Supplementary File

1. SPIRIT Checklist
2. Consent form - Guatemala - English Versions, Separate Control and Intervention Forms
3. Consent form - India - English Versions, Separate Control and Intervention Forms
4. Sample data collection forms - English Versions
5. Protocol: Summary and Detailed Versions

SPIRIT 2013 Checklist: Recommended items to address in a clinical trial protocol and related documents*

Section/item	Item No	Description	Addressed manuscript section
Administrative information			
Title	1	Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym	Title/Abstract /Cover sheet
Trial registration	2a	Trial identifier and registry name. If not yet registered, name of intended registry	Title/Abstract /Cover sheet
	2b	All items from the World Health Organization Trial Registration Data Set	Reference to online registries
Protocol version	3	Date and version identifier	Title/Abstract /Cover sheet
Funding	4	Sources and types of financial, material, and other support	Title/Abstract /Cover sheet/Footnotes
Roles and responsibilities	5a	Names, affiliations, and roles of protocol contributors	Title/Abstract /Cover sheet
	5b	Name and contact information for the trial sponsor	Title/Abstract /Cover sheet
	5c	Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities	Title/Abstract /Cover sheet
	5d	Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team, and other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee)	Title/Abstract /Cover sheet

Introduction			
Background and rationale	6a	Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention	Introduction
	6b	Explanation for choice of comparators	Introduction
Objectives	7	Specific objectives or hypotheses	Introduction
Trial design	8	Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), allocation ratio, and framework (eg, superiority, equivalence, noninferiority, exploratory)	Introduction
Methods: Participants, interventions, and outcomes			
Study setting	9	Description of study settings (eg, community clinic, academic hospital) and list of countries where data will be collected. Reference to where list of study sites can be obtained	Study Setting
Eligibility criteria	10	Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centres and individuals who will perform the interventions (eg, surgeons, psychotherapists)	Eligibility criteria
Interventions	11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be administered	Interventions
	11b	Criteria for discontinuing or modifying allocated interventions for a given trial participant (eg, drug dose change in response to harms, participant request, or improving/worsening disease)	N/a
	11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return, laboratory tests)	N/a
	11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial	N/a
Outcomes	12	Primary, secondary, and other outcomes, including the specific measurement variable (eg, systolic blood pressure), analysis metric (eg, change from baseline, final value, time to event), method of aggregation (eg, median, proportion), and time point for each outcome. Explanation of the clinical relevance of chosen efficacy and harm outcomes is strongly recommended	Outcomes
Participant timeline	13	Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic diagram is highly recommended (see Figure)	Participant timeline

Sample size	14	Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting any sample size calculations	Sample size and recruitment
Recruitment	15	Strategies for achieving adequate participant enrolment to reach target sample size	Sample size and recruitment
Methods: Assignment of interventions (for controlled trials)			
Allocation:			
Sequence generation	16a	Method of generating the allocation sequence (eg, computer-generated random numbers), and list of any factors for stratification. To reduce predictability of a random sequence, details of any planned restriction (eg, blocking) should be provided in a separate document that is unavailable to those who enrol participants or assign interventions	Allocation and blinding
Allocation concealment mechanism	16b	Mechanism of implementing the allocation sequence (eg, central telephone; sequentially numbered, opaque, sealed envelopes), describing any steps to conceal the sequence until interventions are assigned	Allocation and blinding
Implementation	16c	Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions	Allocation and blinding
Blinding (masking)	17a	Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how	Allocation and blinding
	17b	If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial	Allocation and blinding
Methods: Data collection, management, and analysis			
Data collection methods	18a	Plans for assessment and collection of outcome, baseline, and other trial data, including any related processes to promote data quality (eg, duplicate measurements, training of assessors) and a description of study instruments (eg, questionnaires, laboratory tests) along with their reliability and validity, if known. Reference to where data collection forms can be found, if not in the protocol	Data collection and management
	18b	Plans to promote participant retention and complete follow-up, including list of any outcome data to be collected for participants who discontinue or deviate from intervention protocols	Data collection and management

Data management	19	Plans for data entry, coding, security, and storage, including any related processes to promote data quality (eg, double data entry; range checks for data values). Reference to where details of data management procedures can be found, if not in the protocol	Data collection and management
Statistical methods	20a	Statistical methods for analysing primary and secondary outcomes. Reference to where other details of the statistical analysis plan can be found, if not in the protocol	Primary statistical analysis
	20b	Methods for any additional analyses (eg, subgroup and adjusted analyses)	Primary statistical analysis
	20c	Definition of analysis population relating to protocol non-adherence (eg, as randomised analysis), and any statistical methods to handle missing data (eg, multiple imputation)	Primary statistical analysis
Methods: Monitoring			
Data monitoring	21a	Composition of data monitoring committee (DMC); summary of its role and reporting structure; statement of whether it is independent from the sponsor and competing interests; and reference to where further details about its charter can be found, if not in the protocol. Alternatively, an explanation of why a DMC is not needed	Data monitoring and safety
	21b	Description of any interim analyses and stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial	N/a
Harms	22	Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct	Data monitoring and safety
Auditing	23	Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor	Data monitoring and safety
Ethics and dissemination			
Research ethics approval	24	Plans for seeking research ethics committee/institutional review board (REC/IRB) approval	Ethics approvals, risks, benefits

Protocol amendments	25	Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC/IRBs, trial participants, trial registries, journals, regulators)	Ethics approvals, risks, benefits
Consent or assent	26a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32)	Informed consent and confidentialit y
	26b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable	N/a
Confidentiality	27	How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial	Informed consent and confidentialit y
Declaration of interests	28	Financial and other competing interests for principal investigators for the overall trial and each study site	Footnotes
Access to data	29	Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators	N/A
Ancillary and post-trial care	30	Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial participation	Ethics approvals, risks, benefits
Dissemination policy	31a	Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other relevant groups (eg, via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions	Disseminatio n policy
	31b	Authorship eligibility guidelines and any intended use of professional writers	Disseminatio n policy
	31c	Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code	Disseminatio n policy
Appendices			
Informed consent materials	32	Model consent form and other related documentation given to participants and authorised surrogates	Supplementa ry Fil
Biological specimens	33	Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial and for future use in ancillary studies, if applicable	N/A

*It is strongly recommended that this checklist be read in conjunction with the SPIRIT 2013 Explanation & Elaboration for important clarification on the items. Amendments to the protocol should be tracked and dated. The SPIRIT checklist is copyrighted by the

Wuqu' Kawoq | Maya Health Alliance
Partners Healthcare
Research Consent Form
Version Date: June 23, 2020

Subject ID:

Protocol Title: An Individualized Approach to Promote Nurturing Care in Low and Middle Income Countries: A Hybrid Effectiveness/Implementation Trial of the International Guide for Monitoring Child Development

Principal Investigator: Peter Rohloff

Site Principal Investigator: Maria del Pilar Grazioso

Description of Study Population: Children under 2 living in rural communities in India and Guatemala

About this Consent Form:

Please read this form carefully, or listen to this form being read carefully. It tells you important information about a research study. A member of our research team will talk to you about giving permission for your child to take part in this research study. People who agree to take part in research studies are called "subjects." This term will be used throughout this consent form.

