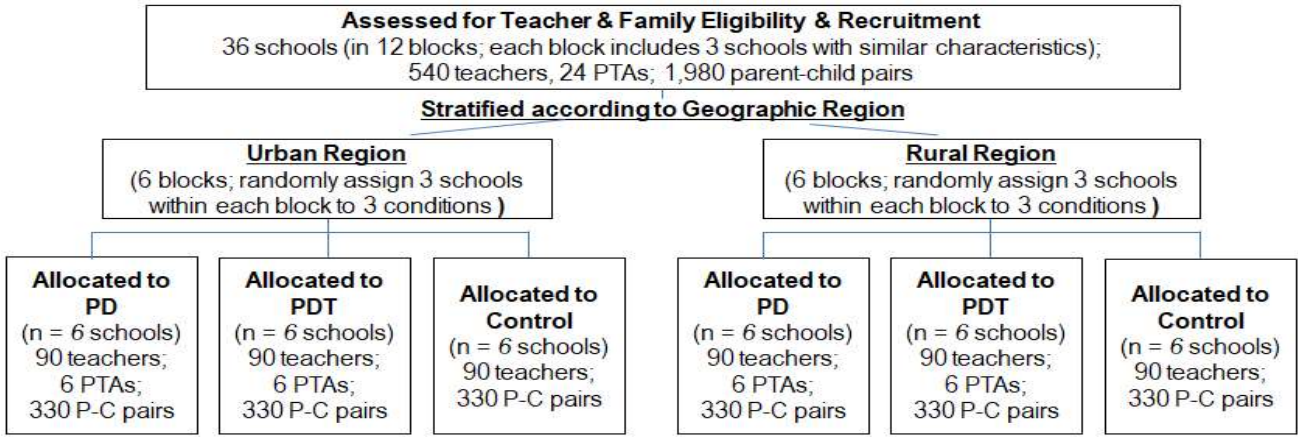
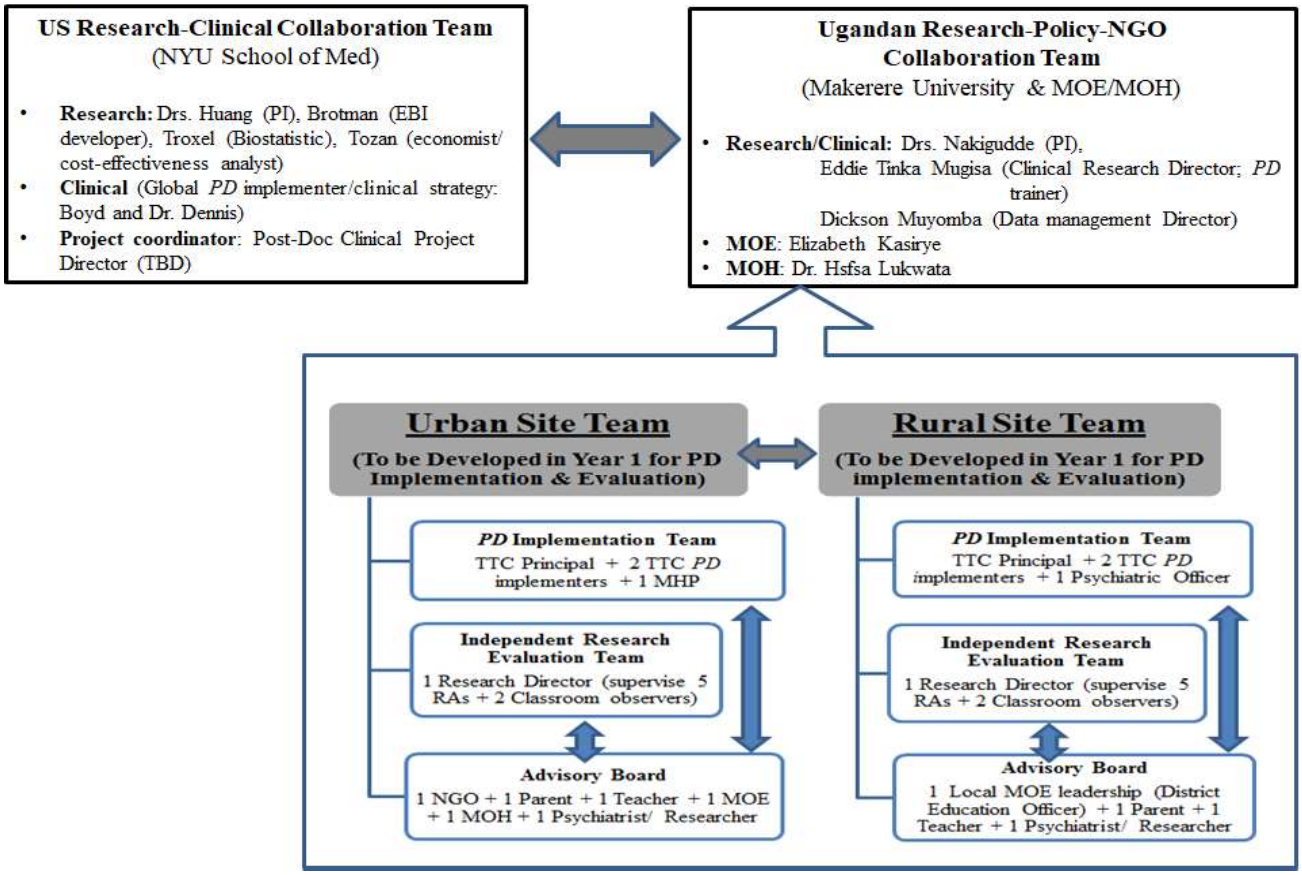


Figure 2. Implementation Partnership and Study Team Structure



Key Roles

Name	Title on Project	Institution	Address	Phone Number	Email	Role and Data Access
Keng-Yen Huang, Ph.D.	Principal Investigator	Department of Population Health, NYU School of Medicine	227 E. 30th Street, Seventh Floor, New York, NY 10016	646-501-2819	Keng-Yen.Huang@nyulangone.org	PI; will oversee all study activities; work with Dr. Toxel on quantitative data analysis; work with Dr. Nakigudde closely to monitor research activities
Laurie Miller Brotman, Ph.D.	Sub-Investigator	Department of Population Health, NYU School of Medicine	227 E. 30th Street, First Floor, New York, NY 10016	646-754-4999	Laurie.Brotman@nyulangone.org	PD developer; lead PD intervention capacity building design; have access to the de-identify data.
Andrea B. Troxel, Sc.D.	Sub-Investigator	Department of Population Health, NYU School of Medicine	180 Madison Ave, New York, NY 10016	212-263-6527	Andrea.Troxel@nyulangone.org	A biostatistician; will oversee analytical models; have access to the de-identify data
Yesim Tozan, PhD	Subcontract Sub-Investigator	College of Global Public Health, NYU	411 Lafayette St. 5FL, New York	212-998-2121	Tozan@nyu.edu	A health economist will oversee cost-effective analysis; will have access to the de-identify data.
Tracy Dennis	Expert Consultant	Director of the Stress, Anxiety, and Resilience Research Center, The City University of New York	695 Park Av. New York, NY 10065	212-650-3878	Tracy.dennis@hunter.cuny.edu	Wellness intervention expert; will work with PI on T-wellness; have access to de-identify data.
Janet Nakigudde, PhD	Ugandan-Local Principal Investigator	Department of Psychiatry, Makerere University	PO Box 33842, Kampala, Uganda	+256-772-407885	Janetnakigudde@gmail.com	Will oversee Ugandan research activities, supervise research staff's work; lead qualitative data analysis.

1 Introduction, Background Information and Scientific Rationale

1.1 Background Information and Relevant Literature

Unmet Needs of Ugandan Children. Children in Uganda comprise 55% of the total population[1,2], and face enormous health and educational challenges[1,3]. More than one-quarter of Ugandan children have externalizing or internalizing mental health problems[4-6] and only 53% achieve grade-level academic competency in 6th grade[3]. The large mental health and educational gaps can be attributed to high rates of chronic poverty (38-43%)[7,8], community violence (53-58%)[8,9], cultural practice of harsh/abusive discipline at home and schools (64-84%)[4], and other health burdens (28% caregiver depression, 56-80% malaria)[8,10,11]. Adverse circumstances experienced early in life interfere with children's brain development and acquisition of adaptive self-regulation[12-21], setting the stage for poor mental health and risky behaviors in adolescence and adulthood[22-24]. Despite the emerging research suggesting the feasibility of adapting and transporting child mental health EBIs to Sub-Saharan Africa (SSA)[25-27], large scale effectiveness research with diverse populations in SSA is still lacking. Most child mental health research in SSA has focused on regional conflict or HIV/AIDS-affected children. Limited effort has been invested in developing accessible preventive child mental health services in communities, promoting population-level early childhood mental health, or understanding mechanisms to provide effective interventions[28].

Public Health Approaches to Address Mental Health of Children in LMIC Settings

Global Agenda and Strategies for Mental Health Burden Control. To address the mental health burden in LMICs, providing informal preventive services to promote population mental health has become a priority. WHO developed the *Comprehensive Mental Health Action Plan*[29] and *the Optimal Mix of Mental Health Services Pyramid* framework[30] to guide the design of mental health systems in LMICs. The *Action Plan* proposes strengthening governance, providing integrated mental health services in communities, and implementing strategies for mental health promotion. The *Service Pyramid* proposes that the majority of mental health service planning should focus on services outside the traditional healthcare delivery system and in communities because of high need and relatively low cost[29,30].

School-Based and Population-level Approaches to Preventive Interventions for Mental Health. In line with this global agenda, systems-oriented school-based prevention offers a solution for promoting child mental health at the population level. The school approach can address a wide range of individual, family, and service needs[31,32]. It has been shown to be a cost-effective approach to reduce health problems (e.g., HIV, nutrition) in LMICs[33,34]. Similarly, a large body of developmental research demonstrates that supporting teachers and families of young children has the potential to have meaningful and life-long benefits for children's health and wellbeing[35,36]. Although a school-based approach can be effective for child population health promotion[37-40], this type of preventive mental health intervention has not been widely applied in LMICs. In Uganda, 95% of children are enrolled in primary (~23% enrollment in pre-primary schools)[3,41], the majority of schools do not have mental health professionals (MHPs). To provide accessible services in schools requires systems intervention and a trained embedded workforce who can implement the EBI strategies to support children and families.

Scalable Strategies to Provide School-Based, Population-level Preventive Interventions in Low-Resource Settings*.* This effectiveness study will integrate *three strategies* that have been identified as effective for providing public health interventions at scale in low-resource settings.

A task-shifting strategy, endorsed by the WHO, offers a solution to overcome workforce barriers in schools. Task-shifting involves redistributing tasks from professionally trained workers to those with less training and fewer qualifications in the specific area of expertise[42,43]. Under the right conditions (e.g., political support, appropriate training), this approach can lead to significant public health gains[44-47]. Uganda, like many other LMICs, has few mental health workers (0.09 psychiatrists and 0.02 psychologists per 100,000 population, compared with 10-60 in developed countries)[48-50]. Ugandan schools also do not have MHPs, and teachers are not trained in mental health promotion. Therefore, redistribution of responsibilities and task-shifting of prevention knowledge and skills from MHPs to teachers/school personnel is required. A successful task-shifting of intervention involves: 1) training teachers to apply evidence-based mental health promotion strategies, including applying EBI strategies in *daily practice* during interactions with children and families and sharing knowledge and strategies with community members; and 2) engaging and providing adequate consultation and support to teachers so that they can confidently and effectively apply EBI strategies.

A system-level intervention strategy that applies an integrated scalable implementation framework, as suggested by the WHO's *Scaling Up*[51] and Chamber et al.'s *Dynamic Sustainability* frameworks[52], can address existing policy implementation gaps. Since 2007, the Ugandan government has proposed a series of reforms aimed at strengthening the country's mental health sectors[53,54]. However, these have not resulted in meaningful changes[55]. Therefore, strengthening the existing system and further developing a scalable implementation structure guided by recommended frameworks are necessary[51,56]. To establish a school-based EBI, the scalable approach must be compatible with local school ecological systems (e.g., policy, practices)[52]. The implementation structure and workforce development needs to match available local resources[51,56] and incorporate strategies to overcome a range of organizational- and system-level barriers[51].

A partnership strategy (including task-sharing and interagency collaboration)[57] relies on each partner's expertise to accomplish an overall objective[57]. Research suggests that a cross-disciplinary and cross-agency partnership strategy can be used to overcome systems barriers when existing structures do not have sufficient capacity for large-scale public health program implementation[56,58,59]. This strategy has been used to provide and sustain EBIs at scale in many countries[60-62]. In Uganda, Teacher Training Colleges (**TTCs**) are core institutions that provide in-service training for teachers. Therefore, they can be served as the key partner to provide school-based EBIs. Most TTCs (96%) are owned and funded by the government, and all TTCs are monitored and supported by the Ministry of Education(MOE)[63]. Although MOE has recommended a holistic approach to improve teacher competencies including strategies for promoting child mental health, such training is underdeveloped in the current system. The Principal Medical Officer at the Ministry of Health (MOH) is in charge of mental health services and is responsible for overseeing public education and mental health programs across the country. Most formal collaborations between the governmental agencies for mental health services and those for primary/community health have focused on adults. Because of the limited number of MHPs in the country, and the lack of child mental health training in TTCs, a formal collaboration among MOH, MOE, TTCs, and MHP training institutions has the potential to create a sustainable structure and curriculum to prepare teachers to promote child mental health[64]. ***ParentCorps-Professional Development* to Address Child Mental Health Needs in LMICs**. The EBI considered in this study is one component of *ParentCorps. ParentCorps* is a multi-component school-based intervention that promotes early childhood mental health and development; it was built on an extensive body of cross-cultural parenting and child development research[23,65-71]. *ParentCorps* includes: 1) a *Professional Development (PD)* component for teachers and school personnel, and 2) a *Family Program* for caregivers and their children. The program is aimed to increase teachers' and caregivers' child mental health knowledge and EBI strategy practices at school and home, and enhance children's social-emotional and behavioral regulation skills foundational for mental health. The *PD* and *Family Program* encourage consistent use of a set of EBI strategies by teachers and families. To achieve population-level reach and impact, *ParentCorps* is embedded in early childhood education programs as part of the normative school experience for all children served in a low-income setting. Two RCTs in the United States (US) found that *ParentCorps* resulted in a broad range of long-term benefits for low-income children, including better mental health and academic performance three years post-intervention[65,72-74]. In the US, *ParentCorps* MHPs provide *PD* to teachers and other school-based MHPs. School-based MHPs implement the *Family Program*. Because most LMICs do not have school-based MHPs, implementing *PD* and the *Family Program* with existing resources is not feasible or scalable. Given these resource limitations in LMICs and efforts to provide preventive intervention broadly in LMIC settings, we carried out *a series of investigations to* ***test one component of ParentCorps-PD as a task-shifting model of mental healthcare*** *in urban Uganda* (RCT in 10 schools; 1R21MH-097115-01A1)[27] and rural Nepal (pre-post change in 30 schools; UBS foundation). *PD* was carried out in cross-agency collaboration with MOE and MOH using appropriate localized implementation models and has reached over 300 teachers and 26,000 students in Uganda and Nepal. <u>These initial *PD* studies focused on 4 efficacy-practice-related questions</u>: 1) Can a train- the-trainer model and US-Uganda a distance capacity building approach be applied to support an implementation team in LMICs to provide *PD* with fidelity?;2) Can teachers be trained to apply EBI strategies in their daily practices and interactions with children and families as a task-shifting strategy[43]?; 3) Is the *PD* content culturally relevant for LMICs, and what adaptations need to be made to improve fit?**;** and 4) What are the estimated impacts of *PD* on child mental health? **Table 1** summarizes *ParentCorps* content, implementation models, and impact evidence (*d*=effect size) from the US and LMIC studies*.* The magnitude of impact from *PD* in LMICs was comparable to US studies of *ParentCorps* and to other teacher-focused EBI training programs (*d*=.22-.57 for child mental health)[75,76]. Collectively, these studies support the transportability of *PD* from US to LMICs and highlight the potential of *PD* alone as an effective approach to achieving population-level impact on child mental health in LMICs. Building on this strong evidence, the proposed study extends the existing partnerships with Ugandan MOE, and MOH, and further develops localized scalable structure for early childhood mental health promotion and examines *PD* effectiveness in multiple regions (both rural and urban)[51,52]. In the US, Co-I Brotman (*ParentCorps* developer) is currently partnering with the State Office of Mental Health and the Local Department of Education in scaling *ParentCorps* throughout New York City, which includes more than 1800 early childhood education sites serving 70,000 four-year-olds annually. Under this scale-up effort (launched in 2015), Brotman and colleagues (including PI Huang and Co-I Troxel) have established the research architecture and partnership processes to conduct three hybrid cRCTs (in nearly 200 schools). These studies address critical policy and practice questions including the relative value of *PD* alone versus the full

ParentCorps model when implemented at scale and in diverse settings.The proposed *PD* study in Uganda will leverage this work and benefit from and contribute to scale-up of partnerships and effectiveness-implementation knowledge both domestically and internationally.

