Study Title: Testing an Adaptive Implementation Strategy to Optimize Delivery of Obesity Prevention Practices in Early Care and Education Settings

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Background and Rationale

By the late 1960s, researchers established that most cancers were related to environmental factors.[1] Fewer than 10 years later, studies showed that diet was just as much a cause of cancer as smoking.[2] Further, excess weight is linked with higher risk of 13 cancers,[3] and the US has the highest rate of cancer attributable to body mass index (BMI).[4] Over 600,000 individuals die, and $80.2 billion are spent each year as a result of cancer in the US.[5] The National Cancer Institute recommends healthy eating and weight management for cancer prevention.[6] However, Arkansas (AR) and Louisiana (LA) are among the states in the US with the highest obesity rates, lowest quality diets, and highest cancer rates.[7] Given the limited economic resources of these states, community systems need obesity prevention efforts that optimize resources through innovative, tailored implementation. Disparate disease burden and high healthcare costs will persist without effective implementation of evidence-based interventions.

Dietary habits and weight trajectories in early life predict later health outcomes;[8,9] thus, obesity prevention efforts must target young children. Specifically, children are 5 times more likely to remain overweight or obese in adulthood if they are overweight in preschool.[10] On average, 60% of US children under age 5 (15 million children) have at least 1 non-parental childcare arrangement per week.[11] Children spend 36 hours a week in ECE settings, on average.[12] Thus, the early care and education (ECE) environment is prime for reaching young children for obesity prevention. Despite the potential for ECE to promote healthy habits, a gap exists between current practices and evidence-based practices (EBPs).[13] This gap indicates a need to "overcome barriers to the adoption, adaptation, integration, and scale-up (PA-19-274)" of research evidence in ECE. Our long-term goal is to increase EBP implementation in ECE to improve child diet and health outcomes.

Consistent with World Cancer Research Fund (WCRF) recommendations,[14] Together, We Inspire Smart Eating (WISE) aims to increase children's intake of carotenoid-rich fruits and vegetables (FV). WISE was co-developed with end users to meet the curricular and budgetary needs of the ECE context[15,16] and is included in the US Department of Agriculture SNAP-Ed toolkit.[17] Research supports each WISE EBP: (1) multiple hands-on exposures to FV support food acceptance;[18–24] (2) role modeling by educators allows children to observe a trusted adult eating FV; [25–27] (3) positive feeding practices support children's self-regulation;[27–29] and (4) mascot use associates a familiar character with FV.[30–35] Each EBP aligns with the Academy of Nutrition and Dietetics' "Benchmarks for Nutrition in Childcare."[36] Evidence also supports WISE as a whole.[37,38] Compared to usual education, WISE increased FV intake[37] (8% increase in healthy carotenoid levels; 4% decrease in unhealthy range).[38] Also consistent with WCRF guidance,[14] parents reported significantly decreased fast food and sugar-sweetened beverages intake after a year of WISE.[37,39] Thus, WISE has a positive impact in areas related to adult cancer risk.

Standard approaches to WISE implementation (training and reminders only) have resulted in challenges and suboptimal fidelity to EBPs.[40] Little research exists to guide solutions. For example, although studies have demonstrated that implementation strategies can promote policy implementation (e.g., menu offerings) and improve the

environment (e.g., access to water),[41] few studies have assisted educators to implement EBPs in ECE.[42] Further, no available studies report on implementation mechanisms in ECE[42,43] (how *and* why strategies work *for whom*) or on cost-effectiveness of implementation strategies in ECE. Thus, practitioners lack data to drive decisions on EBP implementation in ECE.

Theoretical Foundation. The integrated Promoting Action on Research Implementation in Health Services (i-PARIHS) framework posits that components of successful implementation include characteristics of the innovation (the EBPs), recipients, context, and facilitation (i.e., implementation support).[44] Successful implementation takes place when facilitation promotes the acceptance and use of an innovation based on the recipients' and context's needs. Facilitation exists along a continuum.[45] On one end, task-focused support provides technical and practical help. On the other end, holistic facilitation provides enabling support to cultivate shared meaning, connected networks, and personal development.[45] A central tenant of i-PARIHS is that successful implementation requires different levels and kinds of facilitation depending on characteristics of the innovation, the context, and recipients. The i-PARIHS framework guides our proposal in several ways. Our formative work (K01-DK110141) identified determinants of WISE EBP implementation by applying i-PARIHS. These determinants guided engagement with stakeholders to select and tailor the proposed implementation strategies. Stakeholders prioritized facilitation as a key strategy to improve WISE EBP implementation, and we will tailor facilitation to reflect recipient and contextual needs. While i-PARIHS is ideal to inform implementation strategy tailoring, research has not tested it in this way (our Aim 1). Further, i-PARIHS has received limited tests of underlying mechanisms (our Aim 2),[46–48] with most studies in health care.[49,50]

Consistent with i-PARIHS, adaptive implementation strategies reflect that a one-size-fits-all approach may not serve all settings well. [51] Not all sites may need all strategies; giving sites more than they need is expensive and wasteful. An adaptive implementation strategy provides decision points and tailoring variables to optimize resources. **Table 1** presents the design features of an adaptive implementation strategy. In sum, an adaptive implementation strategy provides a "replicable guide" for *who* gets *what* implementation support and *when*.[52]

Table 1. Adaptive Implementation Strategies Decision Rules

Design Features	Definition
Crucial decision points	Which strategies to begin the study (i.e., low intensity)
	How and when response is measured
	What strategies are given to non-responders (i.e., high intensity)
Tailoring variables	Measurement to identify non-responders and inform strategy intensity

Hypothesis *and/or* Specific Aims *or* Objectives

Our proposed project will determine the optimal implementation intensity needed to improve the uptake of WISE EBPs in ECE. The overall objectives of this project are to determine the effectiveness and cost-effectiveness of an adaptive implementation approach to improve adoption of the WISE EBPs while also examining moderators and mediators of response to the strategies. Our central hypothesis is that the addition of

high-intensity strategies at sites that do not respond to low-intensity strategies will improve implementation and health outcomes compared to the continuation of low-intensity strategies. Our long-term goal is to increase EBP implementation in the ECE setting to improve health outcomes for children. Thus, we propose the following specific aims.