If you decide to give permission for your child to take part in this research study, you must given your permission to the person talking with you now about the research. You do not need to sign this form, however. The research team member talking with you will record whether you agree to participate or not.. We will give you a copy of the form to keep.

Who should I contact with questions or concerns about this study?

You can call us with your questions or concerns. Our telephone numbers are listed below. Ask questions as often as you want.

Dr. Maria del Pilar Grazioso PhD is the person in charge of this research study. You can call them at 7840-3112, Monday to Friday from 8 am to 5 pm. You can also call Dr. Peter Rohloff at 7840-3112 from Monday to Friday from 8 am to 5 pm with questions.

If you want to talk with someone not directly involved with this research study, you can contact the Wuqu' Kawoq Human Research Committee office. You can reach them at: 7840-3112.

You can talk to them about:

- Your rights as a research subject
- Your concerns about the research
- A complaint about the research
- Any feeling pressure to take part in or continue the research study

Wuqu' Kawoq | Maya Health Alliance
Partners Healthcare
Research Consent Form
Version Date: June 23, 2020

Subject ID:

Why is this research being done?

This research is being done to test if a new tool called the Guide for Monitoring Child Development can help to promote positive development of young children. The tool is designed especially for use in countries where there are not a lot of resources to help promote child development. Promoting child development means helping children learn to move their bodies, communicate, and relate with others. The tool is designed to be used by community health workers in communities like yours.

Who will take part in this research?

Study Population: We are asking you to give permission for your child to take part in this research. The study is for children aged 0 to 2 years living in communities like your community. We are conducting the study in two countries, in India and in Guatemala.

Number of Participants: About 312 children will participate in this study in Guatemala. We are looking for about 12 children to participate in each of 26 different communities such as yours.

Sponsor Information: The National Institutes of Health of the USA is paying for this research to be done.

What will happen in this research study?

This is a randomized controlled study with two different groups to study the positive benefits of the Guide for Monitoring Children Development. Communities like yours in Guatemala will be divided randomly into two groups. In one group, children will receive monthly visits from community health workers working in the community using the Guide for Monitoring Child Development start from the time they agree to participate for a total of 24 months. In the other group, children will receive monthly visits from community health workers using the Guide for Monitoring Child Development starting 12 months after the time they agree to participate up to 24 months. These visits will last between 45 minutes and 1 hour. Throughout the study, your community health workers will continue to provide all the other services that they normally would, such as monitoring your child's nutrition.

The main difference between these two groups is that one will receive the intervention earlier than the other. This selection is completely random. We cannot and you cannot decide in which group your child will be. **Your community has been selected to be in the later group.**

If you decide to let your child participate, you will have three visits from our research team, first when you sign up and then again around 12 and 24 months later. Each visit will last up to 2 hours. At these visits we will check your child's growth and take a small drop of blood from their heel to check for anemia. We will also ask questions about the home environment and your child's health and diet. Finally, one of our psychologists or pediatricians will use questions and observations of your child to assess their development. We will share the results of these tests with you and explain them to you. During visits from the study, if there are any procedures or questions that make you uncomfortable, you can tell the researcher that you do not want to complete them. You can also decide where in your home is the best place to conduct the visits.

How may we use and share your child's health information for other research?

Wuqu' Kawoq | Maya Health Alliance
Partners Healthcare
Research Consent Form
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Subject ID:

The information we collect in this study may help advance other research. If your child joins this study, we may remove all information that identifies your child (for example, your name and date of birth) and use these de-identified data in other research. It won't be possible to link the information or samples back to your child. This information may be shared with researchers at our hospitals or other academic institutions. You will not be asked to provide additional informed consent for these uses.

Will you get the results of this research study?

The research study we are doing is only a stepping stone in understanding how best to promote child development. Therefore, no information about the results of this research study comparing your child to other participants will be given to you. However, some of the tests we do as part of the research, including growth measurements, tests for anemia, and results from the developmental tests may be useful to your doctor as they care for your child. We will give you copies of these results and explain them to you, so that you can save them or give them to your doctor.

What are the risk and possible discomforts from being in this research study?

If you agree to participate in the study, you will receive visits from our research team plus participate in activities with a community health worker. The main risk from the study is that it will take up some of your time to participate. You may also experience stress or emotional discomfort from answering some questions we ask you. You can skip any question that makes you uncomfortable.

In addition, our research team we will check your child for anemia using a drop of blood from the heel. This is a very safe procedure, but there is a small risk of infection from puncturing the skin and it can cause some mild discomfort to your child.

Sometimes young children can get sick. This is probably not due to the study, but you can still inform the team. If we find a child with severe malnutrition or another very serious health problem, we will help you make sure they get treatment.

We will collect information about your child's health. Because of this, there is a small chance that your information may be seen occasionally by someone other than your doctor, nurse or other trusted person. We will work to prevent this from happening.

Sometimes families make decisions about participating in research projects together. If there is another family member that you feel needs to help you make the decision to participate, then we should talk to that person before you make your decision.

What are the possible benefits from being in this research study?

Since this is a research study, it is possible that you and your child may not benefit from participating. However, some possible benefits of participating include that your child will have access to developmental monitoring tests that they probably would otherwise not have access to. We will make these results available to you and explain them to you. In addition, the visits from the community health workers using the Guide for Monitoring Child Development may help to foster better development for your child and give you more ideas about how to support your child as they develop.

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Research Consent Form
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Subject ID:

Can your child still get medical care if they don't take part in the research study or if they stop taking part?

Yes. Your decision will not change the medical care and other services that you receive from your community health workers or from other people at Wuqu' Kawoq. There will be no penalty, and your child won't lose any benefits your child receives now or has a right to receive.

What should you do if you want your child to stop taking part in the study?

If you child takes part in this research study and you want them to drop out, you should tell us. We will make sure that your child can stop the study.

Also, it is possible that we will have to ask your child to drop out of the study before they finish it. This could happen, for example, if your child develops a medical condition that requires treatment and prevents them from participating. If this happens, we will tell you why and help you arrange care for your child if needed.

Will you or your child be paid to take part in this research study?

You and your child will not be paid for taking part in this research study.

What will you have to pay for if your child takes part in this research study?

There will be no costs for you to participate. You will not be charged for any of the study activities.

What happens if your child is injured while taking part in the research study?

This research study involves very safe procedures, and we don't anticipate that your child will be harmed as a result of participating. However, injuries sometimes happen in research even when no one is at fault. There are no plans to pay you or your child or give you other compensation for an injury, should one occur. However, you or your child are not giving up any of your legal rights by agreeing to participate in this study.

If you think your child has been injured or has experienced a medical problem as a result of taking part in this research study, tell the person in charge of this study as soon as possible. This person's name and phone number are listed on the first page of this form.

If your child takes part in this research study, how we will we protect your child's privacy?

Federal laws of Guatemala and the USA require us at Wuqu' Kawoq and Partners Healthcare to protect the privacy of health information and related information that identifies you.