Table 1. ParentCorps implementation models and impact evidence[27,65,72,73,77-79]

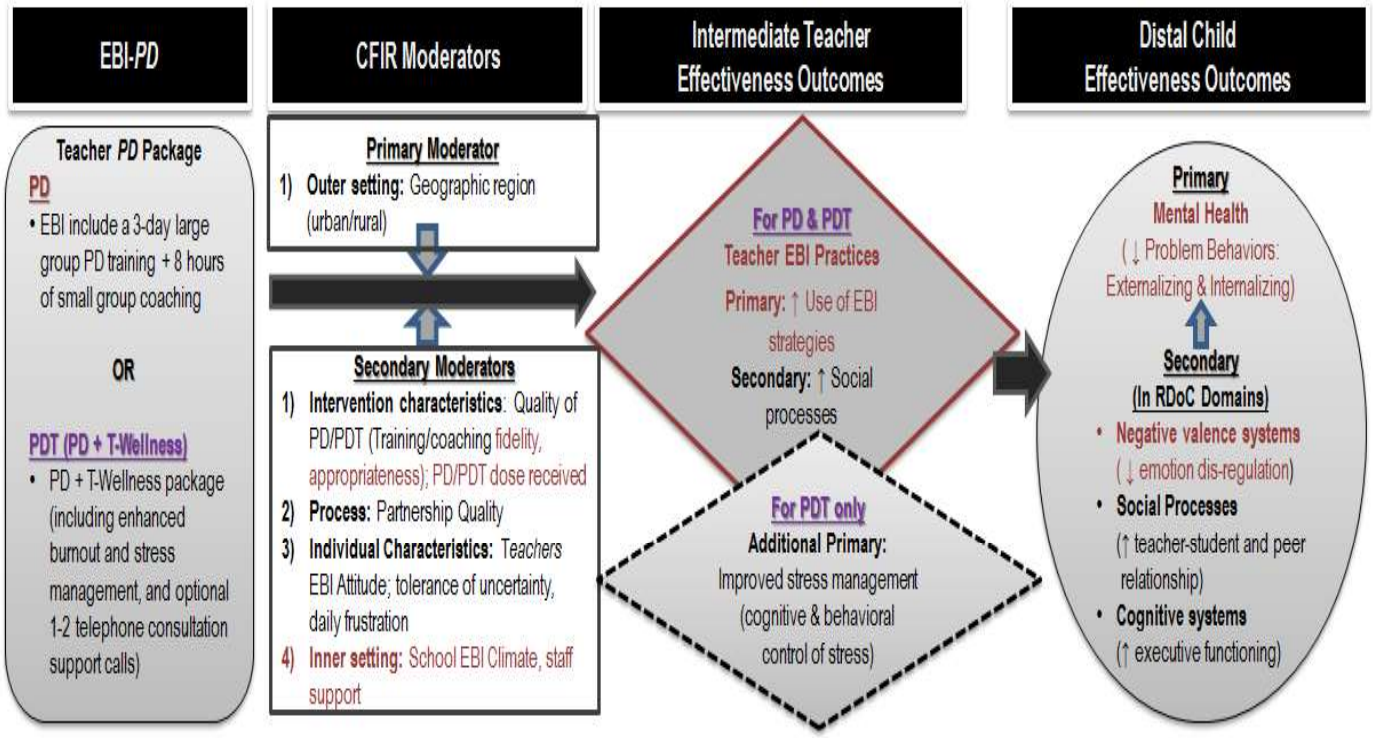
	United States (US)	LMICs- Uganda (urban) & Nepal (rural)
School-based Intervention Components	**PD** (3 days + 1:1 individual coaching) + **Family Program** (14 sessions).	**PD** (3-4 days+ a group coaching model to reduce costs and to align with value for working in groups as the "collective culture" + culturally relevant handout to facilitate discussion around EBI-strategies during parent-teacher meetings)
ParentCorps Contents	• **Core EBI strategies included in PD & Family Program**: Draw on social learning theory and cognitive & behavioral principles that target adults' knowledge, skills, and confidence in an effort to reduce or prevent child social, behavioral, and emotional problems). EBI strategies include: i) proactive behavioral management strategies; ii) social emotional promotion & regulation strategies; iii) managing misbehaviors & noncooperation; iv) school-family connection • **Other EBI strategies included in PD**: i) parent engagement strategies to strengthen school-home connection & support for students; ii) individual planning for supporting high-need students; and iii) coaching support in applying the EBI strategies.	
Implementation model	Mental health professionals (MHPs) from an academic institution and Department of Education (DOE) jointly implemented PD and Family program	**Localized Partnership Implementation Models** **Uganda (Urban)**: MHPs and psychiatric nurses implemented PD **Nepal (Rural)**: MHPs, community health workers (CHWs), and District Education Office staff implemented PD
Targets in the studies	Ethnically diverse Black, Latino & Asian children (aged 4- 6) from low-income urban communities	Ethnically diverse children (aged 3-10) from low-income families in urban Uganda and rural Nepal with diverse tribes and migration backgrounds
Impact evidence (d=effect size)	**Efficacy evidence for ParentCorps** (2 RCTs) • Teachers: EBI practices (d = .42-.85) • Children: Mental health at post and 3 years post intervention (d=.44-.56) • Parents: EBI practices (d=.16-.50)	**Efficacy evidence for PD** (immediate post intervention) **Uganda** (RCT): Teachers: EBI practice (d=.55-1.03); Children: Mental health (d=.39-1.08); and Parents: EBI practices (d=.22-.56 through knowledge sharing). **Nepal** (pre-post): Teachers: EBI practices (d=.32-.69); Children: Mental health (d=.20-.47), school functioning (d=.26-.43); Parents: EBI practices (d=.43-.79)

Additional CHW Engagement Strategies Required to Overcome the Critical Practice Barrier of Teacher Stress in LMICs. Teachers in Uganda and other LMICs are vulnerable to job burnout and stress[80]. Sources that contribute to teacher stress include ***teaching stress*** (i.e., 7 stress domains: poor school environment, student misbehavior, poor working conditions, personal concerns of teachers, relationships with parents, time pressures, and inadequacy of training[81]) and ***out-of-school stress*** (e.g., personal, family, and larger ecological environmental stress). Data from our RCT work in Uganda revealed that 79% of Ugandan teachers reported significant burden of stress (e.g., 70% workload, 41% job effectiveness, 23% emotional distress, 9% job dissatisfaction-related stress). *PD* coaching data also revealed that many Ugandan teachers asked for stress management support from *PD* coaches outside of the *PD* program. Teacher stress can result in anger, frustration, depression, exhaustion, and job ineffectiveness, and can have negative consequences for schools, teachers, students, and importantly long-term EBI effectiveness[82,83]. In planning for a large-scale EBI implementation in high-stress contexts, teacher stress must be considered. Teachers suffering from stress might be less engaged in the *PD*, have reduced motivation and ability to apply EBI strategies over time or difficulty in sustaining the added responsibility resulting from task-shifting. This effectiveness study will test an integrated evidence-based stress-management package (T-Wellness) as a complement to *PD*, and examine underlying mechanisms that teacher stress and stress management contribute to effectiveness and EBI strategy uptake and sustainment. T-Wellness will be optimized before conducting the cRCT (see Research Method below). T-Wellness is based on *Stress and Coping (an EBI)*, which has been shown to reduce stress for Ugandan adults impaired by distress in PI-Nakigudde's prior work[84,85], and *Rational-Emotive Health Education Intervention,* which has been shown to be effective in reducing teacher stress and burnout in LMICs[80,86] (described in detail below).

1.2 Rationale

This study involves efforts to advance the science of prevention in early childhood mental health in low-resource communities. We will investigate the effectiveness, practical implementation strategies, and underlying mechanisms of the *PD* in urban and rural Uganda. We will compare effectiveness of two *PD* implementation approaches (with and without T-Wellness) using a hybrid effectiveness-implementation cRCT[87]. **Figure 3** shows the conceptual model for *PD* and *PDT* Theory of change in LMIC contexts, which considers *intermediate intervention effectiveness outcomes* (teacher EBI practice) and *distal effectiveness outcomes* (including primary child mental health outcomes and secondary child behavioral outcomes, defined in Table 2). *PD* is expected to change teachers' EBI practices; and the impact of *PD* on distal child mental health outcomes will be mediated primarily through changes in teachers' practice of EBI strategies. Similarly, we expect that *PDT* (PD+T-Wellness) will also have impact on distal child mental health outcomes, and this will be mediated primarily through improvement in both teachers' EBI practices/behaviors and teachers' stress management skills (cognitive and behavioral control/ coping of stress). We anticipate *changes in child behaviors will be observed in the secondary outcome domains before the mental health outcomes* (primary distal outcomes). Because *PD/PDT* will be implemented in diverse contexts, our theory of change also considers moderators from aspects of the Consolidated Framework for Implementation Research (CFIR)[88], which proposes that five domains of contextual factors can impact effectiveness-implementation. Specifically, we expect that certain *individual, intervention implementation, and school contexts* may also influence (or moderate) intervention effectiveness [44,88-91]. We consider geographic region (urban/ rural) as the primary moderator, and other CFIR factors listed in the figure as secondary moderators. This theory of change has been partially tested (constructs in 'red' in Figure 3) and supported in previous *PD* studies[27]. This study will formally examine the cost-effectiveness and test the *PD/PTD* theory of change with a larger diverse sample and using scalable approaches. We select a foreign low-resource country as our study site because it provides an ideal setting to test how a mental health system can be strengthened through careful consideration of strategies while simultaneously examining effectiveness outcomes of an EBI. Also, Ugandan context is similar to other underserved and under-resourced communities in the US and other LMICs. Therefore, knowledge generated from our study will be relevant globally.

Figure 3. Hypothesized Mechanisms for PD & PDT impact on Teachers and Children



INNOVATION

The project is innovative in its scale, methods, scientific contribution, and structure. **1)** We have brought together a team of international experts in policy, intervention content development, large-scale program implementation, biostatistics, and health economics to launch the largest population-based early childhood mental health prevention trial in low-resource African contexts paired with a comprehensive plan to support MOH, MOE, and TTC to set up a sustainable school-based preventive mental health training and service structure. **2)** Studying effectiveness and theory of change of a population-based mental health preventive intervention in Ugandan and US context simultaneously is innovative. In partnership with public stakeholders, *PD* is currently being tested in the US context (also led by this investigation team, but with separate funding sources). The support from NIH of this *PD* scale-up effort in Uganda will provide a unique opportunity to study effectiveness as well as to compare underlying mechanisms across two countries. Lessons learned from this effectiveness and theory of change testing will inform generalizability of intervention and theory across contexts, as well as facilitate new innovations to address similar mental health disparities in countries with similar adversity and resource barriers globally. **3)** Our localized scalable implementation models (for urban and rural Uganda) and teacher task-shifting preventive service model is innovative in LMIC contexts. Our scalable approaches integrate MOH and MOE policy efforts and consider a localized multi-stakeholder task-shifting/ task-sharing collaborative approach. This approach ensures local fit and adaptability of implementation systems to support EBIs in diverse contexts. Furthremore, by training teachers to apply mental health promotion EBI strategies in daily practice, it has the potential to not only promote children's mental health, but also to strengthen school mental health systems and service (e.g., increase workforce, EBI knowledge sharing from teachers to other community members). Our approach also lays out a service model for WHO's *Action Plan and Service Pyramid* frameworks, which suggest providing accessible population-based child mental health preventive intervention in schools. **4)** Studying workforce/teacher stress management strategies and underlying mechanisms using the MOST design in the context of effectiveness RCT is innovative. Our study addresses a critical CHW workforce stress/job burden issue that has been frequently reported in LMICs. Applying the pragmatic MOST design increases reserach efficiency, provides an opportunity to further optimize EBIs, and ensures expected T-Wellness impact before conducting the cRCT. Our study contributes to new knowledge and new solutions that may overcome workforce stress, which may also maximize EBI uptake, effectiveness, and sustainability. Findings will also inform policy decisions in EBI programming and workforce development. **5)** Our design integrating multiple implementation science frameworks is innovative. We integrate several recently developed conceptual models from scale-up and implementation science[51,52,88]. This provides a new way to synthesize conceptual models that is more in line with complex real-world large-sale intervention implementation. Evidence from our research can inform new integrated frameworks to guide scaling-up research and better understand practice relevant behavioral change processes.

1.3 Potential Risks & Benefits

1.3.1 Known Potential Risks

There are no known physical risks associated with the study. However, there is the possibility that teachers, principals, PTAs, parents or students will experience some inconvenience, embarrassment, or distress while completing the interviews/questionnaires or when being observed. In addition, because teacher recruitment and intervention program implementation will be carried out in a group format (including Pre-primary to Primary 1-4 grade teachers from study schools), it is not feasible to guarantee complete confidentiality to teachers who decline to participate, as other participating teachers may notice teachers who are not present in the training. Furthermore, adult participants will be made aware of the limits to confidentiality, especially in adhering to legal status regarding reporting to child protection agencies information if study children are found to be at-risk for abuse or neglect or are being abused or neglected. To minimize these risks, we have developed plans to protect research participants through consents, preventive actions, and risk mitigation.

1.3.2 Known Potential Benefits

The training of the TTC faculty, school teachers and PTAs can strengthen local child mental health preventive service capacity. Teachers/PTAs/TTC staff who participate in PD/PDT may develop new knowledge and skills that are useful to promote their children/students' mental health. They may also benefit from the support of professionals and their colleagues. In addition, parents and children of the participated schools will benefit from their teachers. Teachers/PTAs may improve skills in promoting parent involvement and child social emotional and mental health. The minor risks of participation are considered reasonable in relation to the anticipated benefits to subjects and the knowledge that may result from this study.

2 Objectives and Purpose

Aim 1. To evaluate the short- and longer-term effectiveness of PD and PDT.
Hypotheses: (a) PD, implemented using localized scalable approaches, is more effective than control; and (b) PDT is more effective for CHWs/teachers than PD alone; and (c) PDT has a more favorable cost-effectiveness ratio than PD alone.

Aim 2. To examine effectiveness mechanisms and theory of change underlying the EBIs.
Hypotheses: the mediational mechanisms of PD (teacher EBI strategy use as a mediator between intervention and child outcomes) and PDT (teacher stress management and EBI strategy use as mediators) will be supported.

Aim 3. To examine implementation contextual factors and mechanisms that contribute to CHWs' (teachers') uptake and sustainment of EBI strategies within PD and PDT schools

2.1 Primary Objective

The primary teacher effectiveness outcomes (or intermediate effectiveness outcomes) are teachers' EBI strategy use, teacher stress management. The primary child effectiveness outcome is child mental health (externalizing and internalizing problems)

2.2 Secondary Objectives (if applicable)

The secondary child effectiveness outcomes are three behavioral-cognitive domains: emotion regulation), social relationships (student-teacher & peer relationship), and executive functioning (cognitive system function).

3 Study Design and Endpoints

3.1 Description of Study Design

Study Overview. We will study the effectiveness and mechanisms of PD/PDT in diverse Ugandan contexts. Year 1 will be the preparation period, in which we will establish localized scalable PD implementation structures in two study regions, and to optimize the T-Wellness by caring out a user-centered testing study with 4 schools (~60 teachers) (in a 4-6 month time frame in Year 1). In Years 2-4, we will carry out a cRCT to study effectiveness, cost-effectiveness, and underlying mechanisms. Drs. Troxel and Huang with expertise in RCTs and quantitative analyses will guide the effectiveness and mechanism analyses. For the cost-effectiveness comparisons, Dr. Tozan will guide the planning and analyses. Dr. Nakigudde, with expertise in stress management and qualitative studies, will guide the T-Wellness testing and qualitative analyses.

4 Study Enrollment and Withdrawal

4.1 Inclusion Criteria

In order to be eligible to participate in this study, an individual must meet all of the following criteria:

1. The inclusion criteria for the school staff (teachers, head teachers) are: they must be in the recruited study schools and teaching in Pre-Primary to Primary 4 classrooms or holding the head teachers/administration leadership position in school. The inclusion criteria for Parent Leaders are: they must be at least 18 years old and have served as a Parent-Teacher-Association member or Parent Leader in the school for at least 1 year.