<u>Specific Aim 1.</u> Determine the effectiveness of an adaptive implementation strategy that tailors the intensity of implementation support versus a low-intensity strategy.

<u>Specific Aim 2.</u> Examine moderators and mediators of implementation outcomes in a mixed-methods design.

<u>Specific Aim 3.</u> Assess the incremental cost-effectiveness of the adaptive implementation strategy.

Study Design and Procedures

We will use an enhanced non-responder trial[51] design to determine the effectiveness (Aim 1) and incremental cost-effectiveness (Aim 3) of an adaptive implementation strategy for WISE, while examining moderators and mediators of the strategy effect (Aim 2). In this trial, we will randomize sites that do not respond to low-intensity strategies to either (a) continue receiving low-intensity strategies or (b) receive high-intensity strategies (See Figure 1). This design will determine the effect of an adaptive implementation strategy that adds high intensity versus one that continues with low intensity among non-responder sites. This trial design has two key advantages. [51] First, data collection across the entire study informs identification of moderators to inform improvements to the adaptive implementation strategy guide (i.e., who needs what and when). Second, secondary analyses can consider the time course of response (i.e., whether some sites need more time with low intensity, if early responders maintain response).

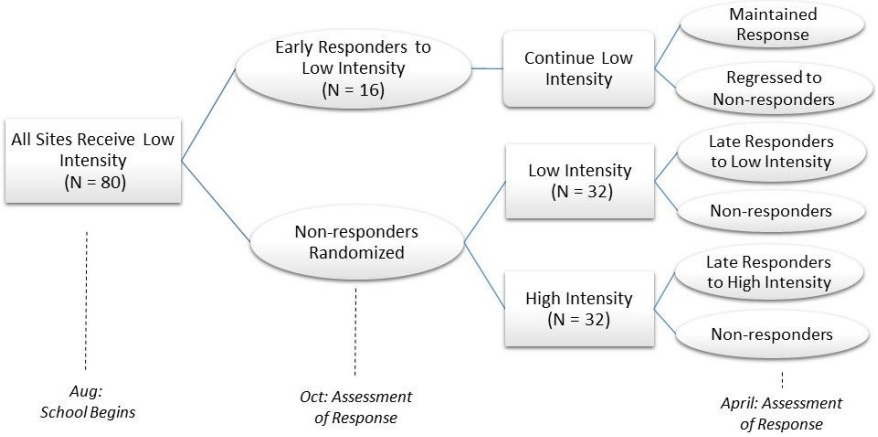

Figure 1. Cluster-Randomized Enhanced Non-Responder Trial

Study Population

Sites will be from 4 geographic regions: Central AR, AR River Valley, North Central LA, and Southeast LA. A site is one ECE location; a site may have multiple classrooms with up to 20 children per classroom. A director provides leadership at each site; educators implement WISE in their classrooms.

Site Inclusion/Exclusion Criteria: Sites within a 100-mile radius of staff offices; participating in the Child and Adult Care Food Program (CACFP) and the state's quality rating system; serving 15+ children ages 3 to 5 years; agreeing to participate in data collection; and not currently using WISE can be included. We will exclude sites unwilling to adopt WISE for all classrooms. Focusing on CACFP will maximize equitable reach, generalizability, and study impact. A focus on CACFP builds upon our prior work that documented gaps in adoption and significant barriers to EBP use in CACFP-funded sites (i.e., all USDA/K01 sites were CACFP).[53] While CACFP provides sound meal pattern guidance, this guidance has neither reliably improved educators' knowledge or practice[54] nor children's healthy food intake.[54] Further, studies demonstrate implementation of the most recent CACFP standards at fewer than 23% of CACFP sites in some states.[55] Most importantly, CACFP is a federal system that serves 3 million children per year,[56] "targeting benefits to those children most in need."[57] CACFP provides snack funds, removing the barrier of food costs for WISE implementation.

Classroom Inclusion Criteria: All classrooms at a site will receive the same implementation strategies and participate in data collection. *This reflects stakeholder input that sites would not participate unless all classrooms are treated equally*. For analyses, we will include only classrooms that are non-responders. In this way, we avoid contaminating analyses with classrooms that respond to the low-intensity strategy against the site trend. Based on our ECE experience, we expect 3 non-responding classrooms per site, on average; we have powered accordingly. Thus, we plan to include 192 total classrooms at 64 sites in our primary analyses. The early responder sites and classrooms (16 sites, 48 classrooms) will be included in exploratory analyses.

Child Inclusion Criteria: We will select one classroom at random per site to participate in collection of child outcomes (N = 64 classrooms, 15 children per classroom = 960 children total). Specifically, all classrooms at the site will be assigned a number (e.g., 1-10 at a site with 10 classrooms). Next, the biostatistician will use a random number generator to select a number. The classroom corresponding to that number will be targeted for child participation. Children will be between 3 and 5 years of age.

Relevance of Results to the Community. Community partnership is key to reduce cancer-related health disparities.[122,123] To this end, we will draw on Evidence-Based Quality Improvement (EBQI) methods, in which we are well-versed. [81,124,125] This process will develop researcher–stakeholder partnerships for joint decision making,[81,124–129] consistent with Community-Engaged Dissemination and Implementation principles.[130] Our EBQI panel will include educators, directors, and staff from ECE as well as state policy leaders who can inform WISE scale-up. For example, at least 3 professional networks could use the adaptive approach we develop: CACFP sponsors, Childcare Resource and Referral (CCR&R) agents, and USDA Cooperative Extension agents (See **LOS**). The panel will meet 3 times per year and provide input into study recruitment, roll out of study protocol, interpretation of findings, and future planning. We will also disseminate our results back to participants and stakeholders through infographic-style summaries and presentations at community events. We will pay stakeholders $50 for participation in these meetings.