In this study we will collect identifiable information from your child from the research procedures described above, including tests and questionnaires.

The following entities may see, use, or share your child's identifiable information:

- Researchers and staff at Wuqu' Kawoq and Partners Healthcare involved in this study.
- The sponsor of this study or people or groups who are hired by them to audit the research
- Other researchers at other institutions involved in this study

Subject ID:

- Members of the ethics board at Wuqu' Kawoq and Partners Healthcare overseeing this research
- Federal agencies in Guatemala or the USA that oversee, evaluate, and audit research
- Public health or safety authorities, if we learn information that could mean harm to your child or others (for example, we are required to make reports about child abuse)

Because research is an ongoing process, we cannot give you an exact date when we will either destroy or stop sharing your child's identifiable information. Your permission to use this information does not expire.

The results of this research study may be published in a medical book or journal, or used to teach others. However, your child's name or other identifiable information will not be used for these purposes.

Your Child's Privacy Rights

You have the right to not agree to participate in this research. However, if you don't agree to the details of the research in this document, your child can't take part in the research study.

You have the right to withdraw your permission for us to use or share your child's identifiable information. If you want to withdraw your permission, you must notify the person in charge of this study listed at the start of this form. If you withdraw your permission, your child cannot continue in the study. If you withdraw your permission, we will not be able to take back information that has already been used or shared, and this information may continue to be used for certain purposes, such as to comply with the law or to maintain the reliability of the study.

Informed Consent and Authorization:

Statement of Person Giving Informed Consent and Authorization

- I have read this consent form or had it read aloud to me
- This research study has been explained to me, including risks and possible benefits, procedures, and other important things about the study
- I have had the opportunity to ask questions
- I understand the information given to me.

Documentation of Consent of Parent/Guardian of Child

I hereby certify that the parent/guardian ____ HAS or _____ HAS NOT given verbal consent for their child to take part in this research study and agrees to allow their health information to be used and shared as described above.

Signature of Study Doctor or Person Obtaining and Certifying Verbal Consent:

Statement of Study Doctor or Person Obtaining Consent

- I have explained the research to the parent(s)/guardian and child.
- I have answered all questions about this research study to the best of my ability.
- I am fluent in the preferred language of the parent/guardian and have conducted this conversation in that language

_____ _____

Study Doctor or Person Obtaining Consent Date

Mahatma Gandhi Institute of Medical Sciences
Partners Healthcare
Research Consent Form
Version Date: June 23, 2020

Subject ID:

Protocol Title: An Individualized Approach to Promote Nurturing Care in Low- and Middle-Income Countries: A Hybrid Effectiveness/Implementation Trial of the International Guide for Monitoring Child Development

Principal Investigator: Peter Rohloff

Site Principal Investigator: Subodh Gupta

Description of Study Population: Children under 2 living in rural communities in India and Guatemala

About this Consent Form:

Please read this form carefully, or listen to this form being read carefully. It tells you important information about a research study. A member of our research team will talk to you about giving permission for your child to take part in this research study. People who agree to take part in research studies are called "subjects." This term will be used throughout this consent form.

If you decide to give permission for your child to take part in this research study, you must sign this form to show that you want them to take part. We will give you a signed copy of the form to keep.

Who should I contact with questions or concerns about this study?

You can call us with your questions or concerns. Our telephone numbers are listed below. Ask questions as often as you want.

Dr. Subodh Gupta, MD is the person in charge of this research study. You can call them at XXXX, Monday to Friday from XX to XX. You can also call ALTERNATE PERSON at ALTERNATE TELEPHONE from Monday to Friday from XX to XX with questions.

If you want to talk with someone not directly involved with this research study, you can contact the Mahatma Gandhi Human Research Committee office. You can reach them at: PHONE.

You can talk to them about:

- Your rights as a research subject
- Your concerns about the research
- A complaint about the research
- Any feeling pressure to take part in or continue the research study

Mahatma Gandhi Institute of Medical Sciences
Partners Healthcare
Research Consent Form
Version Date: June 23, 2020

Subject ID:

Why is this research being done?

This research is being done to test if a new tool called the Guide for Monitoring Child Development can help to promote positive development of young children. The tool is designed especially for use in countries where there are not a lot of resources to help promote child development. Promoting child development means helping children learn to move their bodies, communicate, and relate with others. The tool is designed to be used by community health workers in communities like yours.

Who will take part in this research?

Study Population: We are asking you to give permission for your child to take part in this research. The study is for children aged 0 to 2 years living in communities like your community. We are conducting the study in two countries, in India and in Guatemala.

Number of Participants: About 312 children will participate in this study in India. We are looking for about 12 children to participate in each of 26 different communities such as yours.

Sponsor Information: The National Institutes of Health of the USA is paying for this research to be done.

What will happen in this research study?

This is a randomized controlled study with two different groups to study the positive benefits of the Guide for Monitoring Children Development. Communities like yours in India will be divided randomly into two groups. In one group, children will receive monthly visits from community health workers working in the community using the Guide for Monitoring Child Development start from the time they agree to participate for a total of 24 months. In the other group, children will receive monthly visits from community health workers using the Guide for Monitoring Child Development starting 12 months after the time they agree to participate up to 24 months. These visits will last between 45 minutes and 1 hour. Throughout the study, your community health workers will continue to provide all the other services that they normally would, such as monitoring your child's nutrition.

The main difference between these two groups is that one will receive the intervention earlier than the other. This selection is completely random. We cannot and you cannot decide in which group your child will be. **Your community has been selected to be in the later group.**

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How may we use and share your child's health information for other research?

The information we collect in this study may help advance other research. If your child joins this study, we may remove all information that identifies your child (for example, your name and date of birth) and use these de-identified data in other research. It won't be possible to link the

information or samples back to your child. This information may be shared with researchers at our hospitals or other academic institutions. You will not be asked to provide additional informed consent for these uses.

Will you get the results of this research study?

The research study we are doing is only a stepping stone in understanding how best to promote child development. Therefore, no information about the results of this research study comparing your child to other participants will be given to you. However, some of the tests we do as part of the research, including growth measurements, tests for anemia, and results from the developmental tests may be useful to your doctor as they care for your child. We will give you copies of these results and explain them to you, so that you can save them or give them to your doctor.

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Sometimes young children can get sick. This is probably not due to the study, but you can still inform the team. If we find a child with severe malnutrition or another very serious health problem, we will help you make sure they get treatment.

We will collect information about your child's health. Because of this, there is a small chance that your information may be seen occasionally by someone other than your doctor, nurse or other trusted person. We will work to prevent this from happening.

Sometimes families make decisions about participating in research projects together. If there is another family member that you feel needs to help you make the decision to participate, then we should talk to that person before you make your decision.

What are the possible benefits from being in this research study?

Since this is a research study, it is possible that you and your child may not benefit from participating. However, some possible benefits of participating include that your child will have access to developmental monitoring tests that they probably would otherwise not have access to. We will make these results available to you and explain them to you. In addition, the visits from the community health workers using the Guide for Monitoring Child Development may help to foster better development for your child and give you more ideas about how to support your child as they develop.