2. The inclusion criteria for the PD/PDT program implementers are: they must have current employment with eligible partners (i.e., medical/mental health institutions, Teacher Training Colleges), with professional experiences in teacher training or mental health training.

3. The inclusion criteria for parents are: caregivers must be at least 18 years old, their children must be enrolled in Pre-Primary or Primary 1 to 4 classes (or between 3 to 10 years old) in the recruited schools, and willing to have their child to be assessed by research staff. Parents and children will have diverse characteristics (e.g., randomly selected from school student lists). About 10% families will be randomly selected from the student lists. The proposed study will be open to both men and women caregivers

4.2 Exclusion Criteria

An individual who meets any of the following criteria will be excluded from participation in this study:

1. Evidence of psychopathology or cognitive impairment severe enough to preclude giving consent, or completing the survey instruments or the focus group of the study.

2. Minors (age <18) will also be excluded. Additional criteria should be included as appropriate for the study design and risk.

4.3 Vulnerable Subjects

The key intervention targets for this study are teachers, and evaluate whether impacts on teachers will improve child mental health. For schools where the principal agree to participate in the PD/PDT, individual teachers will still have the right to refuse to participate at any time during the study. Research staff will ensure that the school staffs are aware of this during the consent process. To ensure that non-participating teachers are not discriminated against by principals, school personnel, or participating teachers, we have worked with MOE partners and developed several policies, which will be in place from the start of the study. One, we will apply a recruitment approach that will “normalize” the decision not to participate. Specifically, when consenting principals and teachers, we will explicitly explain that the study aims to test a new school approach to help promote students’ health and development, and that we are asking for volunteer schools and teachers to participate and provide their feedback. We will notify principals upfront that teacher participation is completely voluntary and does not reflect on the community or researchers’ views about principals’ leadership or the image of their school and teachers. We will also notify teachers that there are many reasons why some teachers may not participate, including having unique responsibilities (either personal or professional) that other teachers may not have. We will strongly urge school teachers to be respectful of others’ choices to not participate, given a range of possible circumstances. This recruitment approach will likely minimize any potential feelings of discomfort for non-participating teachers, and will minimize potential discrimination toward non-participating teachers.

Although the intervention is not directly targeted on children, and there will be indirect benefit on children (through positive changes on teachers). Because the primary effectiveness outcomes are focusing on children; therefore, we will include children as our study subjects and ask children's own perception of their behaviors and environment. We will obtain parent's permission/consent (which will be documented) and the study child's assent before conducting child assessment. The child assessment will be conducted by trained research staff, and will take about 20-30 minutes. All research staff who conduct child testing/assessment will be trained and equipped with skills to manage children distress. Research staff will also work with the targeted students' teachers to schedule appropriate time for assessments, so it will not interrupt study children's class activities or impact on their right to attend classes. If children have limited capability and cannot reasonably respond to assessment questions, research staff will stop the assessment. The intervention and child assessment are no greater than minimal risk, and the child assessments can help better understand impacts through children's own perspective. This research presents an opportunity to further the understanding children's need and impacts of prevention.

4.4 Strategies for Recruitment and Retention

The target of the intervention for this proposed project is school staff (i.e., teachers and Parent-Teacher-Association [PTA] members/Parent Leaders). The intervention is at a system-level, which is to train school staff to provide preventive intervention to students and parents. Subjects for the teacher and children's effectiveness outcomes will be reported by teachers, parents, and students. Objective observation (by trained study staff) on teachers' EBI practice in classrooms will also be conducted.

Recruitment and Referral Sources:
• Intervention Implementer/ Trainer: Drs. Huang and Nakigudde We will work with TTC and, MOE, and MOH to finalize the referral and recruitment process. Trainers will be identified and invited to participate. Participation will be completely voluntary, with no consequence for opting out of participation due to personal reasons.

• Schools: We will work with Ministry of Education (MOE) to finalize the referral and recruitment procedure. In general, public primary schools in targeted districts will be identified from governmental school lists in two study districts (urban and rural) provided by MOE. Principals of these schools will be invited to attend one of the information sessions hosted by the Ugandan intervention implementation team. During the recruitment session, principals will be provided with details of study requirements and intervention. They will have an opportunity to ask questions and also complete a questionnaire that seeks to gather information on school demographics, commitment to remain in a randomized condition, willingness to facilitate data collection, and allocate staff time to participate in the study. Eligible schools will be selected based on school leaders' and principals' expressed of interest and their agreement to allow teachers' voluntary participation. To ensure approximately similar characteristics in the intervention and control conditions, a statistician, unfamiliar with study schools, will match schools on size (i.e., number of teachers and students), location (urban/rural), and quality/performance from the eligible school list. A stratified-block randomization design will be applied. We will work with MOE to finalize a systematic approach to select the final 36 schools.

• Teachers and PTA Members: For the selected 36 schools, all pre-primary and Primary 1 to 4 teachers, serving students between 3 and 10 years old will be eligible to participate. Teachers' participation will be completely voluntary, with no consequence for opting out of participation due to personal reasons (see human subjects section for detail about teacher protection). PTA members from 24 intervention schools will be recruited to participate. For schools that do not have a PTA, Parent Leaders will be recruited. PTA members and Parent Leaders that are actively involved and have at least a year of experience in working with schools will be eligible. We will work with the intervention school to plan for recruitment and training of one PTA member from each intervention school (control schools will not have an identified PTA members). We anticipate that 540 teachers from 36 schools will participate in the evaluation study; and 360 intervention school teachers will be participated in intervention.

• Families (Parent & child pairs): Ugandan primary schools have on average about 550 students. Given the large numbers of students in schools, research staff will randomly select 10% of students and families from each school based on student lists provided by teachers (using random number generator software). Teachers will be informed of the students randomly selected for participation in the assessments and asked to introduce the study to the selected parents or primary caregivers. Targeted parents will be invited to consent for interviews, for teachers to complete ratings on their child's behavior, and for research staff to carry out objective assessments with their child.

Procedures for monitoring enrollment and tracking/retaining participants for follow-up assessments:

We have developed a procedure to ensure timely subject enrollment and data collection. Because of multiple samples (school staff & families), our monitoring and data collection procedure will occur in blocks based on sources of sample and carried out using a multiple-team-approach (a teacher/school staff data collection team, a parent-interview team, a child-assessment team, and a teacher EBI practice observation team). Designated research coordinators will be responsible for coordinating, tracking and collecting data from the school staff (head teachers, teachers, PTA) and families.

Research teams and coordinators will be trained to use a secure data tracking system to track and monitor the data tracking system on a weekly basis during enrollment or data collection periods. The monitoring will be conducted at the school level. For schools that do not meet the expected enrollment or assessment numbers will be flagged for additional actions. Research coordinators will follow up on those flagged schools to ensure they complete assessment according to the study timeline. The research coordinators will meet weekly with PIs to discuss the progress and share experience. We have applied this tracking approach in our previous studies.

Strategies for Ensuring a diverse, representative sample:

For teacher sample, all primary school teachers are eligible to participate. No one will be excluded. For families, they will be randomly selected from student lists provided by schools/teachers. Only 10% families will be selected for the evaluation study. Therefore, it is expected that our teacher and family recruitment samples will be representative.

Potential recruitment/enrollment challenges and strategies for overcoming shortfalls:

For school personnel recruitment, we anticipate that most teachers (>90%) will sign up for the study based on our prior experience. However, we anticipate some teachers will be on maternity leave, sick leave, or transferred to different schools during the study period. For those teachers, we will work with principals to determine alternative approaches to contact these teachers to gather data. A phone interview may be applied if such contact option is appropriate.

For families, we anticipate parents with low-literacy or struggling with poverty related stressors might be difficult to reach. If the situation happens, we will reach out to teachers and PTA for assistance in family recruitment and engagement. We will also applied strategies that we have learned from our previous studies, including sending home a reminder note to parent with students; calling parents; carrying out parent interview through home visits or phone calls.

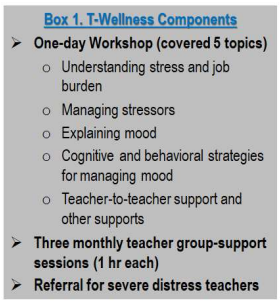
Evidence to support the feasibility of enrollment

Our research team has track record in conducting large scale studies both in the US and in Ugandan contexts. We have developed family and school engagement strategies to ensure high rate of enrollment. We have also applied a multiple-team approach (by having multiple research coordinators) and a partnership approach (partnering with research network, academic social science/public health departments, and community networks to utilize additional network strategies) to ensure target enrollment and timely data collection. Given our prior experience, we have demonstrated the feasibility of our enrollment approach

4.5 Duration of Study Participation

During Year 1, we will establish a localized scalable PD implementation team structure and train a group of PD/PDT implementers (N=8; using a TTC-MOE-Mental Health partnership structure) [51,52,57]. We will train an implementation team that includes 6 TTC trainers and 2 MHPs (i.e., clinical psychologists, senior psychiatric nurses) and additional educational stakeholders (i.e., governmental stakeholders from MOE, MOH) from the 2 regions. As with the methods that we have applied before, we will refine and formalize the partnership by using a muli-stakeholder participatory approach[60,92] and principles of effective partnership[57]. Our partnership process, meetings, field interview notes, and qualitative data will be documented and analyzed. The implementation team members will participate in the study for 4 years.

T-Wellness Package User-Centered & Optimization Study (N=60). T-Wellness Package will be based on the *Stress and Coping (SC),* a group-approach EBI that has been shown to reduce stress for Ugandan adults impaired by distress in PI-Nakigudde's prior RCT work (effect size *d*=.35)[84,85]. The *SC* focuses on understanding personal stress/adversity, and strategies for managing problems/stress, mood, strengthening social support, and staying well[84,85]. To effectively address teacher burnout, we will add additional strategies from the Rational-Emotive Health Education Intervention (REHET), which focuses on evidence-based strategies to improve cognitive-behavioral skills and techniques to help teachers manage workplace burnout stress and overcome irrational beliefs in teaching[86]. These strategies have shown to be effective in reducing teacher burnout related stress in LMICs[80,84,86]. Our T-Wellness package will optimize these two core components of the evidence-based stress and support interventions that are relevant to teacher stress and have been reported in the literature[84,93-96](see Box1 for T-Wellness contents). To ensure the expected impacts for T-Wellness, we will recruit 4 study schools and applying factorial design to test the effect of each component (1 Common Stress management; 1 Burnout Stress management; 1 Combined Common and Burnout Stress management; 1 control; with ~15 teachers in each condition). Teacher participants will participate in the study for 4-6 months. We will collect pre- and post-intervention data using a mixed-methods design to evaluate the effect of each component on stress management indicators (e.g., stress management skills, competency, burnout, general personal stress). Results will be used to optimize stress intervention components to be included in the Year 2-4 RCT). PI Nakigudde and consultant Dr. Dennis with stress management expertise will lead this effort.



Two Advisory Boards (N=10; 1 rural and 1 urban advisory board) will be established to ensure that the *PD* effectiveness-implementation study aligns with Ugandan school/health system policies and practices in communities to pave the way for a sustainability policy plan should the intervention be effective. The Board in the urban setting will include 6 representatives, including 2 Ministry stakeholders, 1 researcher, 1 NGO stakeholder, 1 teacher, and 1 parent leader. The Board in the rural setting will include 4 representatives, including 1 local-MOE leader, 1 researcher, 1 teacher, and 1 parent leader. The teacher and parent leader will be selected based on school stakeholders' recommendation. The advisory boards will meet regularly (2 times a year) throughout the 4 study years and provide guidance on programming, finding interpretation, and dissemination. Meeting notes will be documented for analyses.

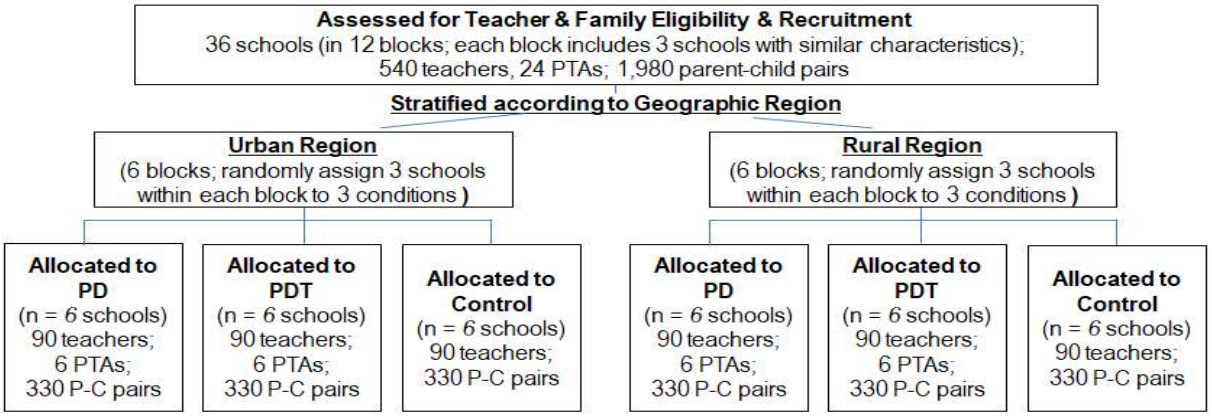
In Years 2-4, we will carry out a cluster randomized controlled trial to study effectiveness and mechanisms of intervention with 36 schools. Implementation and evaluation activities will be carried out in two-cohort sequence by recruiting school staff and families (children and their caregivers).

- *Primary school teachers and selected school leadership staff* (Head teacher, PTA leaders) will participate in the evaluation study for 2 years. Teachers (i.e., pre-primary and primary 1st to 4th grade, serving students between the ages of 3 and 10 years) and PTA leaders are the primary targets of the PD/PDT.

- *Children and caregivers* will participate in the Year 2-4 RCT evaluation study for 18 months which will include surveys/Questionnaires/Individual Interviews for the caregivers and game-like activities for children that assess childrens' attention, memory, and social emotional wellbeing.

4.6 Total Number of Participants and Sites

This study is carried out in Uganda with support from the US. Recruitment, informed consent, intervention, and evaluation of all school staff and participating families will occur in Uganda. For the PD/PDT effectiveness evaluation, participants will include 540 school staff (i.e., teachers/principals from 36 schools), 24 PTA members from intervention schools, and 8 implementers (from TTCs and mental health institutions). There will be 1980 parent-child pairs (including 1980 parents/caregivers and 1980 children). We expect that most teachers and primary caregivers/ parents will be female (75%), and equal % for children will be male and female (50% for each group). Participants numbers break down by site (rural and urban) are presented in the figure below.



4.7 Participant Withdrawal or Termination

4.7.1 Reasons for Withdrawal or Termination

Participant will be free to withdraw from participation in the study. Participants can request to discontinue participation at any time. The decision to participate or not participate, or to withdraw, will not affect participant employment and/education opportunity

4.7.2 Handling of Participant Withdrawals or Termination

To leave the study, Ugandan participants will be asked to send a written notice to Janet Nakigudde and Keng-Yen Huang, Ph.D. at the following address: (Department of Psychiatry, Makerere University, Kampala, Uganda), or email Drs. Nakigudde and Huang.

4.7.3 Premature Termination or Suspension of Study

This study may be temporarily suspended or prematurely terminated if there is sufficient reasonable cause. If the study is prematurely terminated or suspended, the PIs will promptly inform the IRB and will provide the reason(s) for the termination or suspension.

Circumstances that may warrant termination or suspension include, but are not limited to:

- Determination of unexpected, significant, or unacceptable risk to participants
- Insufficient compliance with protocol requirements
- Data that are not sufficiently complete and/or evaluable
- Determination of futility

5 Behavioral/Social Intervention

The EBI considered in this study is ParentCorps-Professional Development (PD), a school-based EBI and preventive service provision model that supports teachers and school personnel to apply EBI strategies to promote young children's mental health in impoverished areas. The PD approach represents a task-shifting model of mental healthcare by shifting mental health preventive duties from professionals to teachers to optimize school children's mental health. Therefore, teachers are considered as CHWs. Two efficacy studies of PD from our work in urban Uganda (RCT in 10 schools; 1R21MH-097115-01A1) and rural Nepal (pre-post comparison in 30 schools; UBS Foundation) demonstrate feasibility, acceptability, and positive impacts on teachers' use of EBI strategies and students' mental health. The current study builds on this work and further tests scalable PD implementation approaches and investigates PD effectiveness in multiple regions (urban and rural) in Uganda. In addition, based on previous findings that nearly 80% of Ugandan teachers (the EBI strategy users) experience occupational stress that threatens PD uptake, effectiveness, and sustainment, this study will also test a teacher stress management package (T-Wellness, adapted from EBIs) as an enhancement to PD.