Specific Aim 1. Determine the effectiveness of an adaptive implementation strategy that tailors the intensity of implementation support versus a low-intensity strategy.

Table 2. Aim 1 Measures & Data Collection Plan

Constructs	Measures	Frequency
Fidelity	WISE fidelity[64]	Oct, Jan, April of school year
Acceptability, feasibility, appropriateness of innovation *and* strategies	Weiner et al. pragmatic measures[59]	Aug, Jan, April of school year
Adoption	WISE delivery survey[40]	Monthly during implementation year
Sustainability	WISE delivery, WISE fidelity[64]	Fall of following school year
Child health outcomes	RRS,[130] BMI,[60] consumption[127]	Aug & April of school year

Table 3 presents the Aim 1 data collection plan. Measures align with Proctor's Outcomes for Implementation Research taxonomy.[58] The school year calendar informs measurement timing. **The primary outcome is fidelity to the WISE EBPs at the classroom level.** We will use the WISE fidelity observational measure.[64] The measure includes 2 to 3 items per EBP on a 1 to 4 scale to receive an average, continuous fidelity score with 4 representing the highest fidelity. For each item, values are anchored to concrete, observable behaviors. Trained and field-reliable staff blinded to the study condition will collect fidelity data consistent with published protocols.[64]

Secondary implementation outcomes are adoption as well as acceptability, feasibility, and appropriateness of WISE *and* the implementation strategies.[59] We will collect secondary outcomes through *self-report from educators* on the schedule in **Table 2.** The WISE delivery survey[40] captures the number/content of lessons delivered and material dissemination to parents. In the next school year, we will assess EBP sustainment (i.e., delivery and fidelity 12-18 months after initial implementation). All measures will be submitted to the IRB for approval before use in the study.

To measure the effect on child health outcomes, we will use Resonance Raman Spectroscopy (RRS), which measures skin carotenoid levels as a biomarker for colorful FV intake[61] with an optical hand scan.[62,63] RRS reflects intake over the prior 4 weeks and is sensitive to individual differences and experimental changes.[64,65] Trained staff will assess BMI with a standardized protocol[60] and interpret the data with 2000 CDC growth charts.[66] Finally, we will observe children's target food intake with a standardized protocol used by our team in prior studies.[127–128] We will weigh food portions (to the nearest 0.1 g) before and after observation.

Implementation Processes. First, site leadership will meet with WISE facilitators to discuss the formal commitment and implementation blueprint. Next, all staff will receive WISE training. At training, educators will receive the "reminder cutting board," showing the 4 WISE EBPs for use during lessons. Next, sites will select a "champion" to be a liaison between the site and WISE facilitator. Champions receive standardized training to navigate WISE implementation before September.

Facilitation. In the low intensity group, WISE facilitators will provide monthly task-focused facilitation targeted to site directors and champions. Facilitation in the low-

intensity group will monitor implementation, identify and solve problems related to contextual barriers, and assist with navigating structural changes needed for WISE. In the high intensity group, WISE facilitators will provide holistic, enabling facilitation tailored to the needs of the educators twice per month and more upon request. Facilitation in the high-intensity group will support educators in a one-on-one fashion, helping to set goals, fostering peer networking, developing shared vision among leaders and staff, and building meaningful relationships that support change efficacy. This will include the provision of tailored educational materials and coaching based on observed fidelity reports. Each study region will have 2 trained facilitators with experience in the ECE setting and/or WISE. Further, all facilitators will receive standard training and toolkits (e.g., sample scripts, testimonials, motivational interview examples). This is based on the Veterans Health Administration Implementation Facilitation Training,[70] which 2 study staff completed in 2019. This training has been adapted for WISE and delivery in a 4-hour session. After training, new facilitators will accompany experienced facilitators for 2 field visits to observe. The new facilitators will lead at least 2 visits with support and feedback from the experienced facilitator. Facilitators will take part in monthly reflective supervision calls led by the PI. All facilitators will log their activities (e.g., visits, calls, emails, champion contacts). The PI will compare the facilitator logs against the core implementation facilitation activities checklist for fidelity monitoring [71] and provide corrective guidance as needed.

Specific Aim 2. Examine moderators and mediators of implementation outcomes in a mixed-methods design.

We will use an explanatory, sequential mixed methods design (QUANT→qual) to provide a nuanced understanding of implementation mechanisms and contextual factors.[72,73] Quantitative analyses will test 2 moderators and 3 mediators specified a priori (See **Figure 2),** while qualitative methods will provide detail and elaborate on potential additional candidate moderators and mediators at a subset of sites of purposively selected sties based on response type.

Quantitative Procedures. During the baseline period (prior to Oct), educators at participating sites will complete assessments of potential moderators and mediators. Educators will also complete surveys mid-year and at the school year end to assess proposed mediators. We expect 2 educators per classroom to complete the survey, 6 per site on average. This follows the best practice of assessing moderators before randomization[74,75] and assessing mediators at a minimum of three points in time.[76,77] Further, our design includes key features to establish causal inference including temporality and experimental manipulation of dosages of facilitation.[78] Educator responses will reflect site experiences, and we will aggregate educator responses to the site level for analyses. Teachers will complete surveys at baseline, mid-point, and follow up. We will pay them $15 per survey ($45 total). The research team will collect these data in person with paper surveys or emailed survey links (reflecting technology access and use in ECE). We will capture data with REDCap for secure storage. All classroom staff (lead and assistants) will complete assessments; assessments will be submitted for IRB approval prior to use in the study. These measures will be compiled and

submitted for approval in the first 6 months of the study while site recruitment efforts are underway.

Moderation. Organizational culture predicts care quality in health care[79,80] and moderates response to implementation strategies.[81] Further, research by our team and others has linked early educator background with personal nutrition and EBP use,[82–85] suggesting it as a prime target for moderation of response.