Can your child still get medical care if they don't take part in the research study or if they stop taking part?

Yes. Your decision will not change the medical care and other services that you receive from your community health workers or from other people at the Mahatma Gandhi Institute of Medical

Sciences. There will be no penalty, and your child won't lose any benefits your child receives now or has a right to receive.

What should you do if you want your child to stop taking part in the study?

If you child takes part in this research study and you want them to drop out, you should tell us. We will make sure that your child can stop the study.

Also, it is possible that we will have to ask your child to drop out of the study before they finish it. This could happen, for example, if your child develops a medical condition that requires treatment and prevents them from participating. If this happens, we will tell you why and help you arrange care for your child if needed.

Will you or your child be paid to take part in this research study?

You and your child will not be paid for taking part in this research study.

What will you have to pay for if your child takes part in this research study?

There will be no costs for you to participate. You will not be charged for any of the study activities.

What happens if your child is injured while taking part in the research study?

This research study involves very safe procedures, and we don't anticipate that your child will be harmed as a result of participating. However, injuries sometimes happen in research even when no one is at fault. There are no plans to pay you or your child or give you other compensation for an injury, should one occur. However, you or your child are not giving up any of your legal rights by agreeing to participate in this study.

If you think your child has been injured or has experienced a medical problem as a result of taking part in this research study, tell the person in charge of this study as soon as possible. This person's name and phone number are listed on the first page of this form.

If your child takes part in this research study, how we will we protect your child's privacy?

Federal laws of India and the USA require us at the Mahatma Gandhi Institute of Medical Sciences and Partners Healthcare to protect the privacy of health information and related information that identifies you.

In this study we will collect identifiable information from your child from the research procedures described above, including tests and questionnaires.

The following entities may see, use, or share your child's identifiable information:

- Researchers and staff at Mahatma Gandhi Institute of Medical Sciences and Partners Healthcare involved in this study.
- The sponsor of this study or people or groups who are hired by them to audit the research
- Other researchers at other institutions involved in this study
- Members of the ethics board of Mahatma Gandhi Institute of Medical Sciences and Partners Healthcare overseeing this research
- Federal agencies in India or the USA that oversee, evaluate, and audit research

Mahatma Gandhi Institute of Medical Sciences
Partners Healthcare
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Subject ID:

- Public health or safety authorities, if we learn information that could mean harm to your child or others (for example, we are required to make reports about child abuse)

Because research is an ongoing process, we cannot give you an exact date when we will either destroy or stop sharing your child's identifiable information. Your permission to use this information does not expire.

The results of this research study may be published in a medical book or journal, or used to teach others. However, your child's name or other identifiable information will not be used for these purposes.

Your Child's Privacy Rights

You have the right to not agree to participate in this research. You have the right to not sign this form. However, if you don't sign it, your child can't take part in the research study.

You have the right to withdraw your permission for us to use or share your child's identifiable information. If you want to withdraw your permission, you must notify the person in charge of this study listed at the start of this form. If you withdraw your permission, your child cannot continue in the study. If you withdraw your permission, we will not be able to take back information that has already been used or shared, and this information may continue to be used for certain purposes, such as to comply with the law or to maintain the reliability of the study.

Informed Consent and Authorization:

Statement of Person Giving Informed Consent and Authorization

- I have read this consent form or had it read aloud to me
- This research study has been explained to me, including risks and possible benefits, procedures, and other important things about the study
- I have had the opportunity to ask questions
- I understand the information given to me.

Signature of Parent/Guardian of Child

I give my consent for my child to take part in this research study and agree to allow his/her health information to be used and shared as described above.

_____ _____

Parent(s)/Guardian for Child Date

Signature of Study Doctor or Person Obtaining Consent:

Statement of Study Doctor or Person Obtaining Consent

- I have explained the research to the parent(s)/guardian and child.
- I have answered all questions about this research study to the best of my ability.
- I am fluent in the preferred language of the parent/guardian and have conducted this conversation in that language

_____ _____

Study Doctor or Person Obtaining Consent Date

Wuqu' Kawoq | Maya Health Alliance
Partners Healthcare
Research Consent Form
Version Date: June 23, 2020

Subject ID:

Protocol Title: An Individualized Approach to Promote Nurturing Care in Low and Middle Income Countries: A Hybrid Effectiveness/Implementation Trial of the International Guide for Monitoring Child Development

Principal Investigator: Peter Rohloff

Site Principal Investigator: Maria del Pilar Grazioso

Description of Study Population: Children under 2 living in rural communities in India and Guatemala

About this Consent Form:

Please read this form carefully, or listen to this form being read carefully. It tells you important information about a research study. A member of our research team will talk to you about giving permission for your child to take part in this research study. People who agree to take part in research studies are called "subjects." This term will be used throughout this consent form.

If you decide to give permission for your child to take part in this research study, you must given your permission to the person talking with you now about the research. You do not need to sign this form, however. The research team member talking with you will record whether you agree to participate or not.. We will give you a copy of the form to keep.

Who should I contact with questions or concerns about this study?

You can call us with your questions or concerns. Our telephone numbers are listed below. Ask questions as often as you want.

Dr. Maria del Pilar Grazioso PhD is the person in charge of this research study. You can call them at 7840-3112, Monday to Friday from 8 am to 5 pm. You can also call Dr. Peter Rohloff at 7840-3112 from Monday to Friday from 8 am to 5 pm with questions.

If you want to talk with someone not directly involved with this research study, you can contact the Wuqu' Kawoq Human Research Committee office. You can reach them at: 7840-3112.

You can talk to them about:

- Your rights as a research subject
- Your concerns about the research
- A complaint about the research
- Any feeling pressure to take part in or continue the research study

Wuqu' Kawoq | Maya Health Alliance
Partners Healthcare
Research Consent Form
Version Date: June 23, 2020

Subject ID:

Why is this research being done?

This research is being done to test if a new tool called the Guide for Monitoring Child Development can help to promote positive development of young children. The tool is designed especially for use in countries where there are not a lot of resources to help promote child development. Promoting child development means helping children learn to move their bodies, communicate, and relate with others. The tool is designed to be used by community health workers in communities like yours.

Who will take part in this research?

Study Population: We are asking you to give permission for your child to take part in this research. The study is for children aged 0 to 2 years living in communities like your community. We are conducting the study in two countries, in India and in Guatemala.

Number of Participants: About 312 children will participate in this study in Guatemala. We are looking for about 12 children to participate in each of 26 different communities such as yours.

Sponsor Information: The National Institutes of Health of the USA is paying for this research to be done.

What will happen in this research study?

This is a randomized controlled study with two different groups to study the positive benefits of the Guide for Monitoring Children Development. Communities like yours in Guatemala will be divided randomly into two groups. In one group, children will receive monthly visits from community health workers working in the community using the Guide for Monitoring Child Development start from the time they agree to participate for a total of 24 months. In the other group, children will receive monthly visits from community health workers using the Guide for Monitoring Child Development starting 12 months after the time they agree to participate up to 24 months. These visits will last between 45 minutes and 1 hour. Throughout the study, your community health workers will continue to provide all the other services that they normally would, such as monitoring your child's nutrition.