The 24 schools assigned to the intervention conditions will receive PD (12 with and 12 without T-Wellness) during their 1st year of participation. In the PD group, teachers and PTAs will participate in a 3-day ParentCorps-PD training before the 1st school term. For the PDT group, one additional training day will be added for stress management). Teachers in both PD implementation conditions will also receive 8 sessions (12 hours) of face-to-face group-based coaching during the 1st and 2nd terms. Coaching sessions are to help teachers apply EBI strategies in their classrooms, engage families, and develop competencies. For the teachers in the PDT group, additional stress management group coaching activities will also be integrated into the 8 sessions (3 additional monthly 1-hr wellness sessions for teachers as a group in each school) and receive a total 15 hours of coaching.

6 Study Procedures and Schedule

6.1 Study Procedures/Evaluations/Procedures/Timeline

The three effectiveness and mechanism testing aims (Aim 1-3) will be accomplished by applying a matched-pair cRCT and hybrid effectiveness-implementation design[87,97]. A mixed methods design with qualitative and quantitative data collection will be applied. The school will be the unit of randomization because the program is applied at the school-level and builds a "school community" of teachers who promote students' mental health. The three-arm cRCT design allows us to simultaneously test *PD* effectiveness and study the added value of a package (T-Wellness) to address a critical practical task-shifting challenge (teacher stress). In addition, the Hybrid design that considers CFIR domains of implementation contexts (in Figure 1) allows us to rigorously study other EBI effectiveness-implementation mechanisms, which can further inform decisions about optimal deployment and generalized impact, and may accelerate the introduction of other valuable innovations into practice[87]. Study tasks and timeline are listed in Table 1 below.

For effectiveness, intervention theory of change (mediation mechanisms), and cost-benefit evaluations, the child and teacher effectiveness outcomes will be assessed and evaluated across 3 time points- baseline (**T1**, before PD), immediately after the PD/PTD (**T2**, about 3-4 months after T1), and 12 months later (**T3**, about 18 months after T1). Data from **multiple sources** will be collected. For child effectiveness outcomes, the primary outcome is mental health (externalizing and internalizing problems), and the secondary outcome is behavioral and cognitive domains (see Table 2 for measures). Parent and child report data will be used. Parents of target students will be interviewed by trained research staff (using English or Luganda, lasting 30-45 minutes). Child assessment will be carried out in school by research staff (lasting about 20-30 mins). For teacher effectiveness outcomes, the primary teacher outcome is EBI practice, which will be based on objective observation by an independent observation team (primary data source) and teacher-report (secondary data source). The observation measure has been validated and published in our previous trial study (see Huang KY, Nakigudde J, et al. Transportability of an Evidence-based Early Childhood Intervention in a Low-Income African Country: Results of a Cluster Randomized Controlled Implementation Study. Prevention Science. 2017;18:964-75). The secondary teacher outcome will be social process (i.e., teacher-student and teacher-family relationship), based on parent and child report. All primary outcomes and most secondary outcome measures have been used and validated in our previous Ugandan studies[77,98,99] (see Table 2 for measures and reliability information from our Ugandan studies). Costs will be measured using an activity-based micro-costing approach[100] in the intervention cluster (school), and in the extended implementation phase in all clusters from 6 through 12 months (n=36 clusters). Costs of the intervention will include all program costs incurred (for *PD/PDT* training, coaching, and materials/resources). Research costs will be excluded. Cost data collection will utilize existing standardized cost extraction forms and procedures that have been validated from Co-I Tozan's work in Uganda and LMICs[101-105]. Prior to use, these tools will be tailored and customized. **Research staff for *family and observation data* collection will be masked** to intervention conditions. To ensure masking, we will have an independent assessment team (led by a separate research coordinator), and members will not participate in any intervention activities. We will also train implementation team on protocol to prevent releasing assigned condition information. Teacher-report data collection will not be masked. The tablet and team approach of data collection that we used in our previous studies will be applied.

For study implementation moderation mechanisms, the selected key moderators from the 5 CFIR domains include target individuals' charateristics (teachers and childrend), school, and intervention implementation contexts will be studied (listed in Table 2). Most CFIR measures have been validated in our previous *PD* pilot trial[98,99]. *PD/PDT* implementation fidelity will be assessed, characterized, and examined for moderation effects (on teacher effectiveness outcomes). Four fidelity measures[106] will be considered, including *adherence* (the extent to which the TTC trainers deliver the core intervention content and as per program guidelines), *quality of program implementation* (assessed based on teacher satisfaction with the PD/PDT and ratings of TTC Coaches' competence); *engagement* (assess trainees' level of *PD* knowledge improvement from pre- to post-training[72]); and *exposure* (measured by attendance of *PD* and coaching sessions)[106].

To have a more comprehensive understanding of possible mechanisms, we also plan to conduct qualitative interviews, which will purposively select *PD* trainers (n=8), teachers (n=40; 20 from intervention and 20 from control across two sites) and our Advisory Board members, and conduct interviews at 4 time points (T1, T2, T3,

and Year 4). Interview guides will comprise semi-structured questions relating to experience with *PD/PDT*. Participants will also be asked to provide a narrative account of partnership approaches, efforts to implement *PD/PDT*, including barriers and facilitators experienced. The group interview guides will be adapted from our previous pilot *PD* implementation studies.

Table 1. Study Timeline (including recruitment and assessment timeline)

	Year 1			Year 2				Year 3				Year 4				
	2020 School Year			2021 School Year				2022 School Year				2023 School Year				
	Term 2	Term 3	Term 4	Term 1	Term 2	Term 3	Term 4	Term 1	Term 2	Term 3	Term 4	Term 1	Term 2	Term 3	Term 4	Term 1
Project oversight (Month 1-6)	X	X														
Technology-Assistant Monitoring System	X	X														
T-Wellness Optimization Study	X	X														
Training Study Team (Months 7-9)	X	X	X													
Implementing PD/PDT																
Cohort 1 (C1): 18 schools: 12 intervention (Int.) & 6 Control (Cont)				cRCT in C1 (18 schools)												
Cohort 2 (C2): 10 schools: 12 int. (6 PD, 6 PDT) & 6 Cont.								cRCT in C2 (10 schools)								
Implement T-Wellness for Control Only (after completion of effectiveness evaluation)										T-Wellness for C1				T-Wellness for C2		
Effectiveness Data Collection-School/Teacher level Cohort 1 (18 schools; 270 school staff)				C1/T1	C1/T2				C1/T3							
Cohort 2 (18 schools; 270 school staff)								C2/T1	C2/T2				C2/T3			
Family/Student level data collection Cohort 1 (18 schools; 990 families)				C1/T1	C1/ T2				C1/T3							
Cohort 2 (18 schools; 990 families)								C2/T1	C2/ T2		C2/T3		C2/T3			
T-Wellness Post Int. Assessment: *Control Schools Only (teacher & family data)*												C1/T4				C2/T4
Data Management, Analysis, Reporting				X	X	X	X	X	X	X	X	X	X	X		
Mental Health Promotion Advisory Board	X		X		X		X		X		X		X		X	X

Note. **Project oversight activities** include IRB approval, finalizing the intervention PD/PDT manual, implementation strategy tools, assessment protocols (including fidelity system/procedures), and forming Advisory Boards. Training study teams includes formalize partnership with Teacher Training Colleges (TTCs), and training implementation (TTC faculty and mental health professionals) and research teams. Term= school term. T1-T4 = Time 1-Time 4 evaluation time points. T1=baseline, T2= immediate post PD/PDT (about 3-4 months after T1); T3= 6-7 moths after T2 (or 10-11 month after T1). T4= 5-6 months after T3.

Table 2. Key Study Measures for Effectiveness-Implementation Study: Constructs and Measures

Dimensions	Constructs & Data Sources	Measures
Child Effectiveness Outcomes (T1-T3)	**a) Mental Health (Primary):** Externalizing & Internalizing **b) RDoC domains (Secondary)**: *Negative valence* (emotion disregulation), *social processes* (student-teacher & peer relatinship); *cognitive system* (executieve functioning)	**a)** Strengths & Difficulties Questionnaire (α=.63-.80)[107] (P); **b)** Emotion-regulation (α=.90)[108] (P); Relationship with Teachers (C)(α=.78)[77] & Peer relationship (P)(α=.75)[108]; Comprehensive Computerized Battery for Child Psychological Assessment (C) (for cognitive system, executive functioning)[109]
Teacher Effectiveness Outcomes (T1-T3)	**a) Teacher EBI Practice (Primary):** EBI Practices (including a range of behavior management and social emotional promotion practices (T & O); **b) Teacher Stress &Management** (Primary for PDT)(T) **c) Teacher social process (secondary)**- relationship (P)	**a)** Teacher EBI Practices: Classroom Observation (O) (α=.68-.72) [110]; PD Strategies Practice Questionnaire (T) (α=.69-.80)[77,111,112]; Determinants of Implementation Behavior Questionnaire (DIBQ)[113] **b)** Teacher Stress: Stress Questionnaire (T) [114]; Stress Management: Irrational Belief Questionnaire [80,114]; Responses to Stress Questionnaire[115,116] **c)** Family and Teacher Relationship Quality (P)[117]
Contextual Moderators (Pre/T1 and Post PD training, and during PD implementation)	**a) Outer setting: Urban/rural region** (Primary moderator) **b) Fidelity**: 4 PD/PDT measures (F, T) **c) Inner setting**: School EBI climate (e.g., work environment, team work alliance, leadership) (T); **d) Individual/Teacher characteristics** (e.g., EBI readiness/attitude; wellness) (T) **e) Intervention characteristics**: Acceptability; Appropriateness (T) **f) Processes:** Partnership Quality (e.g., TTC and teacher/PTA partnership) (T)	**b)** 4 Fidelity measures[118] (1) Adherence (F) (deliver the core content): *PD/PDT* Fidelity Checklists (completed after each training day & coaching session) (2) Quality of implementation (T) (Teacher Satisfaction (T) (post PD training and T2)(α=.72)[99] and ratings of Coaches' competence]; (3) Engagement (T) Strategy Knowledge[72] (T) (EBI knowledge gain before-after training) (test-retest r=.35-.43)[72];(4) Exposure (F): Attendance tracking[99]; **C)** School Environment Survey[119]; Organization Climate Questionnaire (α=.65-.85) [120,121]; **d)** Teacher demographic[119]; PHQ-mental health [122,123]; EBP Attitude Scale[124]; **e)**Applied Mental Health Research Dissemination and Implementation Measurements (AMHRG)[125]; **f)** Partnership Questionnaire[57,126]
Demo (T1)	Family/Student Demo (e.g., parenting, well-being) (P)	Family: Demo[127]; Parent EBI Practices (P) (α=.69-.80)[77,111,112].PHQ (α=.90) [123]
PD/PDT Cost	Program implementation costs;	Implementation costs: actual program costs (with & without monitoring cost)[128]

Note. For ***child effectiveness outcomes***, primary data source is parent-report (P); and secondary data source is child-report/testing (C). For ***teacher effectiveness outcomes,*** primary data sources is classroom observation (O) & teacher report (T); and secondary data sourc is Parent (P) report. ***CFIR contextual data*** will be gathered from from Training/coaching session tracking data from facilitator report (F) and teachers-report (T). **Suicidal behaviors** are NOT included because this study focuses on preventive intervention and young children (ages 4-10 years). The measures used in young children usually do not include suicidal items. However, parent, teacher, and child reported depressive symptoms will be included.

7 Safety and Adverse Events

The definitions below are included in the protocol as part of the template provided by the NYU School of Medicine IRB.

7.1.1 Definitions

Unanticipated Problems Involving Risk to Subjects or Others
Any incident, experience, or outcome that meets all of the following criteria:

- Unexpected in nature, severity, or frequency (i.e. not described in study-related documents such as the IRB-approved protocol or consent form, the investigators brochure, etc)
- Related or possibly related to participation in the research (i.e. possibly related means there is a reasonable possibility that the incident experience, or outcome may have been caused by the procedures involved in the research)
- Suggests that the research places subjects or others at greater risk of harm (including physical, psychological, economic, or social harm).

An ***adverse event*** (AE) is any symptom, sign, illness or experience that develops or worsens in severity during the course of the study. Intercurrent illnesses or injuries should be regarded as adverse events. results in study withdrawal

- is associated with a serious adverse event
- is associated with significant increased clinical signs or symptoms and impair functioning
- is considered by the investigator to be of clinical significance

Serious Adverse Event
Adverse events are classified as serious or non-serious. A ***serious adverse event*** is any AE that is:

- fatal
- life-threatening
- requires or prolongs hospital stay
- results in persistent or significant disability or incapacity
- an important medical event

All adverse events that do not meet any of the criteria for serious should be regarded as ***non-serious adverse events***.

Severity of Event

For AEs not included in the protocol defined grading system, the following guidelines will be used to describe severity.

- **Mild** – Events require minimal or no treatment and do not interfere with the participant's daily activities.
- **Moderate** – Events result in a low level of inconvenience or concern with the therapeutic measures. Moderate events may cause some interference with functioning.
- **Severe** – Events interrupt a participant's usual daily activity and may require systemic drug therapy or other treatment. Severe events are usually potentially life-threatening or incapacitating.}

7.1.2 Relationship to Study Intervention

All AEs will have their relationship to study intervention or study participation assessed with a level of specificity appropriate to the study design.

- ***Related*** *– The AE is known to occur with the study intervention, there is a reasonable possibility that the study intervention caused the AE, or there is a temporal relationship between the study intervention and event. Reasonable possibility means that there is evidence to suggest a causal relationship between the study intervention and the AE.*
- ***Not Related*** *– There is not a reasonable possibility that the administration of the study intervention caused the event, there is no temporal relationship between the study intervention and event onset, or an alternate etiology has been established.*

7.2 Time Period and Frequency for Event Assessment and Follow-Up

The occurrence of an AE or SAE may come to the attention of study personnel during study visits and interviews of a study participant. All AEs including local and systemic reactions not meeting the criteria for SAEs will be captured on the appropriate RF. Information to be collected includes event description, time of onset, staff's assessment of severity, relationship to study intervention (assessed only by those with the training and authority), and time of resolution/stabilization of the event. All AEs occurring while on study must be documented appropriately regardless of relationship. All AEs will be followed to adequate resolution.

The PI will record all reportable events with start dates occurring any time after informed consent is obtained until 7 (for non-serious AEs) or 30 days (for SAEs) after the last day of study participation. At each study visit, the investigator will inquire about the occurrence of AE/SAEs since the last visit. Events will be followed for outcome information until resolution or stabilization.

All unresolved adverse events should be followed by the investigator until the events are resolved, the subject is lost to follow-up, or the adverse event is otherwise explained. At the last scheduled visit, the investigator should instruct each subject to report any subsequent event(s) that the subject, or the subject's personal physician, believes might reasonably be related to participation in this study. The investigator should notify the study sponsor of any death or adverse event occurring at any time after a subject has discontinued or terminated study participation that may reasonably be related to this study.

7.2.1 Event Reporting

The Investigators will be responsible for recording and reporting adverse events and unanticipated problems, as defined by the NYU School of Medicine IRB. The Investigators will ensure that they are knowledgeable of the definitions for safety and adverse events. All adverse events occurring during the course of the study will be recorded. The current study includes surveys and interviews, and does not involve diagnostic procedures or clinical treatment. Should an adverse event occur, the event will be recorded and followed until resolution, stabilization or until it has been determined that participation in the study was not the cause of the adverse event. Serious adverse events that are ongoing at the end of the study will be followed up to determine the final outcome. All serious and unexpected adverse events (e.g., hospitalizations, life threatening events, death) or other unanticipated problems that involve risk to study participants or others and whether these appeared related to the research assessment protocols will be reported to the NYU School of Medicine IRB, the Uganda's National Science and Technology IRB, and the Chair of the DSMB. The DSMB has the authority to halt the preventive trial if it perceives that harm is occurring due to the program. Summaries of adverse events reports will be also made to Clinicaltrials.gov bi-annual update/report and NIH in the yearly progress report, unless the nature of a particular event is such that it bears reporting to NIH immediately.

7.3 Safety Oversight

DSMB: An independent group of experts that advises the study investigators. The primary responsibilities of the DSMB are to 1) periodically review and evaluate the accumulated study data for participant safety, study conduct and progress, and, when appropriate, efficacy, and 2) make recommendations concerning the continuation, modification, or termination of the trial.