Moderation Measures. Moderation measures will include The Organizational Readiness to Change Assessment (ORCA),[86] which we adapted and tested in ECE in our prior work. For this study, we will focus on the context subscale, which is consistent with our focal moderator and based on i-PARIHS. The baseline survey will also capture educator background including years of experience and type/ frequency of prior nutrition and feeding training to create a composite educator experience variable.

Mediation. Lewis et al.[87] recommend a process for examining mediators in implementation research: (1) specify implementation strategies, (2) generate strategy–-mechanism linkages, and (3) identify proximal and distal outcomes. For both the low- and high-intensity strategies, implementation facilitation provides the umbrella under which other implementation strategies are used. Thus, we will focus on mechanisms theorized to be activated by facilitation. First, we hypothesize that facilitation will decrease the perceived barriers to implementation (e.g., by helping to identify problems and solutions).[45] The presence of fewer perceived barriers has been associated with improved EBP use.[88] Second, we expect that facilitation will improve implementation climate (e.g., by developing shared meaning,[45] assisting with boundary navigation, and supporting role clarity[45,89]). Implementation climate has been associated with positive attitudes towards EBPs,[90] success in medication management implementation,[91] and improvements in evidence-based psychotherapy use.[92] Finally, we hypothesize that facilitation will improve implementation leadership and the knowledge and behaviors leaders leverage to support EBP implementation[93] (e.g., by navigating group interests, modeling empowerment, and building organizational structures[45,89]). Implementation leadership has been associated with positive attitudes toward EBPs,[90] success in medication management implementation and EBP use in acute care,[94] and implementation improvement in evidence-based psychotherapies and community mental health.[95] For steps (2) and (3), **Figure 2** presents our proposed model that links facilitation to the proposed mediators (proximal outcomes) and targeted implementation outcomes (distal outcomes).

Mediation Measures. Facilitation (e.g., dose, target) will be measured using the facilitation logs described in Aim 1; however, we will conceptualize facilitation dichotomously for analyses (high and low intensity). We will apply widely used and validated measures of proposed mechanisms, including the Implementation Climate Scale[96] and Implementation Leadership Scale,[93] recently adapted for educational settings;[97] the perceived barriers measure[53] is a checklist of challenges educators reported in our formative work and used in the K01.

Qualitative Procedures. We will use qualitative data to provide detailed understanding of response to low- and high-intensity strategies. Specifically, quantitative data from the enhanced non-responder trial will identify 5 categories of

response to implementation strategies (**Figure 1**): (1) early responders to low-intensity (by Oct), (2) late responders to low-intensity (by school year end), (3) non-responders to low-intensity, (4) responders to high-intensity, and 5) non-responders to high intensity. Through purposive site visits, we will collect qualitative data within each response type. We expect to target 3 sites per response type to reach a total sample of 15 sites (split across state and study years). We expect to reach saturation with 15 sites, but we are prepared to increase to 20 if needed to reach saturation. During site visits, the research team will conduct semi-structured, key informant interviews with directors and focus groups with educators (4 to 6 educators per Krueger[72,98]). This format is cost-effective and will allow educators to share experiences (independent of directors).[72] All participants in focus groups and interviews will receive a $25 incentive.

Table 3. Sample interview questions by i-PARIHS constructs.

Context	*What is it like to work at this center? How did that influence implementing WISE? How did your leadership get involved?*
Innovation	*Tell me about how WISE worked in your classroom.*
Recipients	*As you implemented WISE, what was most helpful to you? Least helpful?*
Facilitation	*Who was your WISE coach? How did you interact with them? What did the WISE coach do that helped? What do you wish they had done to better support you?*

Qualitative Measures. Both director interviews and educator focus groups will probe to provide an in-depth understanding of our proposed moderators and mediators while exploring additional unanticipated ones. Director interviews and educator focus groups will elicit perceived reasons why the strategies worked (or failed) at their site, practical strategies of leadership

support, and relevant factors in the implementation climate. Concepts from the i-PARIHS framework will inform interviews and focus groups guides (Table 4). Additionally, the research team will capture field notes of the site activities, processes, and interactions that may influence response to the strategies. We will submit interview guides for IRB approval prior to collection of qualitative data.

Specific Aim 3. Assess the incremental cost-effectiveness of the adaptive implementation strategy.

Cost-effectiveness analysis (CEA) constructs an incremental cost-effectiveness ratio (ICER) to estimate the marginal difference in costs and effectiveness of 2 implementation strategies. We will use CEA to estimate the incremental differences seen with continuing low-intensity strategies versus augmenting with high-intensity strategies on costs and (a) fidelity and (b) child health outcomes.

Measures. We will calculate implementation strategy costs based on time and travel data in the facilitation log and known material purchase costs. Based on work by Ritchie et al.,[99] facilitators will log all activities and travel time using REDCap, which was tested and found feasible in our prior work.

Risks and Benefits

Minimal risk is anticipated. However, the following possible risks have been identified:

1. Discomfort: The open-ended interviews and surveys with educators may include questions that some teachers may experience discomfort in answering.

2. Confidentiality: Classroom observations will record behaviors specific to each teacher. Disclosure of this information could be damaging to the teachers, both personally and professionally. Further, a risk to study participants is the potential for loss of confidentiality of study data.

3. Parents may prefer that their child not participate in RRS, BMI, and child consumption assessments.

Protection Against Risk

1. Discomfort: Teachers may choose not to answer survey questions or to stop interviews at any time. Directors will also be assured they can withdraw participation at any time. We do not expect the questions to elicit a strong emotional response.

2. Confidentiality: Each center will be informed of the private nature of the teacher surveys/interviews and classroom observations and that these records will not be accessible by their agency. The audio and transcription files will be deidentified and stored electronically on a secured server. Physical copies of the interviews and interview notes will be stored in locked filing cabinets in an office suite. Interviews and observations will be tracked with neutral identification numbers, never including teacher names, addresses, or birthdates.