The main difference between these two groups is that one will receive the intervention earlier than the other. This selection is completely random. We cannot and you cannot decide in which group your child will be. **Your community has been selected to be in the early group.**

If you decide to let your child participate, you will have three visits from our research team, first when you sign up and then again around 12 and 24 months later. Each visit will last up to 2 hours. At these visits we will check your child's growth and take a small drop of blood from their heel to check for anemia. We will also ask questions about the home environment and your child's health and diet. Finally, one of our psychologists or pediatricians will use questions and observations of your child to assess their development. We will share the results of these tests with you and explain them to you. During visits from the study, if there are any procedures or questions that make you uncomfortable, you can tell the researcher that you do not want to complete them. You can also decide where in your home is the best place to conduct the visits.

How may we use and share your child's health information for other research?

Wuqu' Kawoq | Maya Health Alliance
Partners Healthcare
Research Consent Form
Version Date: June 23, 2020

Subject ID:

The information we collect in this study may help advance other research. If your child joins this study, we may remove all information that identifies your child (for example, your name and date of birth) and use these de-identified data in other research. It won't be possible to link the information or samples back to your child. This information may be shared with researchers at our hospitals or other academic institutions. You will not be asked to provide additional informed consent for these uses.

Will you get the results of this research study?

The research study we are doing is only a stepping stone in understanding how best to promote child development. Therefore, no information about the results of this research study comparing your child to other participants will be given to you. However, some of the tests we do as part of the research, including growth measurements, tests for anemia, and results from the developmental tests may be useful to your doctor as they care for your child. We will give you copies of these results and explain them to you, so that you can save them or give them to your doctor.

What are the risk and possible discomforts from being in this research study?

If you agree to participate in the study, you will receive visits from our research team plus participate in activities with a community health worker. The main risk from the study is that it will take up some of your time to participate. You may also experience stress or emotional discomfort from answering some questions we ask you. You can skip any question that makes you uncomfortable.

In addition, our research team we will check your child for anemia using a drop of blood from the heel. This is a very safe procedure, but there is a small risk of infection from puncturing the skin and it can cause some mild discomfort to your child.

Sometimes young children can get sick. This is probably not due to the study, but you can still inform the team. If we find a child with severe malnutrition or another very serious health problem, we will help you make sure they get treatment.

We will collect information about your child's health. Because of this, there is a small chance that your information may be seen occasionally by someone other than your doctor, nurse or other trusted person. We will work to prevent this from happening.

Sometimes families make decisions about participating in research projects together. If there is another family member that you feel needs to help you make the decision to participate, then we should talk to that person before you make your decision.

What are the possible benefits from being in this research study?

Since this is a research study, it is possible that you and your child may not benefit from participating. However, some possible benefits of participating include that your child will have access to developmental monitoring tests that they probably would otherwise not have access to. We will make these results available to you and explain them to you. In addition, the visits from the community health workers using the Guide for Monitoring Child Development may help to foster better development for your child and give you more ideas about how to support your child as they develop.

Wuqu' Kawoq | Maya Health Alliance
Partners Healthcare
Research Consent Form
Version Date: June 23, 2020

Subject ID:

Can your child still get medical care if they don't take part in the research study or if they stop taking part?

Yes. Your decision will not change the medical care and other services that you receive from your community health workers or from other people at Wuqu' Kawoq. There will be no penalty, and your child won't lose any benefits your child receives now or has a right to receive.

What should you do if you want your child to stop taking part in the study?

If you child takes part in this research study and you want them to drop out, you should tell us. We will make sure that your child can stop the study.

Also, it is possible that we will have to ask your child to drop out of the study before they finish it. This could happen, for example, if your child develops a medical condition that requires treatment and prevents them from participating. If this happens, we will tell you why and help you arrange care for your child if needed.

Will you or your child be paid to take part in this research study?

You and your child will not be paid for taking part in this research study.

What will you have to pay for if your child takes part in this research study?

There will be no costs for you to participate. You will not be charged for any of the study activities.

What happens if your child is injured while taking part in the research study?

This research study involves very safe procedures, and we don't anticipate that your child will be harmed as a result of participating. However, injuries sometimes happen in research even when no one is at fault. There are no plans to pay you or your child or give you other compensation for an injury, should one occur. However, you or your child are not giving up any of your legal rights by agreeing to participate in this study.

If you think your child has been injured or has experienced a medical problem as a result of taking part in this research study, tell the person in charge of this study as soon as possible. This person's name and phone number are listed on the first page of this form.

If your child takes part in this research study, how we will we protect your child's privacy?

Federal laws of Guatemala and the USA require us at Wuqu' Kawoq and Partners Healthcare to protect the privacy of health information and related information that identifies you.

In this study we will collect identifiable information from your child from the research procedures described above, including tests and questionnaires.

The following entities may see, use, or share your child's identifiable information:

- Researchers and staff at Wuqu' Kawoq and Partners Healthcare involved in this study.
- The sponsor of this study or people or groups who are hired by them to audit the research
- Other researchers at other institutions involved in this study

Subject ID:

- Members of the ethics board at Wuqu' Kawoq and Partners Healthcare overseeing this research
- Federal agencies in Guatemala or the USA that oversee, evaluate, and audit research
- Public health or safety authorities, if we learn information that could mean harm to your child or others (for example, we are required to make reports about child abuse)

Because research is an ongoing process, we cannot give you an exact date when we will either destroy or stop sharing your child's identifiable information. Your permission to use this information does not expire.

The results of this research study may be published in a medical book or journal, or used to teach others. However, your child's name or other identifiable information will not be used for these purposes.

Your Child's Privacy Rights

You have the right to not agree to participate in this research. However, if you don't agree to the details of the research in this document, your child can't take part in the research study.

You have the right to withdraw your permission for us to use or share your child's identifiable information. If you want to withdraw your permission, you must notify the person in charge of this study listed at the start of this form. If you withdraw your permission, your child cannot continue in the study. If you withdraw your permission, we will not be able to take back information that has already been used or shared, and this information may continue to be used for certain purposes, such as to comply with the law or to maintain the reliability of the study.

Informed Consent and Authorization:

Statement of Person Giving Informed Consent and Authorization

- I have read this consent form or had it read aloud to me
- This research study has been explained to me, including risks and possible benefits, procedures, and other important things about the study
- I have had the opportunity to ask questions
- I understand the information given to me.

Documentation of Consent of Parent/Guardian of Child

I hereby certify that the parent/guardian ____ HAS or _____ HAS NOT given verbal consent for their child to take part in this research study and agrees to allow their health information to be used and shared as described above.