We shall include the following:

- An expert in the conduct of preventive trials and all phases of intervention research (i.e., Dr. Laurie Brotman)
- Two professionals with substantive expertise in the area of child health promotion (i.e., two Ph.D. level researchers: Dr. Demy Kamboukos from the US and Dr. Nakasujja Noeline from Uganda).
- A biostatistician with expertise in prevention trials (i.e., Dr. Andrea Troxel)
- The DSMB will perform the following activities:
    - Review the research protocol and plans for data and safety monitoring.

- Evaluate the progress of the prevention program implementation, including periodic assessments of data quality and timeliness, participant recruitment, accrual and retention, participant risk versus benefit, performance of trial sites, and other factors that can affect study outcome.

- Monitors will also consider factors external to the study when interpreting the data, such as scientific or behavioral problem development that may have an impact on the safety of the participants or the ethics of the study.

- Make recommendations to the IRB and investigators concerning continuation or conclusion of the trial(s).

- Protect the confidentiality of the trial data and the results of monitoring.

The DSMB will meet with PI Huang, subcontract-PI Nakigudde and the sub-Investigators yearly to review adverse events reports and dropout rates. Data will be provided at those meetings by the investigators on key variables that may indicate harm. The DSMB biostatistician will evaluate confidentiality and integrity of the database, and the procedures for recording and storing confidential files. The DSMB will also review the elements of the plan to deal with emergencies.

8 Clinical Monitoring

In the event of a clinical emergency or other crisis, research staff and trainer/implementers (MHPs & TTC faculty) will be trained in basic crisis management. Staff will be trained in a manualized protocol for handling a variety of crises that may be presented to staff at the schools. The protocol for handling these issues addresses the safety of both study participants and study staff. The protocol also details the need for supervision in all instances. They will also notify Ugandan PI and Co-I (clinicians and researchers) or contact them by mobile phone if needed. Ugandan PI and the Clinical Research Director will oversee our program for the study schools and children. If medical attention or follow-up is needed, they will refer them to local Hospital or other health agencies. If additional medical consultation is needed regarding the adverse event, we will consult with the needed specialists or consulting services.

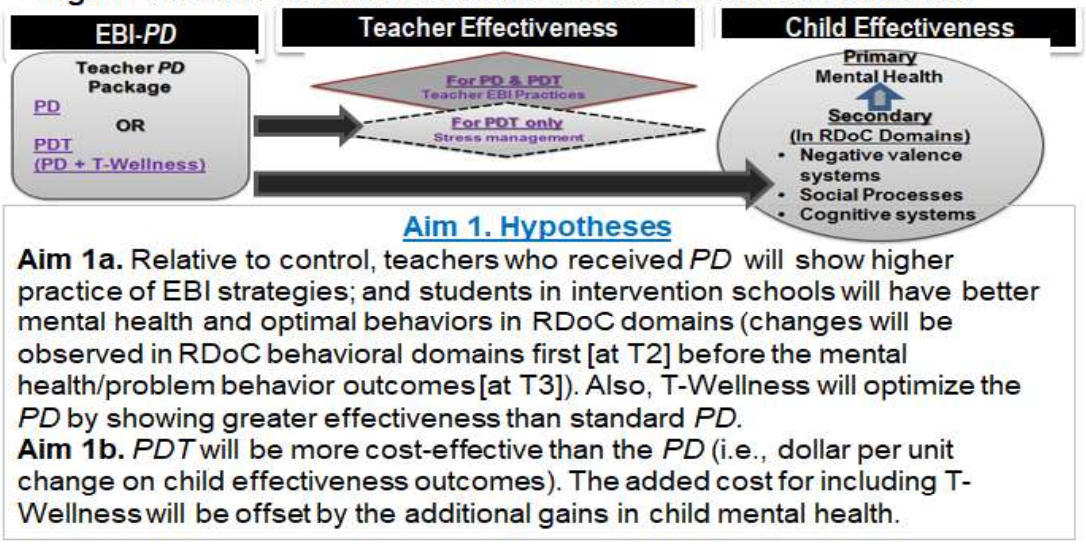
Research staff will also be available to talk individually with any participant who becomes distressed during program participation, and referrals will be made for participants as needed (e.g., teachers who expresses concern about their students' well-being).>

9 Statistical Considerations

Data Analysis Plan for Aim 1. Prior to any outcome analyses, we will generate summary statistics for all data, summarizing with means and standard deviations for continuous variables and frequencies for categorical variables. The distribution of study variables and missing data patterns will be inspected. To estimate effectiveness, we will apply intention-to-treat (ITT) analyses and first focus on between-subject comparisons of intervention vs. control (comparing *PD* to control, comparing *PDT* to control, and comparing *PD* to *PDT*). We will estimate the impact of *PD* on children and teachers post-intervention (T2, 4-5 months after T1) and at one-year follow up (T3, 18 months after T1, or 12 months after T2). **Figure 4** below describe the model to be tested under Aim 1. School and class nesting will be considered, and a multiple imputation strategy[128] will be applied to account for missing data. Linear mixed effect models[129], using SAS PROC MIXED[130], will be applied to examine short and longer-term impacts. We will first examine the immediate impact by modeling post-intervention outcomes (T2) as a function of intervention, adjusting for T1 outcome measures. The model accounts for between-subject (within-school and -class) correlation by including school- and classroom-level (when appropriate) random intercepts. The outcomes will be modeled as: $Y_{ij} = \beta_1 I_j + \beta_2 C + \beta_3 X_{ij} + \gamma_j + \gamma_k + \epsilon_{ijk}$, where Y_{ij} is the outcome for the student i in school j. I_j is intervention status (a categorical variable, with 3 levels) for school j, representing two dummy variables (control as the reference). C is the cohort indicator for

school, where *C*= 1 if is in the second cohort, 0 for the 1st cohort. X_{ij} is the baseline value of the outcome for student i in school j. In the models, β_1 represents the intervention impact, β_2 is the effect of the second cohort, β_3 is the effect of baseline measure, γ_j is the school-level random effect and γ_k is the class-level random effect (when appropriate), and $\epsilon_{ijk}$is the error term for student i in school j and *k* class. Next, we will study longer-term effectiveness outcomes (T2 to T3) by applying growth curve models and using repeated assessments over time. In these growth models, we will add time-relevant parameters to the model above, including school-level random slopes. The post-baseline scores will be modeled as a linear function of time/slopes, intervention indicator, and intervention-by-time interactions, adjusting for T1 scores and cohort. The long-term outcome will be modeled as: $Y_{ij} = \beta_1 I_j + \beta_2 t + \beta_3 I_j * t + \beta_4 C + \beta_5 X_{ij} + \gamma_j + \gamma_k + \epsilon_{ijk}$. A significant β_3 would indicate the effect of the intervention depends on time; in this case, we will estimate the slopes for each condition, and the difference between the conditions with respect to the mean outcome scores. The analytical methods that we propose have been applied successfully in our previous US and LMIC studies. Cost-effectiveness analysis of *PD* and *PDT* implementation models will be examined using approaches that have been applied in previous school-based and parenting-based child mental health promotion research[131-136]. The analysis will center on incremental cost-effectiveness ratios (ICERs), where the numerator represents the cost difference between the intervention arms and the control, and the denominator represents the difference in average intervention effects. To that end, the cost-effectiveness analysis of the intervention will involve examining how much the *PD/PDT* intervention costs to achieve a unit of effect relative to the control group. The effects of the intervention will be estimated using the effect sizes *d* (standardized mean difference between comparison groups) from an ITT approach. For the effectiveness outcomes, we will use an effect size of 0.2-0.4 as a benchmark; this corresponds to a small to medium effect size according to Cohen. We will calculate the ICERs and compute the per-participant cost per 0.2-0.4 SD change for each effectiveness outcome. Reporting of the analysis will follow the Consolidated Health Economic Evaluation Reporting Standards (CHEERS)[137].

Figure 4. Aim 1 Effectiveness and Cost-Effectiveness Mechanisms



Aim 1. Hypotheses

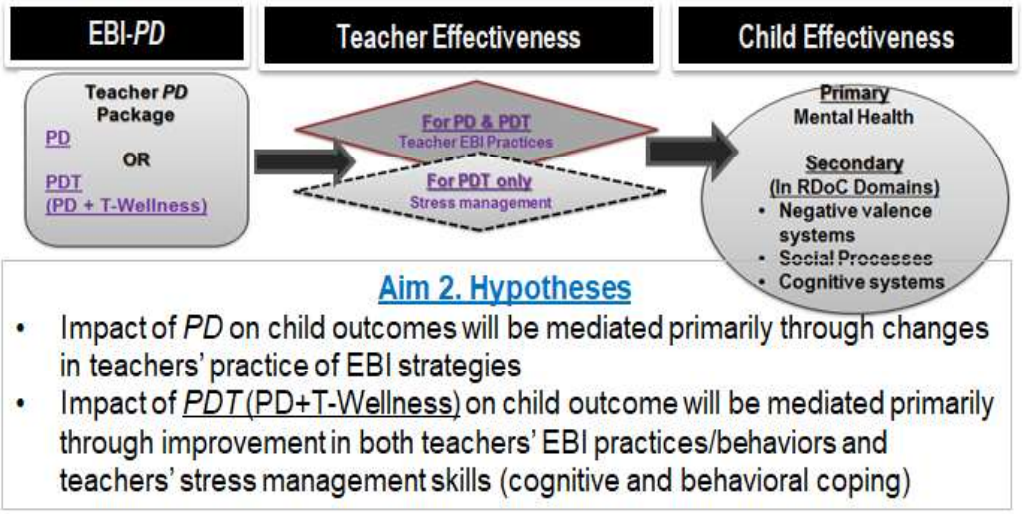
Aim 1a. Relative to control, teachers who received *PD* will show higher practice of EBI strategies; and students in intervention schools will have better mental health and optimal behaviors in RDoC domains (changes will be observed in RDoC behavioral domains first [at T2] before the mental health/problem behavior outcomes [at T3]). Also, T-Wellness will optimize the *PD* by showing greater effectiveness than standard *PD*.

Aim 1b. *PDT* will be more cost-effective than the *PD* (i.e., dollar per unit change on child effectiveness outcomes). The added cost for including T-Wellness will be offset by the additional gains in child mental health.

Data Analysis Plan for Aims 2. For testing *PD/PDT* theory of change, Preacher's Multilevel Structural Equation Modeling (SEM)[138,139] and MacKinnon's mediation model testing principles/strategies[140,141] will be applied. Figure 5 below describes the model to be tested under Aim 2. Mediators (primary and secondary) will be examined separately. Only intermediate outcomes that show significant improvement will be examined in the mediation model testing. The mediation model will build on the effectiveness evaluation model (Aim 1 model), by including changing scores of mediators (T2-T1) and T2 to T3 child outcome trajectory because a mediation model is ideally tested in a design demonstrating time precedence in which the intervention occurs before the outcome[142,143]. The mediation mechanism will be modeled as: $Y_{ij} = \beta_1 I_j + \beta_2 t + \beta_3 I_j * t + \beta_4 \boldsymbol{M_j} + \beta_5 C + \beta_6 X_{ij} + \gamma_j + \gamma_k + \epsilon_{ijk}$. M_j is the value of the mediator at T2 and/or T3 for school j. γ_j *and* γ_k are the school- and class-level random effects. We will compare β_1 and β_3 from this model with the β_1 and β_3 from the effectiveness models that are not included the moderator ($Y_{ij} = \beta_1 I_j + \beta_2 t + \beta_3 I_j * t + \beta_4 C + \beta_5 X_{ij} + \gamma_j + \gamma_k + \epsilon_{ijk}$). A significant effect of β_1 and β_3 in the mediation model will suggest a mediation effect. A conventional

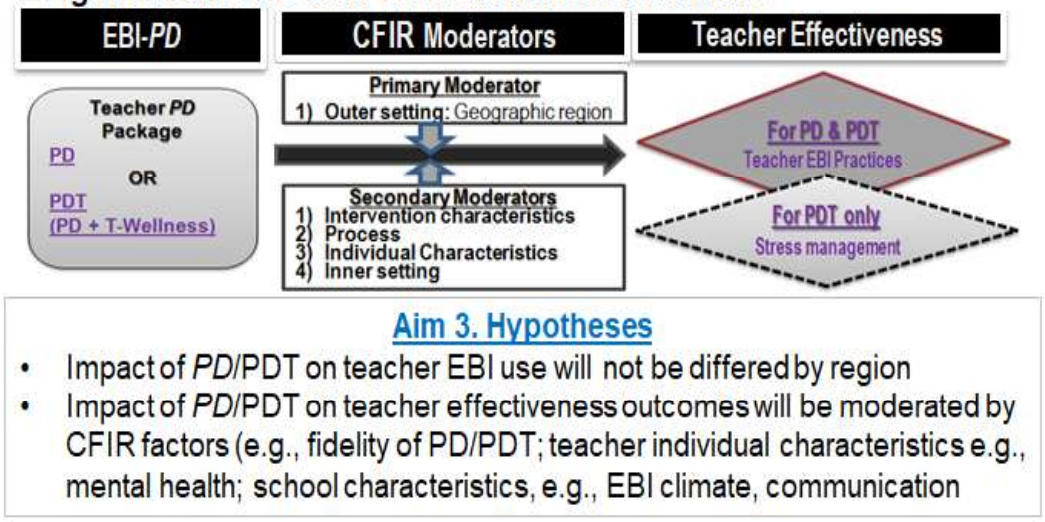
Sober test described by Baron and Kenny will be applied next to test the significance of the mediation model[144]. This modeling approach has been applied in our previous work[145,146]. To confirm the model, Multilevel SEM[138,139] will also be conducted (using Mplus[147]).

Figure 5. Aim 2 PD and PDT Mediation Mechanisms



Data Analysis Plan for Aims 3. For moderation model testing, we will apply similar approaches as in Aim 1 and add the moderator and moderator-by-intervention interaction terms in the analysis. Figure 6 below describes the model to be tested under Aim 3. For models with a significant moderator-by-intervention term on teacher effectiveness outcomes, we will then further test mediation-moderation mechanisms by expending the mediation model described above. These methods have been utilized in our previous studies[79,146,148].

Figure 6. Aim 3 PD and PDT Moderation Mechanisms



For **qualitative interview data**, we will apply qualitative analysis methods. Data from partnership meetings, partnership processes survey[126], field interviews, teacher stress survey, and observational notes will be documented and analyzed using quantitative and qualitative analytic approaches. Interview data will be transcribed and analyzed using Atlas.ti software. To better understand partnership/scalable approaches, coding will focus on themes related to the partnership development process, usefulness of partnership frameworks in formalizing processes, scalable strategies, intervention implementation barriers, teacher stress, and strategies for overcoming teacher stress and other practices (considering CFIR). These analyses will help identify facilitators and barriers for partnership and implementation for carrying out the effectiveness study. For

effectiveness-implementation mechanisms, qualitative analysis will focus on themes related to implementation barriers, facilitators, and contextual factors and processes that influence teacher intermediate and child effectiveness outcomes. Coding of qualitative data will follow a *constant comparative analysis* approach, where data are analyzed for themes that reflect project aims, which are then confirmed by further data analysis, followed by a third review of the data to identify additional themes[149-151].

10 Quality Assurance and Quality Control

QC procedures will be implemented beginning with the data entry system and data QC checks that will be run on the database will be generated. Any missing data or data anomalies will be communicated to the site(s) for clarification/resolution.

Following written SOPs, the monitors will verify that the clinical trial is conducted and data are generated, documented (recorded), and reported in compliance with the protocol, GCP, and the applicable regulatory requirements (e.g., Good Laboratory Practices (GLP), Good Manufacturing Practices (GMP)).

The investigational site will provide direct access to all trial related sites, source data/documents, and reports for the purpose of monitoring and auditing by the sponsor, and inspection by local and regulatory authorities.

11 Ethics/Protection of Human Subjects

11.1 Ethical Standard

The investigator will ensure that this study is conducted in full conformity with Regulations for the Protection of Human Subjects of Research codified in 45 CFR Part 46.

11.2 Institutional Review Board

The protocol, informed consent forms, recruitment materials, and all participant materials will be submitted to the both NYU and Makerere University (Uganda) IRB for review and approval. Approval of both the protocol and the consent forms must be obtained before any participant is enrolled. Any amendment to the protocol will require review and approval by the both NYU and Makerere University (Uganda) IRB before the changes are implemented to the study. All changes to the consent form will be IRB approved; a determination will be made regarding whether previously consented participants need to be re-consented.