3. No child will be included in study activities if a parent has indicated they do not want their child to participate.

There may be some indirect benefit to participants taking part in this study. As early care and education programs learn more about effective practices for obesity prevention through the findings of this project, they may provide better training opportunities and support for teachers. Additionally, educators in prior studies have reported WISE training and food experiences as beneficial to their personal health. Stakeholders have reported service on EBQI panels as highly rewarding as well. It is also possible that participants will experience no direct benefit as a result of participation. However, the potential benefit to others outside the research study is great. Development and evaluation of implementation strategies to support obesity prevention will provide critical knowledge on the value of investments in adding implementation support strategies to existing obesity prevention interventions. Specifically, this study will give information about what level of implementation support is likely to be beneficial and for whom. Further, we believe that information gained will contribute to future uptake and sustainability of environmental interventions to improve diet of children.

The Data Safety and Monitoring board will assess the balance or risks and benefits throughout the study period (See Appendix A).

Data Handling and Recordkeeping

For all quantitative data, we will use REDCap software to securely collect and store all survey data. We will also use RedCap software for quantitative assessments at site visits because REDCap has offline secure storage capacity. For these observations, data collectors will observe teachers in the classroom to complete ratings of feeding practices. All quantitative data will be transferred into SPSS, a statistical processing software. In-depth interviews and focus groups (Aim 2) will be audio-recorded and transcribed and imported into Nvivo for analyses. All data will be paired with a neutral identification number. This information will only be accessible to the PI and research assistant. Names will be removed from all files after the follow-up data collection.

BMI data will be captured using paper data forms and then entered into SPSS. Resonance Raman Spectroscopy information is captured by the device computer and sent to a secure server. All data will be paired with a neutral identification number. The same process will be followed for child consumption observations. Containers will be labeled and weights recorded alongside a neutral identification number. A key file linking ID numbers with participant names will only be kept between pre and post assessments to be able to link participants across time. This information will only be accessible to the PI, LA Site lead, and site Project managers.

The Principal Investigator will carefully monitor study procedures to protect the safety of research subjects, the quality of the data and the integrity of the study. All study staff will be certified in human subjects research. All study subject material Information obtained will be summarized without identification. Participants will have no identifying information linked with their responses. Study documentation will be kept in a locked file in the principal investigator's office, if hardcopy, or on a password-protected server. We will destroy identifiers and contact of study participants after final data collection and analysis are complete and results of the project shared with participants. We expect this to take up to 7 years.

Multisite Research

The University of Arkansas for Medical Sciences (UAMS) will serve as the single IRB for this study for all participating sites, including Louisiana Tech University and the University of Colorado. The UAMS IRB is registered with the federal Office for Human Research Protections per 45 CFR 46 Part E. The UAMS IRB has the professional competence necessary to review the proposed research. Louisiana Tech University (LA Tech) and the University of Colorado Anschutz Medical Campus have expressed their willingness to rely upon the review of a single IRB of Record for this study. The Anschutz Medical Campusand UAMS are already participants in the SMART IRB agreement (NIH's National Center for Advancing Translational Sciences [NCATS] Streamlined, Multi-site, Accelerated Resource for Trials [SMART] IRB Reliance Platform). LA Tech will use the UAMS reliance agreement to cede IRB oversight.

The UAMS PI (Swindle) will:

- Coordinate communication between sites
- Request and receive information and documentation from sites

- Develop template materials for review by the UAMS IRB and for limited modification by relying sites
- Submit materials from all sites to the UAMS IRB and coordinate responses to any IRB queries
- Provide documentation to relying sites

Relying sites will follow local procedures to coordinate, collect, and verify information such as:

- Site variations in areas such as recruiting, informed consent, HIPAA, populations
- Conflict of interest disclosure and management
- Completion of ancillary reviews
- Training and qualifications of study team
- Continuing review or closure information
- Reportable events

Relying sites will provide necessary information or assurances to the UAMS study team for submission to the UAMS IRB. The UAMS IRB office will communicate directly with the UAMS study team as the proxy for all relying sites. Relying sites will follow their local procedures for dissemination of information and documentation.

UAMS will maintain records of the authorization/reliance agreements and of the communication plan.

Data Analysis

We will use SPSS Statistics v25 (IBM) for Aim 1 analyses. Analysts will examine data for missing values, extreme scores, and variable distributions. We expect missing values on the primary outcome to be minimal because study staff will collect these data. If the missing values percentage exceeds 5%,[101] we will use a multiple imputation approach for analyses. For our primary analysis, we will use linear mixed-effects regression models[102] to test for group differences in fidelity outcomes at the school year end, while accounting for classroom nesting within site. Covariates will include state, site size, cohort, turnover rate, October fidelity, quality rating, and demographics. The statistical significance of the treatment group predictor (alpha =.05) will be used to determine significant differences in fidelity outcomes for the low- vs high-intensity groups. Additional analyses will include repeated outcomes from all time points to test for treatment group differences across time and time-by-treatment effects. We will repeat these analyses for secondary implementation outcomes. We will also examine child-level outcomes using linear mixed-effects regression models, which account for a child's nesting within classrooms and sites. Parallel to primary analyses, we will first test treatment group differences at the spring assessment and then examine treatment and time-by-treatment effects using all time points. For all analyses, a significant, positive effect of treatment group will support the effectiveness of applying high-intensity strategies at sites that do not respond to low-intensity strategies initially. An exploratory

analysis is to describe the number of sites that were early responders and maintained response until the April assessment (versus regressing to non-responders over time).