Signature of Study Doctor or Person Obtaining and Certifying Verbal Consent:

Statement of Study Doctor or Person Obtaining Consent

- I have explained the research to the parent(s)/guardian and child.
- I have answered all questions about this research study to the best of my ability.
- I am fluent in the preferred language of the parent/guardian and have conducted this conversation in that language

_____ _____

Study Doctor or Person Obtaining Consent Date

Mahatma Gandhi Institute of Medical Sciences
Partners Healthcare
Research Consent Form
Version Date: June 23, 2020

Subject ID:

Protocol Title: An Individualized Approach to Promote Nurturing Care in Low- and Middle-Income Countries: A Hybrid Effectiveness/Implementation Trial of the International Guide for Monitoring Child Development

Principal Investigator: Peter Rohloff

Site Principal Investigator: Subodh Gupta

Description of Study Population: Children under 2 living in rural communities in India and Guatemala

About this Consent Form:

Please read this form carefully, or listen to this form being read carefully. It tells you important information about a research study. A member of our research team will talk to you about giving permission for your child to take part in this research study. People who agree to take part in research studies are called "subjects." This term will be used throughout this consent form.

If you decide to give permission for your child to take part in this research study, you must sign this form to show that you want them to take part. We will give you a signed copy of the form to keep.

Who should I contact with questions or concerns about this study?

You can call us with your questions or concerns. Our telephone numbers are listed below. Ask questions as often as you want.

Dr. Subodh Gupta, MD is the person in charge of this research study. You can call them at XXXX, Monday to Friday from XX to XX. You can also call ALTERNATE PERSON at ALTERNATE TELEPHONE from Monday to Friday from XX to XX with questions.

If you want to talk with someone not directly involved with this research study, you can contact the Mahatma Gandhi Human Research Committee office. You can reach them at: PHONE.

You can talk to them about:

- Your rights as a research subject
- Your concerns about the research
- A complaint about the research
- Any feeling pressure to take part in or continue the research study

Mahatma Gandhi Institute of Medical Sciences
Partners Healthcare
Research Consent Form
Version Date: June 23, 2020

Subject ID:

Why is this research being done?

This research is being done to test if a new tool called the Guide for Monitoring Child Development can help to promote positive development of young children. The tool is designed especially for use in countries where there are not a lot of resources to help promote child development. Promoting child development means helping children learn to move their bodies, communicate, and relate with others. The tool is designed to be used by community health workers in communities like yours.

Who will take part in this research?

Study Population: We are asking you to give permission for your child to take part in this research. The study is for children aged 0 to 2 years living in communities like your community. We are conducting the study in two countries, in India and in Guatemala.

Number of Participants: About 312 children will participate in this study in India. We are looking for about 12 children to participate in each of 26 different communities such as yours.

Sponsor Information: The National Institutes of Health of the USA is paying for this research to be done.

What will happen in this research study?

This is a randomized controlled study with two different groups to study the positive benefits of the Guide for Monitoring Children Development. Communities like yours in India will be divided randomly into two groups. In one group, children will receive monthly visits from community health workers working in the community using the Guide for Monitoring Child Development start from the time they agree to participate for a total of 24 months. In the other group, children will receive monthly visits from community health workers using the Guide for Monitoring Child Development starting 12 months after the time they agree to participate up to 24 months. These visits will last between 45 minutes and 1 hour. Throughout the study, your community health workers will continue to provide all the other services that they normally would, such as monitoring your child's nutrition.

The main difference between these two groups is that one will receive the intervention earlier than the other. This selection is completely random. We cannot and you cannot decide in which group your child will be. **Your community has been selected to be in the early group.**

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How may we use and share your child's health information for other research?

The information we collect in this study may help advance other research. If your child joins this study, we may remove all information that identifies your child (for example, your name and date of birth) and use these de-identified data in other research. It won't be possible to link the

information or samples back to your child. This information may be shared with researchers at our hospitals or other academic institutions. You will not be asked to provide additional informed consent for these uses.

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We will collect information about your child's health. Because of this, there is a small chance that your information may be seen occasionally by someone other than your doctor, nurse or other trusted person. We will work to prevent this from happening.

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Since this is a research study, it is possible that you and your child may not benefit from participating. However, some possible benefits of participating include that your child will have access to developmental monitoring tests that they probably would otherwise not have access to. We will make these results available to you and explain them to you. In addition, the visits from the community health workers using the Guide for Monitoring Child Development may help to foster better development for your child and give you more ideas about how to support your child as they develop.

Can your child still get medical care if they don't take part in the research study or if they stop taking part?

Yes. Your decision will not change the medical care and other services that you receive from your community health workers or from other people at the Mahatma Gandhi Institute of Medical

Sciences. There will be no penalty, and your child won't lose any benefits your child receives now or has a right to receive.

What should you do if you want your child to stop taking part in the study?

If you child takes part in this research study and you want them to drop out, you should tell us. We will make sure that your child can stop the study.

Also, it is possible that we will have to ask your child to drop out of the study before they finish it. This could happen, for example, if your child develops a medical condition that requires treatment and prevents them from participating. If this happens, we will tell you why and help you arrange care for your child if needed.

Will you or your child be paid to take part in this research study?

You and your child will not be paid for taking part in this research study.

What will you have to pay for if your child takes part in this research study?

There will be no costs for you to participate. You will not be charged for any of the study activities.

What happens if your child is injured while taking part in the research study?

This research study involves very safe procedures, and we don't anticipate that your child will be harmed as a result of participating. However, injuries sometimes happen in research even when no one is at fault. There are no plans to pay you or your child or give you other compensation for an injury, should one occur. However, you or your child are not giving up any of your legal rights by agreeing to participate in this study.

If you think your child has been injured or has experienced a medical problem as a result of taking part in this research study, tell the person in charge of this study as soon as possible. This person's name and phone number are listed on the first page of this form.

If your child takes part in this research study, how we will we protect your child's privacy?

Federal laws of India and the USA require us at the Mahatma Gandhi Institute of Medical Sciences and Partners Healthcare to protect the privacy of health information and related information that identifies you.

In this study we will collect identifiable information from your child from the research procedures described above, including tests and questionnaires.

The following entities may see, use, or share your child's identifiable information:

- Researchers and staff at Mahatma Gandhi Institute of Medical Sciences and Partners Healthcare involved in this study.
- The sponsor of this study or people or groups who are hired by them to audit the research
- Other researchers at other institutions involved in this study
- Members of the ethics board of Mahatma Gandhi Institute of Medical Sciences and Partners Healthcare overseeing this research
- Federal agencies in India or the USA that oversee, evaluate, and audit research

Mahatma Gandhi Institute of Medical Sciences
Partners Healthcare
Research Consent Form
Version Date: June 23, 2020

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- Public health or safety authorities, if we learn information that could mean harm to your child or others (for example, we are required to make reports about child abuse)

Because research is an ongoing process, we cannot give you an exact date when we will either destroy or stop sharing your child's identifiable information. Your permission to use this information does not expire.

The results of this research study may be published in a medical book or journal, or used to teach others. However, your child's name or other identifiable information will not be used for these purposes.

Your Child's Privacy Rights

You have the right to not agree to participate in this research. You have the right to not sign this form. However, if you don't sign it, your child can't take part in the research study.

You have the right to withdraw your permission for us to use or share your child's identifiable information. If you want to withdraw your permission, you must notify the person in charge of this study listed at the start of this form. If you withdraw your permission, your child cannot continue in the study. If you withdraw your permission, we will not be able to take back information that has already been used or shared, and this information may continue to be used for certain purposes, such as to comply with the law or to maintain the reliability of the study.