11.3 Informed Consent Process will be conducted in Uganda by Uganda research Staff under PI Nakigudde supervision

Informed Consent and Assent. All procedures and forms for recruiting, obtaining consent, enrolling subjects, and collecting data will be reviewed for compliance with regulations by the NYU School of Medicine IRB, Ugandan IRBs, and NIH Clinical Trial guideline. Participation will be voluntary. Consent will be obtained in the participants' native language (English or local language Luganda). As we have done in previous studies, trained research staff will be available in the schools to present the study and answer questions during recruitment. Feedback regarding the study procedures and the effect of data collection procedures on school operations will be sought from school administrators, faculty and staff on an ongoing basis by PIs. The consent process provides an opportunity for school staff, PTAs and parents to question the research team so that they have full clarity about study procedures, their rights and confidentiality. All research participants will be inform related to posting of clinical trial information and results through ClinicalTrials.gov, and sharing de-identify trial evaluation data via the National Database for Clinical Trials related to Mental Illness (NDCT).

To consent school principals, principals from the final selected schools (16 urban and 16 rural) will be given a written consent form, which provides the names and contact information of the NYU and Ugandan investigators and IRB, a description of the study, a description of potential risks and benefits, a statement of confidentiality, and an indication of the right to refuse or withdraw at any time without any consequence. The

project PIs will review this form in detail with school principals to ensure informed consent. Principals will sign the consent forms if they agree to have their schools participate in the study.

To consent teachers, teachers from participating schools will be given a written consent form, which provides the names and contact information of the NYU and Ugandan investigators and Institutional Review Boards, a description of the study (including completing surveys, being observed in the classroom), a description of potential risks and benefits, a statement of confidentiality, and an indication of the right to refuse or withdraw at any time without any consequence. The Ugandan PI and/or research staff from Uganda will review this form in detail with teachers to ensure informed consent. Teachers who agree to participate in the study will sign the informed consent form and the observation consent forms, which will allow the research team to collect survey data, conduct live observation in their classrooms (to evaluate teachers' behavioral practices, ParentCorps strategies utilization). These data collected from multiple sources will be used for evaluation of effectiveness and quality of implementation.

For schools where the principal consents to participate in the ParentCorps-PD or PDT, individual teachers will still have the right to refuse to participate at any time during the study (as indicated in the proposal, only schools that expressed interest to participate and Principals agree to allow teacher voluntary participation will be eligible). Research staff will ensure that the school staffs are aware of this during the consent process. Because teacher training and program implementation activities will be carried out in a group format, it is not feasible to guarantee complete confidentiality to teachers who decline to participate, as other participating teachers may notice teachers who are not present in the training. To ensure that non-participating teachers are not discriminated against by principals, school personnel, or participating teachers, we have worked with MOE partners and developed several policies, which will be in place from the start of the study. One, we will apply a recruitment approach that will "normalize" the decision not to participate. Specifically, when consenting principals and teachers, we will explicitly explain that the study aims to test a new school approach to help promote students' health and development, and that we are asking for volunteer schools and teachers to participate and provide their feedback. We will notify principals upfront that teacher participation is completely voluntary and does not reflect on the community or researchers' views about principals' leadership or the image of their school and teachers. We will also notify teachers that there are many reasons why some teachers may not participate, including having unique responsibilities (either personal or professional) that other teachers may not have. We will strongly urge school teachers to be respectful of others' choices to not participate, given a range of possible circumstances. This recruitment approach will likely minimize any potential feelings of discomfort for non-participating teachers, and will minimize potential discrimination toward non-participating teachers. Two, reasons for non-participation in ParentCorps (if any) will be documented by research staff (in order to document barriers to participation) but will not be shared with any school staff. The names/identifying information of these teachers will not be attached to any document and will not be disclosed to anyone in the school or community. Three, if any teacher chooses to withdraw from the study, the PIs and Ugandan Program Trainers will help these teachers develop strategies to explain to other participating teachers reasons for their withdrawal (e.g., personal challenges), and will aim to help these teachers minimize any discomfort they may feel regarding interactions with participating teachers. Four, if a non-participating teacher ever feels any discomfort or discrimination for their non-participation, they can contact the PIs and voice their concerns, and the PIs will respond with appropriate actions (e.g., by reiterating confidentiality and non-discrimination practices to the teachers involved in trainings). Our teacher recruitment approach has been successfully applied in our previous studies both in Uganda, Nepal and in the United States.

In both principals' and teachers' consents, we will explain that individual data collected by the research team (as part of the program evaluation and monitoring) will not be shared with any school staff, including principals or other school officials. Specifically, principals and school officials will not have access to the results from assessment of individual teachers (e.g., teacher performance and competence during the PD training). The research team will only analyze and report data at the aggregate level, and will not analyze individual teacher data. Additionally, we will train our research staff and Ugandan PD trainers/implementers and ensure that they will not share individual data/ results with school personnel, teachers or anyone outside of the research team. All these steps are to ensure that teacher performance in the ParentCorps will not impact employment decisions about the participating teachers.

To consent PTA members/Parent leaders, the procedures will be similar to teacher consent. PTAs will be given a written consent form. The Ugandan PI and/or research staff from Uganda will review this form in detail with PTAs to ensure informed consent. PTAs who agree to participate in the study will sign the informed consent form and the observation consent forms, which will allow the research team to collect survey data and conduct live observation. These data collected from multiple sources will be used for evaluation of PD effectiveness and quality of implementation.

To consent parents, written or oral consent will be applied using local language (Luganda) or English, depending on parents' preference. Parents will be inform about the limitation to confidentiality, especially in adhering to legal status regarding reporting to child protection agencies if study children are found to be at-risk for abuse or neglect or are being abused or neglected. For parents who are literate, a written consent will be given, which will provide the names and contact information of the NYU and Ugandan investigators and Institutional Review Boards, a description of the study, including completing interviews (by research staff), allowing their child's teachers to provide data on their child behaviors at schools, allowing research staff to test their children, a description of potential risks and benefits, a statement of confidentiality, and an indication of the right to refuse or withdraw at any time without any consequence. The study staff will review this form in detail with parents to ensure informed consent. Parents who agree to participate in the study will sign the informed consent form. These data will be used for evaluation of PD effectiveness and quality of implementation. For parents who are illiterate or unaccustomed to dealing with forms, an oral consent will be given. Although oral consent does not require providing information on paper, the research staff are required to provide all the necessary information (describe above) to parents before obtaining their consent. For our study, we will provide an Oral Consent Card that provides the consent information in a bulleted listed to parents. Information about the names and contact information of the NYU and Ugandan investigators and Institutional Review Boards Research staff will also be provided. Research staff will document the oral consent using digital recorder and in the research staff's notes. All parents of nursery to 4th grade students in intervention schools will be informed about PD program in their child's school. As part of the universal early childhood program provided by schools, families do not need to be consented. Only those participated in research activities will be consented.

Child assents to research will be obtained from the children above age 7 of parents who consent to the study

11.4 Participant and Data Confidentiality

All procedures for recruiting subjects, obtaining consent, enrolling subjects, and collecting data will be reviewed for compliance with regulations by the IRBs of NYU School of Medicine and Makerere University (Uganda)IRBs. To ensure the protection of the rights of research participants, several aspects of the study protocol will be planned.

- All personnel and members of the study staff will complete training in human subject protection, as required. This training consists of completion of the formalized training program sponsored by the NYU School of Medicine IRB as well as ongoing training by the PI in all aspects of human subjects' protection.

- All study procedures are reviewed with staff from the perspective of ensuring the protection of the rights of study participants. This includes training of study staff in consent and enrollment procedures to minimize coercion and ensure the principles of informed consent, maintaining study material and information in order to protect study participants' privacy and confidentiality, and ensuring that assessment procedures are conducted in a manner that protects study participants' privacy and rights. In addition, NYU provides study participants with access to an independent institutional representative who can discuss with participants their rights. Subjects will be informed that they can discontinue participation in research at any time or choose not to complete a specific questionnaire or answer certain questions.

- Staff will be trained in the requirement to adhere to legal statutes regarding reporting to child protection agencies information obtained in the course of the study that leads a staff member to suspect that a child is at risk for abuse or neglect or is being abused or neglected. There is a protocol detailing the responsibility

of staff members to share information with the PIs immediately or as soon as possible after the information has been obtained. The protocol requires review of the information to determine whether a report to the protection agency is required. In the case of abuse towards the child or caregivers, we will contact the Local Council (LC) administrator for the home community of the child and caregivers. The Local Council for the community where the child and family lives is typically the best person to advise us on the necessity for police action at the district level, depending on what is an appropriate level of response for that occurrence and situation.

- All personnel working on the project will be educated about the importance of strictly respecting subjects and rights to confidentiality. Both study participants and staff will also be made aware of the limits to confidentiality. School staff, PTAs, and parents will be fully informed of these limits at the time of consent.

- All information collected from study participants during the course of the project is kept confidential. This includes information collected and stored in written and electronic form. All procedures for data collection and management have been developed to ensure the confidentiality of data collected. All data will be de-identified and presented at the group level. All responses of individual participants will be kept confidential, and will not include any identifying information. Paper copies of identifying information, assessment measures, and other study materials will be maintained in locked research files in locked offices. Electronic data are secured by server maintenance that includes password protection, limited access to data by staff, different levels of access depending on the person's specific position on the team, and server securities, which, in combination, ensure a high degree of protection from unauthorized users. Information will be coded by participant identification number. Linking of identifying information to research data will be kept to a minimum. The identity of study participants will not be revealed in presentations or publications of study findings.

- One of the risks of participating in research studies is the potential loss of confidentiality. Measures taken to minimize this risk are noted below. The risks of loss of confidentiality are minimal. During our previous studies, there were no adverse events related to loss of confidentiality. The minor risks of participation are considered reasonable in relation to the knowledge that may result from this study.

- At weekly study meetings, participant reactions to obtaining consent and evaluations will be reviewed. PIs (Drs. Huang and Nakigudde) will meet regularly with mental health professionals & implementers (from Teacher Training Colleges) to provide supervision.

- The project staff will continuously evaluate the experience of study participants and risk exposure. Trends in data and findings will be examined yearly in order to identify any changes in risk/benefit ratios that might necessitate a modification of the protocol for assessments. In the unlikely event that monitoring reveals unanticipated or negative findings, the PIs will report these findings to the field and assess what characteristics of the protocol contributed to the findings. As we have done in our previous international research, the study team will secure a Certificate of Confidentiality from the Department of Health and Human Services in order to ensure the privacy of our participants. A Certificate of Confidentiality provides protection to researchers and research institutions from being forced to provide identifying information on study participants to any federal, state or local authority. Authorization comes from NIH through section 301 (d) of the Public Health Service Act (42 U.S.C. 241 (d)) which provides the Secretary of Health and Human Services the authority to protect the privacy of study participants.

12 Data Handling and Record Keeping

All data will be managed and entered into RedCap an electronic data capture system approved by NYU, which will be secure and include password protection, limited access to data by staff and different levels of access depending on the person's position on the research team. Qualtrics will also be used when collecting data in the field through the offline mobile app function. When using Qualtrics offline mobile app no Identifying information will be collected. Qualtrics mobile app uses Transport Layer Security (TLS) encryption (also known as HTTPS) and data entered into the mobile app cannot be re-accessed in the front-end. Only selected staff

members with have access to the data in the back-end through password protected accounts. Data will be entered using only the unique study identification number. Qualtrics data will then be transfer backed into RedCap as our database management system. Implementation data of teachers will be captured through a Ugandan and Makarere IRB approved system. The system is developed and managed by the Uganda team and will use HIPAA-compliant technology (this is part of their scope of work as the subcontract). The implementation data will then be entered into Redcap by the Uganda research staff. Staff entering implementation data will not have access to research data. All final study files for analyses will be captured and finalized ensuring that no personal identifiable information (PII), including students', parents' or teachers' names, and contact information are included. Electronic data entered that include contact identifying information (e.g., master list of consenting information, contact information/address) will be securely saved, and will not be linked to the study data. There will be additional levels of protection and additional restricted access to this information.

Only the approved study staff will have access to the database and identifying information. Files with identifying information will be restricted to the Principal Investigators, Sub-Investigators and research staff with limited access depending on scope. Linking of identifying study information to research data (which will be identified only with a unique study identification number) will be kept to a minimum. The identity of study participants will not be revealed in presentations or publications of study findings.All participants will be assigned a unique study identification number. This identification number will be used to link each participant's assessment (students) and parent survey to measure change across time. School-based assessments with children and parent surveys will be completed with study staff in person or over the phone; responses to the surveys will be captured or entered electronically into an NYU approved system. School-based assessments will not include any personal identifiable information (PII), including site name and participants' names, or capture IP addresses. Parents' contact information will not be part of the study record, and only used for contact purposes. Teacher data and Implementer data will also be enter into a NYU approved system.

Consent containing any identifying information will be stored in locked cabinets separately from other data. Contact forms will not include information (such as a unique study identification number) that can link the participant to research data. For data collection purposes, a master list will be developed with the participants' names and unique study identification number. The master file linking the contact information (i.e., name) to the unique identification number will be stored securely with limited access to study staff, and stored separately from the study data, and will be used for the purposes of contacting parents for the follow-up surveys, and linking surveys over time.

12.1 Study Records Retention

Study documents will be retained for the longer of 3 years after close out or 5 years after final reporting/publication. These documents should be retained for a longer period, however, if required by local regulations. No records will be destroyed without the written consent of the sponsor, if applicable. It is the responsibility of the sponsor to inform the investigator when these documents no longer need to be retain.

12.2 Protocol Deviations

The Principal Investigators will continuously monitor the study procedures and timelines (on a weekly basis).and will identify and report deviations to the protocol, within 5 working days of the protocol deviation, or within 2 working days of the scheduled protocol-required activity. Protocol deviations will be reported to the NYU School of Medicine IRB, and the Makerere University IRB, per their guidelines. The Principal Investigators will be responsible for knowing and adhering to the IRB guidelines.

12.3 Publication and Data Sharing Policy

This study will comply with the NIH Public Access Policy, which ensures that the public has access to the published results of NIH funded research. It requires scientists to submit final peer-reviewed journal manuscripts that arise from NIH funds to the digital archive PubMed Central upon acceptance for publication.

13 Study Finances

13.1 Funding Source

This study will be funded by NIMH

13.2 Costs to the Participant

There is no cost to participant to be part of this study.

13.3 Participant Reimbursements or Payments

Because the training will be provided during non-school days and outside of the school, each teacher will receive US $50 to compensate for travel and time. For PTAs' participation in training and engaging families, a small stipend of US $30/month will be provided for the month they provide support. To increase control school motivation to participate and assist with data collection, a donation of US $400 will be provided to each school at the end of the 1st year of participation in the study. In the later 2nd year of participation (after completion of the effectiveness evaluation), control schools will receive a one-day T-Wellness workshop (without PD) and 3 monthly follow-up group-support session.

14 Study Administration

14.1 Study Leadership

The study team includes implementation research leadership teams from the US and Uganda. The leadership teams are to collaborate with Ugandan Ministry of Education (MOE) and Ministry of Health (MOH) to develop

infrastructure, and to coordinate, integrate, monitor, implement, and disseminate knowledge related to ParentCorps-Professional Development (PD) across sites. Overall, the US research-clinical team (lead by Dr. Huang) will work closely with the Ugandan Research-Policy-NGO leadership team to set-up a system to support PD implementation and evaluation. The US team will also work closely with Ugandan leadership team on research administrative activities, design, data analysis, report writing, and result dissemination. The Ugandan Research-Policy-NGO Leadership team (lead by Dr. Nakigudde) will work closely with Ugandan MOE, MOH, and AfriChild leadership and will play leadership roles in: 1) developing and training localized implementation teams in urban and rural sites that include Teacher Training College (TTC) Principals, TTC teacher trainers/PD trainers, and mental health professional (MHP)/psychiatric medical officer; 2) developing and training independent research monitoring/evaluation teams in urban and rural sites that include Research Directors, data collection Research Assistants (RAs), and independent classroom observers); 3) working with local PD implementation teams from Advisory Boards (one in Urban and one in Rural region) to facilitate regulate Advisory Board meetings (3 times a year) in order to gain guidance related to program improvement, outcome interpretation and result dissemination; 4) providing oversight for all team management and effectiveness study activities; 5) facilitating knowledge sharing and learning collaboration between urban and rural sites; and 6) collaborating with the US team on design, data analysis, report writing, and result dissemination. For Implementation and effectiveness study, two site teams with parallel structure will be established- one for urban site, and the other for rural site. For each site, there will be a PD Implementation Team that leads by the TTC Principal, and an Independent Research Evaluation Team that leads by a Research Director. The TTC Principals from each site will work with Ugandan Research-Policy-NGO leadership team to recruit and train PD trainers (including two TTC Trainers/PD implementers, and one mental health professional or senior psychiatric nurse). The Research Director from each site will work with the Ugandan leadership team to recruit and train 5 part-time RAs and 2 independent classroom observers. They will not involve in any implementation activities (to maintain blind to study conditions). Both local Implementation team and Research Team will also work with the Ugandan Leadership Team to set-up Advisory Boards and conduct regular Advisory Board meetings. The Central Leadership team will also set-up regular cross-site meetings (or conference calls) for two cross-site teams to share knowledge and research/practice strategies.