For power analysis, we used Optimal Design software[103] to accommodate the clustered design of classrooms nested in sites. Our estimated sample size is based on the primary fidelity outcome and is analogous to powering a 2-arm randomized controlled trial. We have powered our study to detect a practically meaningful 1-point difference on our fidelity scale: 1 point would differentiate an educator who implements a practice only somewhat (e.g., score of 2) from an educator who implements a practice to a significant degree (e.g., score of 3). Based on standard deviations from the K01, a 1-point difference would yield Cohen's d effect sizes between .83 (Mascot) and 1.68 (Role Model). Assuming 64 non-responder sites (assigned 1:1) with an average of 3 non-responding classrooms per site (192 classrooms), the largest previously observed 0.20 Interclass Correlation Coefficient (ICC), and 2-sided α =.05, we will have 80% power to detect an effect size of d = 0.49 or larger. We do not anticipate site-level attrition, but even with ~20% attrition (N = 50 sites), we would have 80% power to detect an effect size of d =.56 or greater. Assuming one randomly chosen classroom per site, 15 children per classroom (N=64*15=960), a 0.10 ICC (largest observed child-level ICC in the K01), and 2-sided α =.05, we will have 80% power to detect an effect size of d =.29 or larger for child-level outcomes, which corresponds to an effect size of between small and medium.[104]

Moderator analyses for Aim 2 will be conducted in SPSS using mixed effects logistics regression models with a treatment main effect (low- vs high-intensity), the moderator main effect (organizational readiness and educator experience), and the interaction between the two. The interaction term significance (alpha =.05) will be evaluated to test moderation. Models will account for the classroom nesting within sites and include controls for state, quality rating, and key demographics. For mediation analyses in Aim 2, we will test a multilevel, multiple mediator model in a Structural Equation Modeling (SEM) framework[105] to account for students clustering in classrooms and classrooms within sites using MPLUS software. Specifying a multiple mediator model is less biased than testing single mediators one at a time.[106] Using parametric bootstrapping (Monte Carlo)[107,108] significance tests in SEM are also less biased than sequential hypothesis testing approaches to mediation tests.[109] Using data at three time points, we will be able to model that Y (independent variable) precedes M (mediator) in time, and M precedes Y (dependent variable) in time; prior levels of M and Y can be controlled.For moderator analyses, we will have 80% power detect a Cohen's f^2 of .13 which falls between a small (f^2=.02) and medium (f^2=.15) effect size.[104] In mediation analyses, the indirect effect is the product of 2 regression coefficients and is not distributed normally, which poses a challenge to power calculations.[110] However, Fritz and MacKinnon[111] recommend a bias-corrected bootstrap method for the indirect effect that, in our sample size of 64 sites, would provide 80% power to detect an indirect effect composed of 2 large-sized constituent effects, or a mix of a large-sized and a medium-sized effects.

Qualitative analyses for Aim 2 will focus on identifying similarities and differences between site response types. Transcripts will be matched with observed field notes and

coded using directed content analysis.[112] The i-PARIHS framework will provide a template of sensitizing concepts to label significant, recurrent ideas,[113] particularly ideas that suggest emergent candidate mediators and moderators. We will incorporate inductive codes as we identify additional salient factors.[114] Primary and secondary coders (at least 1 each from AR and LA) will code the same transcripts until inter-rater reliability is established. Minimum reliability will be set at Kappa of 0.75, which reflects excellent agreement between coders.[115] Coding will be independent after establishing reliability. Coders will hold weekly meetings to discuss iterative expansions to the codebook, to reach consensus about unclear codes, and to document tentative patterns in the data. A third-party team member will resolve disagreements.[116] Participants and stakeholders will review site-level summaries of findings. We will conduct analyses of qualitative interviews yearly and use findings to revise the interview guide for subsequent interviews (e.g., identify probing needs, generate new questions). We will use Nvivo software (QSR International) to code and calculate inter-rater reliability. As we interpret Aim 2 findings, we will connect quantitative and qualitative data. This will include: 1) *expansion* of quantitative findings to provide detail through qualitative data and 2) *complementarity* to deepen understanding and identify other potential moderators and mediators not focused on in quantitative analyses. Thus, qualitative data will explain and elaborate on quantitative findings.

For cost analysis in Aim 3, we will calculate the incremental cost-effectiveness ratio in 4 steps:

Step 1: Aim 1 data will provide estimates of fidelity and child outcome changes (i.e., BMI, RRS, target food consumption) for both study conditions. We will aggregate these findings to the site.

Step 2: Calculate the costs associated with implementation at each site. The WISE intervention cost is the same at all sites, and the ECE system does not accrue downstream costs or benefits. Therefore, we focus on implementation costs only, which comprise 4 categories: facilitator salary and benefits, facilitator travel expenses, educational resources, and other classrooms/site resources.These will be collected using a micro-costing approach, and expenses will be applied to the appropriate site.

Step 3: Estimate covariates to adjust for site-level differences in fidelity. We will use the same covariates as in Aim 1 and aggregate child-level covariates to the site. Incremental costs will be calculated using intent-to-treat analysis to measure the effect of treatment allocation. We will use generalized linear models (GLMs) to estimate the effect of implementation intensity on fidelity, child outcomes, and implementation costs. We will impute missing values via the *ice* procedure in STATA v14.0 (StataCorp LLC). We will compute 2 outcome predictions for each site based on the coefficients from the GLM regressions and the covariates.[117] The first prediction will be as if the site was randomized to the high-intensity strategy, and the second prediction will be as if the site was randomized to the low-intensity strategy. The difference between these predictions represents the incremental effect of the implementation strategy on fidelity, child outcomes, or costs.

Step 4: Calculate the incremental cost-effectiveness of adding the high-intensity strategy relative to continuing the low-intensity strategy. The numerator will be the

incremental difference in total implementation costs incurred at sites receiving the high-intensity strategy compared to sites continuing the low-intensity strategy. The denominator will include the difference in the changes in fidelity or child outcomes between the fall implementation and spring implementation assessments for high-intensity vs. low-intensity strategies. We will use a nonparametric bootstrap with replacement method with 1,000 replications to generate an empirical joint distribution of incremental implementation costs and fidelity or child outcome change scores, and acceptability curves representing the probability of falling below cost effectiveness thresholds identified by stakeholders (COBRE work to be completed by March 2021). Analysts will build preliminary models using data from the first cohort (Y2) to promote analysis expedience when all three cohorts are completed (Y4).