Informed Consent and Authorization:

Statement of Person Giving Informed Consent and Authorization

- I have read this consent form or had it read aloud to me
- This research study has been explained to me, including risks and possible benefits, procedures, and other important things about the study
- I have had the opportunity to ask questions
- I understand the information given to me.

Signature of Parent/Guardian of Child

I give my consent for my child to take part in this research study and agree to allow his/her health information to be used and shared as described above.

_____ _____

Parent(s)/Guardian for Child Date

Signature of Study Doctor or Person Obtaining Consent:

Statement of Study Doctor or Person Obtaining Consent

- I have explained the research to the parent(s)/guardian and child.
- I have answered all questions about this research study to the best of my ability.
- I am fluent in the preferred language of the parent/guardian and have conducted this conversation in that language

_____ _____

Study Doctor or Person Obtaining Consent Date

An Individualized Approach to Promote Nurturing Care in Low- and Middle-Income Countries: A Hybrid Effectiveness/Implementation Trial of the International Guide for Monitoring Child Development

FORM VERSION 1.0, 6/18/2020

Sociodemographic data collection form: Guatemala

Subject ID Code					
1. General Information					
1.1	**Interview date**	**dd**	**mm**	**yr**	
1.2	**District**				
1.3	**Village**				
1.4	**Sector**				
1.5	**Interviewer Code**				
1.6	**Caregiver Name**	**Name** **Last Name**			
1.7	**Mark X if Caregiver not the Mother**				
1.8	**Caregiver's Common Name**	**Name** **Last Name**			
1.9	**Caregiver´s relationship to the child**	**Grandmother=1** **Aunt=2** **Sister older than 18 =3** **Father =4** **Other =5**			
1.10	**Telephone**				
1.11	**Physiological state**	**1-Pregnant | 2-Lactating** **3-Both | 4-Neither**			
1.12	**Preferred Language**	**1-Kaqchikel | 2-K'iche'** **3-Spanish | 6-Other (note)**			
2. Child's Data					

2.1 Name and Last Name	**2.2 Sex**	**2.3 Birthdate** (verify)	**2.4 Age** (mm)

An Individualized Approach to Promote Nurturing Care in Low- and Middle-Income Countries: A Hybrid Effectiveness/Implementation Trial of the International Guide for Monitoring Child Development

FORM VERSION 1.0, 6/18/2020

	1 Masculine 2 Feminine	**dd**	**mm**	**yr**	

Notes on house location:

_____

_____

_____

_____

An Individualized Approach to Promote Nurturing Care in Low- and Middle-Income Countries: A Hybrid Effectiveness/Implementation Trial of the International Guide for Monitoring Child Development

FORM VERSION 1.0, 6/18/2020

3. PRENATAL AND POSTNATAL BACKGROUND OF THE CHILD			
3.1	What is [NAME]order of birth? (1st child, 2nd child, etc.)		
3.2	During [NAME] 's pregnancy, did you have prenatal care? **1** Yes **0** No		
3.3	How many months pregnant were you when [NAME] was born?		
3.4	Was [NAME] born before the due date? **1** Yes **0** No • *p 3.6*		
3.5	How many weeks before the due date?		
3.6	Was [NAME] born after the due date? **1** Yes **0** No •*p.3.8*		
3.7	How many weeks after the due date?		
3.8	How many pounds and ounces, did [NAME] weigh when he or she was born? 99 Don´t Know	**Lb**	**Oz**
3.9	Did you have any problems or complications during the delivery? **1** Yes **0** No • *p 3.11*		

3.10	What complications did you have during your delivery? **1** Yes **0** No								
	A	Infection		C	It took a long time		E	The fluid ran out	
	B	Hemorrhage		D	Did not descend		F	Other_____	

3.11	Did [NAME] have a problem or complication after he or she was born? **1** Yes **0** No •*3.12*								
3.12	What complications did your child have after he was born? **1** Yes **0** No								
	A	Born very purple		C	Needed antibiotics		E	Needed light therapy	

An Individualized Approach to Promote Nurturing Care in Low- and Middle-Income Countries: A Hybrid Effectiveness/Implementation Trial of the International Guide for Monitoring Child Development

FORM VERSION 1.0, 6/18/2020

	B	Need an oxygen tube		D	Needed transfusions		F	Other _____	

4. FAMILY HISTORY	
4.1 Are you currently?	|___| Code 1= Single 2= Married/living together; 3=divorce/separated 4=widow 9= does not know /does not answer
4.2 How old are you? (if not the mother, *p. 4.3*)	
4.3. How old is the [NAME]'s mother?	
4.4 Can you read and write?	|___| (Code 1=Only read 2=Only write 3=Yes both 4= No 9=Does not know /does not answer
4.5 What is your highest year of education?	|___| (Code) 1 None 2 Elementary or less 3 Middle High 4 High School 9= does not known /does not answer
4. 6 Is there any child under 5 years of age in this house?	|___| (Code 1=yes 2=no 9= does not know /does not answer

An Individualized Approach to Promote Nurturing Care in Low- and Middle-Income Countries: A Hybrid Effectiveness/Implementation Trial of the International Guide for Monitoring Child Development

FORM VERSION 1.0, 6/18/2020

4.7 If yes, how many?	
4.8 What is the mother/primary caregiver's occupation?	

5. QUICK POVERTY SCORE		
5.1	How many members does the household have? **1** Eight or more **2** Seven **3** Six **4** Five **5** Four **6** Three **7** Two One	
5.2	How many rooms does the household use (excluding kitchen, bathrooms, hallways, garages, or rooms used only for business)? **1** One **2** Two **3** Three **4** Four or more	
5.3	What type of toilet arrangement does the household have? **1** Latrine, covered pit or none **2** Hand-pour toilet, or toilet connected to septic tank or sewer system	
5.4	Is there a refrigerator in the home? **1** Yes **0** No	
5.5	Is there a gas or electric stove in the home? **1** Yes **0** No	
5.6	Do you own or have access to a blender? **1** Yes **0** No	
5.7	Is there an electric iron in the home? **1** Yes **0** No	
5.8	Does the household have cellular-phone service? **1** Yes **0** No	
5.9	Does the household possess, own, or have access to a television with cable service? **1** No **2** Only television (without cable) **3** Cable (regardless of television)	
5.10	Does the household possess, own, or have access to a bicycle, motorcycle or scooter/moped, or passenger car, pick up, van, minivan, SUV, or truck? **1** No **2** Only bicycle (without others) **3** Motorcycle or scooter/moped (without car etc., and regardless of bicycle) **4** Car, pick up, van, minivan, SUV, truck	

6.WATER ACCESS

An Individualized Approach to Promote Nurturing Care in Low- and Middle-Income Countries: A Hybrid Effectiveness/Implementation Trial of the International Guide for Monitoring Child Development