15 Conflict of Interest Policy

There is no conflict of interest.

16 References

1. UNICEF. Uganda Statistics. http://www.unicef.org/infobycountry/uganda_statistics.html. Published 2014. Accessed April, 2014.
2. Population Reference Bureau. 2009 World Population Date Sheet. Population Reference Bureau. http://www.prb.org/pdf09/09wpds_eng.pdf. Published 2009. Updated January 2011. Accessed.
3. Ministry of Education Uganda. Education and Sports Sector Fact Sheet 2002-2016. Ministry of Education and Sports. http://www.education.go.ug/files/downloads/FACT%20%20%20SHEET%202016.pdf. Published 2013. AccessedMay, 2017.
4. Huang K-Y, Gumikiriza JL, Schmidt-Sane M, Abura G, Nakigudde J. The influence of parent childhood abuse experience on parenting practice and child mental health functioning. World Psychiatry Association Regional Conference; 2014; Kampala, Uganda.
5. Belfer ML. Child and adolescent mental disorders: the magnitude of the problem across the globe. *Journal of Child Psychology and Psychiatry.* 2008;49(3):226-236.
6. Huang K-Y. Need Assessment for Children and Families in Disadvantage Neighborhoods in Kampala, Uganda In: iHUG/ NYU Child Study Center; 2010.
7. CPRC. Summary: Does chronic poverty matter in Uganda? 2005. http://www.chronicpoverty.org/uploads/publication_files/2_CPR-Uganda2005_Summary.pdf. Accessed January 2011.
8. UNICEF. Multiple Indicator Cluster Survey - Country Statistics. UNICEF. http://www.unicef.org/statistics/index_countrystats.html. Published 2014. Accessed April, 2014.
9. Koenig MA, Lutalo T, Zhao F, et al. Domestic violence in rural Uganda: evidence from a community-based study. *Bulletin of the World Health Organization.* 2003;81:53-60.
10. Brownstein JN, Bone LR, Dennison CR, Hill MN, Kim MT, Levine DM. Community Health Workers as Interventionists in the Prevention and Control of Heart Disease and Stroke. *American journal of preventive medicine.* 2005;29(5S1):128-133.
11. Huang K-Y, Abura G, Theise R, Nakigudde J. Parental depression and associations with parenting and children's physical and mental health in Sub-Saharan African settings. *Child Psychiatry and Human Development.* 2017;48:517-527.
12. Shonkoff J, Garner A, Committee on Psychosocial Aspects of Child and Family Health, Committee on Early Childhood Adoption and Dependent Care, Section on Developmental and Behavioral Pediatrics. The lifelong effects of early childhood adversity and toxic stress. *Pediatrics.* 2012;129(1):e232-e246.
13. Heckman J. The economics of inequality: The value of early childhood education. *American Educator.* 2011;Spring:31-47.
14. McClelland MM, Morrison FJ, Holmes DL. Children at risk for early academic problems: The role of learning-related social skills. *Early Childhood Research Quarterly.* 2000;15(3):307-330.
15. Moffitt T, Arseneault L, Belsky D, et al. A gradient of childhood self-control predicts health, wealth and public safety. *PNAS.* 2011;108(7):2693-2698.
16. Olds D, Kitzman H, Cole R, et al. Effects of nurse home-visiting on maternal life course and child development: Age 6 follow-up results of a randomized trial. *Pediatrics.* 2004;114(6):1550-1559.
17. Pianta R, Mashbum A, Downer B, Justice L. Effects of web-mediated professional development resources on teacher-child interactions in pre-kindergarten classrooms. *Early Childhood Research Quarterly.* 2008;23:431-451.
18. Raver C, Zigler E. Social competence: An untapped dimension in evaluating Head Start's success *Early Child Research Quarterly.* 1997;12(4):363-385.
19. Raver C, Jones S, Li-Grining C, Zhai F, Bub K, Pressler E. CSRP's impact on low-income preschooler's pre-academic skills: Self-regulation as a mediating mechanism. *Child Development.* 2011;82:362-378.
20. Rhoades B, Warren H, Domitrovich C, Greenberg M. Examining the link between preschool social-emotional competence and first grade achievement: The role of attention skills. *Early Child Research Quarterly.* 2011;26(2):182-191.
21. Brotman LM, Gouley KK, Huang K-Y, Kamboukos D, Fratto C, Pine DS. Effects of a psychosocial family-based preventive intervention on cortisol response to a social challenge in preschoolers at high risk for psychopathology. *Archives of General Psychiatric.* 2007;64(10):1172-1179.
22. Patel V, Fisher AJ, Hetrick S, McGorry P. Mental health of young people: a global public-health challenge. *Lancet.* 2007;369(9569):1302-1313.

23. Lansford JE, Dodge KA. Cultural norms for adult corporal punishment of children and societal rates of endorsement and use of violence. *Parenting: Science & Practice.* 2008;8(3):257-270.
24. Patel V, Kleinman A. Poverty and common mental disorders in developing countries. *Bulletin of the World Health Organization.* 2003;81:609-615.
25. Baumann AA, Powell BJ, Kohl PL, et al. Cultural adaptation and implementation of evidence-based parent-training: a systematic review and critique of guiding evidence. *Children and Youth Services Review.* 2015;53:113-120.
26. Gardner F, Montgomery P, Knerr W. Transporting evidence-based parenting programs for child problem behavior (age 3–10) between countries: systematic review and meta-analysis. *Journal of Clinical Child & Adolescent Psychology.* 2015;18:1-14.
27. Huang KY, Nakigudde J, Ruhule D, et al. Transportability of an Evidence-based Early Childhood Intervention in a Low-Income African Country: Results of a Cluster Randomized Controlled Implementation Study. *Prevention Science.* 2017;18:964-975.
28. Fazel M, Patel V, Thomas S, Tol W. Mental health interventions in schools in low-income and middle-income countries. *The Lancet Psychiatry.* 2014;1(5):388-398.
29. WHO. Mental Health Action Plan 2013-2020. World Health Organization. http://www.who.int/mental_health/action_plan_2013/en/. Published 2013. Accessed2015.
30. WHO. Improving Health Systems and Services for Menatl Health. 2009. http://apps.who.int/iris/bitstream/10665/44219/1/9789241598774_eng.pdf.
31. Huang K-Y, Calzada E, Cheng S, Brotman LM. Physical and mental health disparities among young children of Asian immigrants. *Journal of Pediatrics.* 2012;160:331-336.
32. United Nations Development Programme. MDGs in Uganda. UNDP. http://www.undp.or.ug/mdgs/25#. Published 2008. AccessedFeb 2011.
33. Kinsman J, Nakiyingi J, Kamali A, et al. Evaluation of a comprehensive school-based AIDS education programme in rural Masaka, Uganda. *Health Education Research* 2001;16(1):8-100.
34. Sherman J, Muehlhoff E. Developing a nutrition and health education program for primary schools in Zambia. *Journal of Nutrition Education and Behavior.* 2007;39:335-342.
35. Shonkoff J, Phillips DA. *From Neurons to Neighborhoods: The Science of Early Childhood Development.* Washington, D.C.: National Research Council and Institute of Medicine: National Academy Press; 2000.
36. Minkovitz CS, Strobino D, Mistry KB, et al. Healthy Steps for Young Children: Sustained Results at 5.5 years. *Pediatrics.* 2007;120(3):e658-e668.
37. August GJ, Realmuto, G. M., Hektner, J. M., & Bloomquist, M. L. An integrated components preventive intervention for aggressive elementary school children: The Early Risers Program. *Journal of Consulting and Clinical Psychology.* 2001;69:614-626.
38. Kellam SG, Poduska JM, Brown H, Windham A, Ialongo N. Effects of two universal interventions directed at first grade classroom behavior and achievement on the prevention of tobacco, alcohol and illicit drug use. Paper presented at: 13th Annual Meeting of the Society for Prevention Research2005; Washington, D.C.
39. Reid MJ, Webster-Stratton C, Baydar N. Halting the development of conduct problems in head start children: the effects of parent training. *Journal of Clinical Child & Adolescent Psychology.* 2004;33(2):279-291.
40. Dawson-McClure SR, Sandler IN, Wolchik SA, Millsap R. Risk as a moderator of the effects of prevention programs for children of divorce: A six-year longitudinal study. . *Journal of Abnormal Child Psychology.* 2004;32:175-190.
41. The World Bank. School Enrollement, Primary (% net). The World Bank. http://data.worldbank.org/indicator/SE.PRM.NENR. Published 2014. Accessed April, 2014.
42. PEPFAR, UNAIDS. Task shifting-Global Recommendation and Guidlines. WHO. http://data.unaids.org/pub/Manual/2007/ttr_taskshifting_en.pdf. Published 2007. Updated August 2012. Accessed.
43. WHO. Task shifting to tackle health worker shortages. World Health Organization. http://www.who.int/healthsystems/task_shifting_booklet.pdf. Published 2007. Accessed.
44. Health Resources and Services Administration (HRSA). Community Health Worker National Workforce Study. 2007.

http://bhpr.hrsa.gov/healthworkforce/supplydemand/publichealth/communityhealthworkforcebibliography.pdf.
45. WHO. Treat, train, retain. The AIDS and health workforce plan. Report on the consultation on AIDS and human resources for health. In: Geneva: WHO; 2006: http://www.who.int/hiv/pub/meetingreports/TTRmeetingreport2.pdf. Accessed 2013.
46. Mutamba BB, van Ginneken N, Paintain LS, Wandiembe S, Schellengerg D. Roles and effectiveness of lay community health workers in the prevention of mental, neurological and substance use disorders in low and middle income countries: a systematic review. *BMC health services research.* 2013;13:412.
47. Mendenhall E, De Silva MJ, Hanlon C, et al. Acceptability and feasibility of using non-specialist health workers to deliver mental health care: Stakeholder perceptions from the PRIME district sites in Ethiopia, India, Nepal, South Africa, and Uganda. *Social science & medicine.* 2014;118:33-42.
48. Kigozi F, Ssebunnya J, Kizza D, Cooper, S., Ndyanabangi S, the Mental Health and Poverty Project. An overview of Uganda's mental health care system: results from an assessment using the world health organization's assessment instrument for mental health system (WHO-AIMS). *International Journal of Mental Health System.* 2010;4(1):1-9.
49. International Institute for Legislative Affairs. Mental Health in Kenya: Unpacking the Issues. ILA. Legislative Digest Web site. http://www.unicef.org/about/annualreport/files/Uganda_COAR_2010.pdf. Published 2011. Accessed April, 2014.
50. Semrau M, Evans-Lacko S, Alem A, et al. Strengthening mental health systems in low- and middle-income countries: the Emerald programme. *BMC Med.* 2015;13:79.
51. WHO. Nine steps for developing a sacling-up strategy. 2010. https://apps.who.int/iris/bitstream/handle/10665/44432/9789241500319_eng.pdf?sequence=1.
52. Chambers DA, Glasgow RE, Stange KC. The dynamic sustainability framework: Addressing the paradox of sustainment amied ongoing change. *Implementation Science.* 2013;8.
53. Ssebunnya J, Kigozi F, Ndyanabangi S. Developing a national mental health policy: a case study from Uganda. *PLoS medicine.* 2012;9:e1001319.
54. Uganda Ministry of Health. *Child and Adolescent Mental Health Guideline* Uganda Ministry of Health;2013.
55. Ejuu G. The status of implementation of the education sector early childhood development policy in Uganda. 2012. http://www.education.go.ug/files/downloads/Early%20Childhood%20Development%20Policy%20Review.pdf. Accessed Sep 2014.
56. Iwelunmor J, Blackstone S, Veira D, et al. Toward the sustainability of health interventions implemented in sub-Saharan Africa: a systematic review and conceptual framework. *Implementation science : IS.* 2016;11:43.
57. Huang KY, Kwon SC, Cheng S, et al. Unpacking Partnership, Engagement, and Collaboration Research to Inform Implementation Strategies Development: Theoretical Frameworks and Emerging Methodologies. *Frontiers in public health.* 2018;6:190.
58. Aguirre J, Carrion VG. Integrated behavioral health services: a collaborative care model for pediatric patients in a low-income setting. *Clinical pediatrics.* 2013;52(12):1178-1180.
59. Aupont O, Doerfler L, Connor DF, Stille C, Tisminetzky M, McLaughlin TJ. A collaborative care model to improve access to pediatric mental health services. *Administration and policy in mental health.* 2013;40(4):264-273.
60. Mirzoev TN, Omar MA, Green AT, et al. Research-policy partnership- Experiences of the Mental Health and Poverty Project in Ghana, South Africa, Uganda and Zambia. *Health Research and Policy and Systems.* 2012;10:30.
61. Bower P, Gilbody S, Richards DA, Fletcher J, Sutton A. Collaborative care for depression in primary care: making sense of a coplex intervention: systematic review and meta-regression. *Brtish Journal of Psychiatry.* 2006;189:484-493.
62. Gilbody S, Bower P, Fletcher J, Richard D, Sutton A. Collaborate care for depression: a cumulative meta-analysis and review of longer-term outcomes. *ARCH INTERN Med.* 2006;166:2314-2321.
63. Uganda Ministry of Education and Sports. Teacher Edudation. Uganda, MOE. http://www.education.go.ug/data/smenu/14/Teacher%20Education.html. Published 2017. Accessed May, 2017.

64. WHO, Uganda MOH. WHO-AIMS report on mental health system in Uganda. 2006. http://www.who.int/mental_health/uganda_who_aims_report.pdf.
65. Brotman LM, Calzada E, Huang K-Y, et al. Promoting effective parenting practices and preventing conduct problems among ethnic minority families from low-income, urban communities. *Child Development.* 2011;82:258-276.
66. Calzada E, Huang K-Y, Anicama C, Fernandez Y, Brotman LM. Test of a cultural framework of parenting with Latino families of young children. *Culture Diversity and Ethnic Minority Psychology.* 2012;18:285-296.
67. Huang K-Y, Calzada E, Kamboukos D, et al. Applying public health frameworks to advance the promotion of mental health among Asian American children. *Asian American Journal of Psychology.* 2014;5:145-152.
68. Huang K-Y, Cheng S, Calzada E, Brotman LM. Symptoms of anxiety and associated risk and protective factors in young Asian American children. *Child Psychiatry & Human Development.* 2012;43:761-774.
69. Lawire M. Parenting around the world: Plus ca Change. *Journal of Family Studies Special Issue: Parenting around the world.* 2009;15(3):204-206.
70. Bradley RH, Corwyn RF. Caring for children around the world: A view from HOME. *international Journal of Behavioral Development.* 2005;29(6):468-478.
71. Greenfield PM, Suzuki LK. Culture and human development: Implications for parenting, education, pediatrics, and mental health. In: Sigel IE, Renninger KA, eds. *Handbook of Child Psychology, Vol.4.* 5 ed. NY: Wiley; 1998:1059-1107.
72. Brotman LM, Kingston S, Bat-Chava Y, Caldwell BM, Calzada E. Training school personnel to facilitate a family intervention to prevent conduct problems. *Early Education & Development.* 2008;19(4):622-642.
73. Brotman LM, Dawson-McClure S, Kamboukos D, et al. Effects of ParentCorps in pre-kindergarten on child mental health and academic performance: follow-up of a randomized clinical trial through 8 years of age. *JAMA Pediatrics.* 2016;170:1-7.
74. Dawson-McClure S, Calzada E, Huang K-Y, et al. A population-level approach to promoting healthy child development and school success in low-income, urban neighborhoods: impact on parenting and child condut problems. *Prevention Science.* 2015;16:279-290.
75. Durlak JA, Weissberg RP, Dymnicki AB, Taylor RD, Schellinger KB. The impact of enhancing students' social and emotional learning: a meta-analysis of school-based universal interventions. *Child Dev.* 2011;82(1):405-432.
76. Korpershoek H, Harms T, de Boer H, van Kuijk M, Doolaard S. A Meta-Analysis of the Effects of Classroom Management Strategies and Classroom Management Programs on Students' Academic, Behavioral, Emotional, and Motivational Outcomes. *Review of Educational Research.* 2016;86(3):643-680.
77. Huang KY, Nakigudde J, Rana H, Castillo T. Implementing an Early Childhood School-Based Mental Health Preventive Intervention in Low-Resource Schools in Nepal and Uganda NIMH/Grand Challenges Canada: Transformative Opportunities for Solving the Grand Challenges in Global Mental Health; 2017; Bethesta.
78. Huang K-Y, Nakigudde J, Rhule D, et al. Transportability of an Evidence-Based Early Childhood Intervention in a Low-Income African Country: Results of a Cluster Randomized Controlled Study. *Prevention Science.* 2017.
79. Dawson-McClure S, Calzada E, Huang K-Y, et al. A population-level approach to promoting healthy child development and school success in low-income, urban neighborhoods: impact on parenting and child condut problems. *Prevention Science.* 2014;16:279-290.
80. Ugwoke SC, Eseadi C, Onuigbo LN, et al. A rational-emotive stress management intervention for reducing job burnout and dysfunctional distress among special education teachers: An effect study. *Medicine (Baltimore).* 2018;97(17):e0475.
81. Turk DC, Meeks S, Turk LM. Factors contributing to teacher stress: implications for research, prevention, and remediation. *Behav Couns Q.* 1982;2:3-25.
82. Ugandan Ministry of Education and Sports. Teacher Issues in Uganda: a shared vision for an effective teachers policy. UNESCO. http://unesdoc.unesco.org/images/0022/002297/229777e.pdf. Published 2014. Accessed May, 2017.