Ethical Considerations

This study will be conducted in accordance with all applicable government regulations and University of Arkansas for Medical Sciences research policies and procedures. This protocol and any amendments will be submitted and approved by the UAMS Institutional Review Board (IRB) to conduct the study.

A waiver of documentation of informed consent is requested for teachers in the project who will only participate only in classroom observational activities. This is because WISE will be adopted in all classrooms as a normal educational activity, and open classroom observations are standard practice in early care and education. Completion of surveys will be assumed as consent; we will include language in the introduction to the survey that describes the voluntary and de-identified nature of the survey as well as that refusal will not affect employment. For educators participating in interviews, we will collect verbal consent on the audio recording (i.e., we are requesting waiver of written consent only). For these aims, the only record linking the subject and the study would be the consent document making the principal risk a breach of confidentiality. This research involves no more than minimal risk to the subjects, and waivers will not adversely affect the rights and welfare of the subjects.

For child data collection, teachers and staff will hand out packets to each parent at enrollment. This packet will contain a study information sheet along with the necessary paperwork the parent completes to enroll at the center. We will submit these materials for approval prior to use in the study. The researchers believe that this is a good strategy for ensuring that each parent receives and reads the information sheet. The parent can return the signed form with the rest of the packet if he/she does not want his/her child to participate. We are therefore requesting a waiver of documentation of consent (e.g., "passive consent") for child participants. It is possible that some children would be wards of the state, although this is not our target population.We have a two-pronged plan to balance protection of vulnerable children and unnecessary exclusion.

First, we will summarize our study and protocol in lay-friendly language and share this with the AR and LA state Departments of Human Services (DHS). We will request them to sign a letter stating they understand the protocol and approve participation for all children that are wards of the state. In the event that we are unable to obtain blanket state approval, we will add a check box to the parent information sheet for caregivers to indicate they are providing foster care for the child and are unable to provide permission (i.e., we would exclude wards of the state from participation). . The study is minimal risk, and involves no procedures for which written consent is normally required outside the research context. The parent Information Sheet will be created and submitted for approval in the first 6 months of the study while site recruitment efforts are underway.

To collect child assent, children will be given a brief, developmentally-appropriate description of study activities (e.g., I would like to see how tall you are." "This machine tells about the color of foods you eat."). Then, research staff will ask children if they would like to participate. Children who state they do not want to participate or exhibit non-verbal hesitancy (e.g., crying, non-compliance) will not be pressured further and will not be included in the research assessments. Classrooms teachers assist the research team with identifying children and inviting them to the research activities. If a child's parent does not want them to participate, the teacher (a known and trusted adult) can explain that they will continue with their other normal activities (e.g., "You are having your turn in the block center today; your place is right here with me!). In prior studies (#134665 and #205335), this has prevented child distress about wanting to participate against their parent's wishes. This also avoids additional interaction with the research team, which may also be against the parent's wishes (versus having the child participate but not recording their data).

In accordance with the Management Plans for both Drs. Swindle and Whiteside-Mansell, the following measures will be taken:

- We will disclose our interests in participant consent and recruitment materials as applicable.
- All research partners will receive and sign a copy of the management plans.
- The interest will be disclosed in all publications and presentations.
- All data analysis (both qualitative and quantitative) will be reviewed by non-conflicted co-investigators or biostatisticians.
- All details in the respective Management Plans will be honored including reports on the specified schedule.

Dissemination of Data

We have developed a dissemination plan that makes data and research resources freely available in a timely manner to diverse audiences while safeguarding the privacy of participants and protecting confidential information (see Resource Sharing Plan). We will register our trial with ClinicalTrials.gov and report our results there within one year of the trial completion date. The process of informed consent will include a statement

informing the participants of the posting of our de-identified and aggregated results to ClinicalTrials.gov. The final, anonymized dataset will be made publicly available upon reasonable request or at the requirement of journal submission guidelines.

In addition, we will employ a multi-pronged strategy to ensure that findings from this research are disseminated to participants, scientists and community stakeholders. These efforts will not contain any identifiable information that could be linked to a participant.

Study participants. Results will be returned to participants first. We will share back findings of all stages of the project to participants and partnering agencies. Each participant will be mailed or e-mailed a one-page summary of results. Results will be presented in the form of an infographic that uses understandable words, as well as culturally relevant pictures/ examples. The study team has incorporated careful measures to protect the participants involved in the study. We will disseminate aggregate results and ensure that no personal health information (PHI) is ever shared. During enrollment, we will ask participants how they want to receive the summary of study results (a personal e-mail, or a mailed paper copy), and results will be provided in the manner they select. At that time, we will remind participants that the results will be shared in aggregate form and that no PHI will be shared. The research team will carefully review dissemination materials to reduce the risk of unintentionally identifying or stigmatizing participants when sharing results in small communities.

Local Stakeholders. By design, Evidence-Based Quality Improvement (EBQI) members will be updated on study progress throughout the study, including at the three planned meetings per year. At these meetings, the research team will present updates on enrollment and retention. When the study concludes, we will present the results and lessons learned. We will use easy to understand tools (e.g., infographics) to present results and lessons learned and provide reports stakeholders can distribute to their community members. Aggregate data with no PHI will be shared.

Early Care and Education Stakeholders. To ensure appropriate dissemination to community stakeholders the research team will seek input from stakeholders serving on the EBQI panel as well as The Translational Research Institute and the Center for Health Literacy (see Facilities and Other Resources). Early educators are a primary stakeholder in the findings of this research as well as directors and administrators at early care and education agencies. We will reach stakeholders through presentation at local conferences with an early education focus and at other community events identified by EBQI members.

Scientists. We will disseminate findings to scientists with interests in implementation science, obesity prevention, nutrition education, and early childhood development. We will attend and present at premier conferences in implementation science and nutrition. We will also submit findings for publication to leading journals in the field such as *Implementation Science, Implementation Science Communications, and Appetite.* will also share abstracts and publications with academic listservs and professional social networking sites on which I am a member.