83. Adriaenssens J, De Gucht V, Maes S. Causes and consequences of occupational stress in emergency nurses, a longitudinal study. *J Nurs Manag.* 2015;23(3):346-358.
84. Hemdi A, Daley D. The Effectiveness of a Psychoeducation Intervention delivered via WhatsApp for mothers of children with Autism Spectrum Disorder (ASD) in the Kingdom of Saudi Arabia: A randomized controlled trial. *Child: care, health and development.* 2017;43(6):933-941.
85. Nakigudde J, Ehnvall A, Mirembe F, Musisi S, Airaksinen E. An exploratory study on the feasibility and appropriateness of family psychoeducation for postpartum women with psychosis in Uganda. *BMC Psychiatry.* 2013;8:131.
86. Ugwoke SC, Eseadi C, Igbokwe CC, et al. Effects of a rational-emotive health education intervention on stress management and irrational beliefs among technical college teachers in Southeast Nigeria. *Medicine (Baltimore).* 2017;96(31):e7658.
87. Curran GM, Bauer M, Mittman B, Pyne JM, Stetler C. Effectiveness implementation hybrid designs: combining elements of clinical effectiveness and implementation research to enhance public health impact. *Med Care.* 2012;50(217-226).
88. Damschroder LJ, Lowery JC. Evaluation of a Large-scale weight management program using the consolidated framework for implemenation research (CFIR). *Implementation Science.* 2013;8(51):2-17.
89. Wittkowski A, Gardner PL, Bunton P, Edge D. Culturally determined risk factors for postnatal depression in Sub-Saharan Africa: a mixed method systematic review. *Journal of Affective Disorders.* 2014;163:115-124.
90. Kisia J, Nelima F, Otieno DO, et al. Factors associated with utilization of community health workers in improving access to malaria treament among children in Kenya. *Malaria Journal.* 2012;11(248):1-7.
91. Sengwana MJ, Puoane T. Knowledge, beliefs and attitudes of community health workers about hypertension in the Cape Peninsula, South Africa. *Curationis.* 2004;27(1):65-71.
92. ExpandNet. ExpandNet- Scaling Up for Health Innovations. ExpandNet/WHO. http://www.expandnet.net/. Published 2004. Accessed May, 2017.
93. Gilhooly KJ, Gilhooly ML, Sullivan MP, et al. A meta-review of stress, coping and interventions in dementia and dementia caregiving. *BMC Geriatr.* 2016;16:106.
94. Ploeg J, Markle-Reid M, Valaitis R, et al. Web-Based Interventions to Improve Mental Health, General Caregiving Outcomes, and General Health for Informal Caregivers of Adults With Chronic Conditions Living in the Community: Rapid Evidence Review. *J Med Internet Res.* 2017;19(7):e263.
95. Ploeg J, Ali MU, Markle-Reid M, et al. Caregiver-Focused, Web-Based Interventions: Systematic Review and Meta-Analysis (Part 2). *J Med Internet Res.* 2018;20(10):e11247.
96. DeHoff BA, Staten LK, Rodgers RC, Denne SC. The Role of Online Social Support in Supporting and Educating Parents of Young Children With Special Health Care Needs in the United States: A Scoping Review. *Journal of medical Internet research.* 2016;18(12):e333.
97. Glasgow RE, Lictenstein E, Marcus AC. Why don't we see more translation of health promotion research to practice? Rethinking the efficacy-to-effectiveness transition. *Am J Public Health.* 2003;93:1261-1267.
98. Huang K-Y, Abura G, Nakigudde J. The Influence of Parental Depression on Parenting and Young Children's Health and Development in Uganda. *BMC Psychiatry.* Under Review.
99. Huang KY, Nakigudde J, Calzada E, Boivin M, Ogedegbe G, Brotman LM. A Cluster Randomized Controlled Trial of an Early Childhood School-Based Mental Health Promotion Intervention in Low-Resource Ugandan Schools: Study Protocol *Trials.* Under review
100. Gold MR, Siegel JE, Russell LB, Weinstein MC. *Cost-effectiveness in Health and Medicine.* New York: Oxford University Press; 1996.
101. Opoku-Boateng YN, Kretchy IA, Aryeetey GC, et al. Economic cost and quality of life of family caregivers of schizophrenic patients attending psychiatric hospitals in Ghana. *BMC health services research.* 2017;17:697.
102. Tozan Y, Headley TY, Sewe MO, et al. A Prospective Study on the Impact and Out-of-Pocket Costs of Dengue Illness in International Travelers. *The American Journal of Tropical Medicine and Hygiene.* 2019.
103. Tozan Y, Ratanawong P, Sewe MO, Wilder-Smith A, Kittayapong P. Household costs of hospitalized dengue illness in semi-rural Thailand. *PLOS Neglected Tropical Diseases.* 2017;11:e0005961.
104. Liyanage P, Rocklöv J, Tissera H, Palihawadana P, Wilder-Smith A, Tozan Y. Evaluation of intensified dengue control measures with interrupted time series analysis in the Panadura Medical Officer of

Health division in Sri Lanka: a case study and cost-effectiveness analysis. *The Lancet Planetary Health.* 2019;3:e211-e218.
105. Thalagala N, Tissera H, Palihawadana P, et al. Costs of Dengue Control Activities and Hospitalizations in the Public Health Sector during an Epidemic Year in Urban Sri Lank. *PloS Negl Trop Dis.* 2016;10:e0004466.
106. Carroll C, Patterson M, Wood S, Booth A, Rick J, Balain S. A conceptual framework for implementation fidelity. *Implementation science : IS.* 2007;2:40.
107. Nakigudde J, Bauta B, Wolf S, Huang K-Y. Screening Child Social Emotional and Behavioral Functioning in Low-Income Country Contexts. *Jacobs Journal of Psychiatry and Behavioral Science.* 2016;2:016.
108. Gouley KK, Brotman LM, Huang K-Y, Shrout P. Construct validation of the social competence scale in preschool-age children. *Social Development.* 2007;17:380-398.
109. Fasfous AF, Peralta-Ramirez MI, Pérez-Marfil MN, Cruz-Quintana F, Catena-Martinez A, Pérez-García M. Reliability and validity of the Arabic version of the computerized Battery for Neuropsychological Evaluation of Children (BENCI). *Child Neuropsychology.* 2015;21:210-224.
110. Brotman LM. Classroom Emotional/Behavioral Climate – PIRS. In: NYU; 2008.
111. Webster-Stratton C, Reid MJ, Hammond M. Preventing conduct problems, promoting social competence: A parent and teacher training partnership in Head Start. *Journal of Clinical Child Psychology.* 2001;30:283-302.
112. NECS. User's Manual for the ECLS-K Base Year Public-Use Data Files and Electronic Codebook. The National Center for Education Statistics & Education Statistics Services Institute. http://nces.ed.gov/pubsearch/pubsinfo.asp?pubid=2001029rev. Published 2001. Accessed.
113. Huijg JM, Gebhardt WA, Dusseldorp E, et al. Measuring determinants of implementation behavior: psychometric properties of a questionnaire based on the theoretical domains framework. *Implementation science : IS.* 2014;9:33.
114. Bernard ME. Teacher beliefs and stress. *J Rat-Emo Cognitive-Behav Ther.* 2016;34:209-224.
115. Connor-Smith JK, Compas BE, Wadsworth ME, Thomsen AH, Saltzman H. Responses to stress in adolescence: Measurement of coping and involuntary stress responses. *Journal Of Consulting and Clinical Psychology.* 2000;68(6):976-992.
116. Yao S, Xiao J, Zhu X, et al. Coping and Involuntary Responses to Stress in Chinese University Students: Psychometric Properties of the Responses to Stress Questionnaire. *Journal of Personality Assessment.* 2010;92(4):356-361.
117. OPRE. Family and Provider/Teacher Relationship Quality (FPTRQ) Parent Measure. https://www.acf.hhs.gov/opre/resource/family-and-provider-teacher-relationship-quality-fptrq-parent-measure. Published 2015. Accessed.
118. Brotman LM. ParentCorps Program: A public health approach to promoting parenting and child mental health among ethnically diverse children. In: NYU Child Study Center; 2005.
119. Huang K-Y, Nakigudde J, Warugaba C, et al. Early Childhood Mental Health Promotion in Uganda: a School-Based Approach of Program Planning and Implementation. *The Bulletin of the World Health Organization.* 2014;Under review.
120. Huang K-Y, Nakigudde J, Kizza D, et al. Physical and Mental Health Needs in Primary Schools in Uganda: Implications for service planning in low resource countries. *Public Health.* 2015;Under Review.
121. Tourangeau K, Nord C, Le TN, Pollack JM, Atkins-Burnett S. *Early Childhood Longitudinal Study, Kindergarten Class of 1998-99 (ECLS-K), Combined User's Manual for the ECLS-K Fifth-Grade Data files and Electronic Codebook (NCES 2006-032).* U.S. Department of Education. Washington DC: The National Center for Education Statistics & Education Statistics Services Institute; 2006.
122. Akena D, Joska J, Obuku EA, Stein DJ. Sensitivity and specificity of clinician administered screening instruments in detecting depression among HIV-positive individuals in Uganda. *AIDS Care.* 2013;25.
123. Kroenke K, Spitzer R, Williams JB. The PHQ-9 validity of a brief depression severity measure. *Journal of General Internal Medicine.* 2001;16:606-613.
124. Aarons GA, Glisson C, Hoagwood K, Kelleher K, Landsverk J, Cafri G. Psychometric properties and U.S. National norms of the Evidence-Based Practice Attitude Scale (EBPAS). *Psychol Assess.* 2010;22(2):356-365.
125. Hamdani SU, Akhtar P, Zill EH, et al. WHO Parents Skills Training (PST) programme for children with developmental disorders and delays delivered by Family Volunteers in rural Pakistan: study protocol for

effectiveness implementation hybrid cluster randomized controlled trial. *Glob Ment Health (Camb).* 2017;4:e11.
126. Huang KY, Hoagwood K, Cheng S. Partnership Questionnaire: Implemenation Team Partners Version. In:2018.
127. Ballard T, Coates J, Swindale A, Deitchler M. Household Hunger Scale: Indicator definition and measurement guide. USAID & Fhi360. FANTA III Food and Nutrition Technical Assistance Web site. http://www.fantaproject.org/downloads/pdfs/HHS_Indicator_Guide_Aug2011.pdf. Published 2011. Accessed June, 2013.
128. McEwan PJ. Cost-effectiveness analysis of education and health interventions in developing countries. *Journal of Development Effectiveness.* 2012;4(2):189-213.
129. Diggle PJ, Heagerty P, Liang K-Y, Zeger SL. *Analysis of Longitudinal Data.* New York: Oxford University Press; 2005.
130. SAS Institute Inc. *Base SAS ® 9.3 Procedures Guide.* Cary, NC: Copyright © 2011, SAS Institute Inc.; 2011.
131. Goldstein H. *Multilevel statistical models.* 3rd ed. London: Armold; 2003.
132. Tozan Y, Albrecht J, Olaf M. Evaluation of the Affordable Medicines Facility – malaria. *The Lancet.* 2013;381:1095.
133. Tozan Y, Eili Y, Klein SD, Rajashree P, Ramanan L, Joel GB. Pre-referral rectal artesunate for treatment of severe childhood malaria: a cost-effectiveness analysis. *The Lancet* 2010;379:1910-1915.
134. Tozan Y, Joel N, James OW. Improving rural health and eliminating extreme poverty: A case study on the Millennium Villages Project." In: , (eds). . In: Blas E, Sommerfeld J, Kurup AS, eds. *Social determinants approaches to public health: from concept to practice. .* Geneva: World Health Organization 2011.
135. Tozan Y, Pitcha R, Valérie RL, Pattamaporn K, Annelies W-S. Use of insecticide-treated school uniforms for prevention of dengue in school children: A cost-effectiveness analysis. *PLoS ONE* 2014;9(e108017).
136. Breitenstein SM, Schoeny M, Risser H, Johnson T. A study protocol testing the implementation, efficacy, and cost effectiveness of the ezParent program in pediatric primary care. *Contemp Clin Trials.* 2016;50:229-237.
137. Husereau D, Drummond M, Petrou S, et al. Consolidated Health Economic Evaluation Reporting Standards (CHEERS)--explanation and elaboration: a report of the ISPOR Health Economic Evaluation Publication Guidelines Good Reporting Practices Task Force. *Value in health : the journal of the International Society for Pharmacoeconomics and Outcomes Research.* 2013;16(2):231-250.
138. Preacher KJ. Multilevel SEM strategies for evaluating mediation in three-level data. *Multivariate Behavioral Research.* 2011;46:691-731.
139. Preacher KJ, Zyphur MJ, Zhang Z. A general multilevel SEM framework for assessing multilevel mediation. *Psychological Methods.* 2010;15(3):209-233.
140. MacKinnon D, Fairchild A, Fritz M. Mediation Analysis. *Annual Review of Psychology.* 2007;58:593-614.
141. MacKinnon DP, Lockwood CM, Hoffman JM, West SG, Sheets V. A comparison of methods to test mediation and other intervening variable effects. *Psychological Methods.* 2002;7(1):83-104.
142. Cole DA, Maxwell SE. Testing mediational models with longitudinal data: Questions and tips in the use of structural equation modeling. *Journal of Abnormal Psychology.* 2003;112:558-577.
143. Kraemer HC, Wilson GT, Fairburn CG, Agras WS. Mediators and moderators of treatment effects in randomized clinical trials. *Archives of General Psychiatry.* 2002;59:877-884.
144. Baron RM, Kenny DA. The moderator-mediator variable distinction in social psychological research: conceptual, strategic and statistical considerations. *Journal of Personality and Social Psychology.* 1986;51:1173-1182.
145. Brotman LM, O'Neal CR, Huang K-Y, Gouley KK, Rosenfelt A, Shrout PE. An Experimental Test of Parenting Practices as a Mediator of Preschool Physical Aggression. . *Journal of Child Psychology and Psychiatry.* 2009;50(3):235-245.
146. O'Neal C, Brotman L, Huang KY, et al. Understanding Relations Among Early Family Environment, Cortisol Response, and Child Aggression via a Prevention Experiment. *Child Development.* 2010;81:290-305.
147. Muthén LK, Muthén BO. *Mplus user's guide (6th edition).* Los Angeles, CA: Muthen & Muthen 2010.

148. Theise R, Huang KY, Kamboukos D, et al. Parental depression, stress and support as moderators in a randomized controlled trial: impact for high-risk parents. *journal of Clinical Child & Adolescent Psychology.* 2013.
149. Glaser BG, Strauss AL. *The discovery of grounded theory: Strategies for qualitative research. .* Chicago: Aldine Publishing Co.; 1967.
150. Padgett DL. *Qualitative Methods in Social Work Research.* London, UK: Sage; 1998.
151. Padgett DK. *Qualitative and mixed methods in public health* Sage; 2012.