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APPENDIX A: DATA AND SAFETY MONITORING PLAN

The Data and Safety Monitoring Plan (DSMP) outlined below will adhere to a protocol approved by the University of Arkansas for Medical Science (UAMS) IRB. The Louisiana Tech IRB and University of Colorado Anschutz Medical Campus IRB have agreed that the UAMS IRB will provide oversight for the study. Oversight of the DSM Plan will be provided by a locally appointed DSM Board under the UAMS IRB. The DSM Board will review data on such aspects as site enrollment, site visits, study procedures, forms completion, data quality, site attrition, and other measures of adherence to protocol. The DSM Board will provide recommendations to the PI regarding potential problems. They will provide periodic reports to the PI indicating whether they see any reasons for change and document all their actions. The Chair of the DSM Board will notify the UAMS IRB at 501-686-5667 of any concerns consistent with IRB policy 10.2. The IRB and NIH will also be notified at the time of renewal of the frequency of monitoring, cumulative data, summary of reviews to ensure subject privacy and research data confidentiality, and any changes to anticipated benefit-to-risk ratio of study participation to minimize research associated risk.

Monitoring Frequency

The table below provides information on the timeline of our review for each type of data.

Data type	Frequency of review	Sources	Reviewer
Subject recruitment (including compliance with protocol enrollment criteria)	Quarterly	Electronic files of observations, surveys, audio recordings, and interviews	PI, Biostatistician
Status of data collection plan	Quarterly	Electronic data files	PI, DSM Board, Biostatistician
Data regarding delivery of implementation support	Quarterly	Electronic files of materials delivered	PI, DSM Board
Unanticipated problems, adverse events, and serious adverse events	Per occurrence		PI, DSM Board UAMS IRB Program Manager, NIH

Reporting Process

The PI will report adverse events (AE) to the IRB and serious adverse events (SAEs) to the IRB and NIH in a timely fashion. In the event that the IRB takes an action that affects the day-to-day operations of the study, the PI will report those actions to the NIH Program officer in writing.

1. In accordance with the UAMS IRB AE reporting policy, an AE is reportable is it meets the following criteria:

a) Local adverse events that the investigator determines are: a. unexpected; b. related to the research; and c. involve new or increased risks to subjects or others. An event must meet all three criteria to require reporting under this policy.
b) Non-local adverse events that have been determined to be unanticipated problems involving risks to subjects or others.
c) Unanticipated adverse device effects.
d) Any change or deviation made to the research without prior IRB approval in order to

eliminate apparent immediate harm.

e) An accidental or unintentional change to the IRB-approved protocol that placed one or more subjects at increased risk or affects the rights and welfare of subjects or others.
f) Any new information that indicates an unexpected change to the risks or potential benefits of the research. This includes, but is not limited to: a. revised investigator brochures, package inserts, device manuals; b. publications in the literature; c. data and safety monitoring reports; d. interim results or other findings;
g) A breach in confidentiality that may involve risk to subjects or others. Examples include the loss of a laptop computer on which subject identifiers are stored or the loss of study records on a thumb drive.
h) Any complaint of a participant that indicates an unanticipated risk or any complaint that cannot be resolved by the research team.
i) Incarceration of a subject if study was not previously reviewed with the anticipation of enrolling prisoners.
j) Change in FDA labeling or withdrawal from marketing of a drug, device, or biologic used in a research protocol.
k) Restrictions, suspension or termination of study by the sponsor, investigator, funding agency, regulatory body, or institutional administration.
l) The premature completion of a study.
m) Notifications of pending audits, inquiries, or investigations by federal agencies.
n) Written reports from study monitor that include information that requires reporting under this policy.
o) Any other problem that was unexpected, related to the research and places the subject or others at a greater risk than previously known.

An example of an AE relevant to this study would be a data breach, and we have taken numerous steps to prevent this (See Protection of Human Subjects). Were someone to gain access to the data, they would not be able to identify the participants because these files use subject numbers only. Should this unlikely event happen, UAMS IRB reporting procedures would be followed. Steps would then be taken to identify how the breach occurred and what needs to be done to correct it. Additionally, we will follow any recommendations from the Safety Officer or IRB. An example of an SAE is the possibility of emotional distress at answering survey questions. Participants are not required to answer any questions they choose not to answer or that they are uncomfortable answering, and this will be reiterated to participants. The information provided by the subjects is confidential, and only study staff have access to answers. An example of an unanticipated problem would be if the subject had an unexpected negative response to participation in the study. The participant would be counseled as appropriate and excluded from the study if needed. These events and problems will be reported in accordance with the IRB and NIH policy.

Additional unknown risks may occur and, if so, will be identified through diligent monitoring by the PI throughout the study. During the informed consent process, participants will be advised of the potential minimum risks of participation and reminded throughout the study that the researchers should be promptly informed about any concerns regarding potential side effects or AEs. Participants will also be instructed to notify the PI and/or designee of any suspected AEs immediately if possible. The PI will maintain an electronic record of all reported AEs and notify the Chair of the DSM Board of all reportable events as they occur.. Additionally, the study manager will generate and provide de-identified cumulative administrative human participant semi-annual safety reports for the DSM Board to review.

Within 72 hours after a reportable AE, SAE or unanticipated problem has been reported by the participant, it will be graded by the PI, forwarded to the study's DSM Board for review, and then submitted by the PI to the UAMS IRB. After IRB review and acknowledgment, the PI will forward a copy of the reportable AE, SAE or unanticipated problem and IRB acknowledgment letter to the NIH Program Officer through the UAMS Office of Research within 72 hours. In addition, all cumulative reportable AE, SAE and unanticipated problems included in the DSM reports will be submitted to NIH in the Annual Progress Reports.

Trial Monitoring and Advising

We will form a group of independent investigators and biostatisticians under the guidance of the UAMS IRB to meet quarterly to review study progress, potential risks, and adherence to protocol and timeline. We expect the group to consist of 3 to 4 individuals with unique expertise. We expect to include investigators with expertise in implementation science, research involving children, and research design/statistics.