FORM VERSION 1.0, 6/18/2020

6.1	What is currently the **primary source** of drinking water for your household?	1…Piped water (inside home or land) 2…Stand pipe 3…Borehole/tubewell 4…Protected dug well 5…Unprotected dug well 6…Protected spring 7…Unprotected spring 8…Rainwater collection 9…Small water vendor 10…Tanker truck 11…Bottled water 12…Bagged/sachet water 13…Surface water (pond, river, lake) 14…Other person _____ 15…Other_____ 99-does not know/does not answer
6.2	How long (in minutes) does it take to go to the water source, get water and come back (including wait time)? *(If water source is in household/compound, record 00 minutes)*	_____ minutes
6.3	What is the primary way that your household treats your **drinking** water?	1…Do not treat it 2…Boil 3…Filter 4…Add chemicals 5…Other (Specify): 99. Does not know/ does not answer

7. FOOD INSECURITY EXPERIENCE SCALE		
7.1	You or others in your household worried about not having enough food to eat because of a lack of money or other resources? **1** Yes **0** No **2** Don't know **3** Refused	
7.2	Still thinking about the last 12 MONTHS, was there a time when you or others in your household were unable to eat healthy and nutritious food because of a lack of money or other resources? **1** Yes **0** No **2** Don't know **3** Refused	

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7.3	Was there a time when you or others in your household ate only a few kinds of foods because of a lack of money or other resources? **1** Yes **0** No **2** Don't know **3** Refused	
7.4	Was there a time when you or others in your household had to skip a meal because there was not enough money or other resources to get food? **1** Yes **0** No **2** Don't know **3** Refused	
7.5	Still thinking about the last 12 MONTHS, was there a time when you or others in your household ate less than you thought you should because of a lack of money or other resources ? **1** Yes **0** No **2** Don't know **3** Refused	
7.6	Was there a time when your household ran out of food because of a lack of money or other resources ? **1** Yes **0** No **2** Don't know **3** Refused	
7.7	Was there a time when you or others in your household were hungry but did not eat because there was not enough money or other resources for food? **1** Yes **0** No **2** Don't know **3** Refused	
7.8	Was there a time when you or others in your household went without eating for a whole day because of a lack of money or other resources? **1** Yes **0** No **2** Don't know **3** Refused	

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Sociodemographic data collection form: India

Subject ID Code					
1. General Information					
1.1	**Interview date**	**dd**	**mm**	**yr**	
1.2	**District**				
1.3	**Village**				
1.4	**Sector**				
1.5	**Interviewer Code**				
1.6	**Caregiver Name**	**Name** **Last Name**			
1.7	**Mark X if Caregiver not the Mother**				
1.8	**Caregiver's Common Name**	**Name** **Last Name**			
1.9	**Caregiver´s relationship to the child**	**Grandmother=1** **Aunt=2** **Sister older than 18 =3** **Father =4** **Other =5**			
1.10	**Telephone**				
1.11	**Physiological state**	**1-Pregnant | 2-Lactating** **3-Both | 4-Neither**			
1.12	**Preferred Language**	**1- Marathi | 2-English** **3-Other (note)**			
2. Child's Data					
2.1 Name and Last Name		**2.2 Sex**	**2.3 Birthdate** (verify)		**2.4 Age** (mm)

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	1 Masculine 2 Feminine	**dd**	**mm**	**yr**	

Notes on house location:

_____

_____

_____

_____

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3. PRENATAL AND POSTNATAL BACKGROUND OF THE CHILD			
3.1	What is [NAME]order of birth? (1st child, 2nd child, etc.)		
3.2	During [NAME] 's pregnancy, did you have prenatal care? **1** Yes **0** No		
3.3	How many months pregnant were you when [NAME] was born?		
3.4	Was [NAME] born before the due date? **1** Yes **0** No • *p 3.6*		
3.5	How many weeks before the due date?		
3.6	Was [NAME] born after the due date? **1** Yes **0** No •*p.3.8*		
3.7	How many weeks after the due date?		
3.8	How many pounds and ounces, did [NAME] weigh when he or she was born? 99 Don´t Know	**Lb**	**Oz**
3.9	Did you have any problems or complications during the delivery? **1** Yes **0** No • *p 3.11*		

3.10	What complications did you have during your delivery? **1** Yes **0** No								
	A	Infection		C	It took a long time		E	The fluid ran out	
	B	Hemorrhage		D	Did not descend		F	Other_____	
3.11	Did [NAME] have a problem or complication after he or she was born? **1** Yes **0** No •*3.12*								
3.12	What complications did your child have after he was born? **1** Yes **0** No								
	A	Born very purple		C	Needed antibiotics		E	Needed light therapy	

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	B	Need an oxygen tube		D	Needed transfusions		F	Other _____	

4. FAMILY HISTORY	
4.1 Are you currently?	|___| Code 1= Single 2= Married/living together; 3=divorce/separated 4=widow 9= does not know /does not answer
4.2 How old are you? (if not the mother, *p. 4.3*)	
4.3. How old is the [NAME]'s mother?	
4.4 Can you read and write?	|___| (Code 1=Only read 2=Only write 3=Yes both 4= No 9=Does not know /does not answer
4.5 What is your highest year of education?	|___| (Code) 1 None 2 Elementary or less 3 Middle High 4 High School 9= does not known /does not answer
4. 6 Is there any child under 5 years of age in this house?	|___| (Code 1=yes 2=no 9= does not know /does not answer

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4.7 If yes, how many?	
4.8 What is the mother/primary caregiver's occupation?	

5. QUICK POVERTY SCORE		
5.1	How many members does the household have? **1** Eight or more **2** Seven **3** Six **4** Five **5** Four **6** Three **7** Two One	
5.2	What is the general education level of the female head/spouse? **1** Primary or below, or not literate **2** Middle **3** Secondary or higher **4** No female head/spouse	
5.3	Does the house possess a refrigerator? **1** Yes **0** No	
5.4	Does the house possess a stove/gas burner **1** Yes **0** No	
5.5	Does the house possess a pressure cooker/pressure pan? **1** Yes **0** No	
5.6	Does the house possess a television? **1** Yes **0** No	
5.7	Does the house possess an electric fan? **1** Yes **0** No	
5.8	Does the household possess an almirah/dressing table? **1** Yes **0** No	
5.9	Does the household possess a chair, stool, bench, or table? **1** Yes **0** No	
5.10	Does the household possess a motorcycle, scooter, motor car, or jeep? **1** Yes **0** No	

6.WATER ACCESS		
6.1	What is currently the **primary source** of drinking water for your household?	1…Piped water (inside home or land) 2…Stand pipe 3…Borehole/tubewell 4…Protected dug well 5…Unprotected dug well 6…Protected spring 7…Unprotected spring 8…Rainwater collection 9…Small water vendor

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		10…Tanker truck 11…Bottled water 12…Bagged/sachet water 13…Surface water (pond, river, lake) 14…Other person _____ 15…Other_____ 99-does not know/does not answer
6.2	How long (in minutes) does it take to go to the water source, get water and come back (including wait time)? *(If water source is in household/compound, record 00 minutes)*	_____ minutes
6.3	What is the primary way that your household treats your **drinking** water?	1…Do not treat it 2…Boil 3…Filter 4…Add chemicals 5…Other (Specify): 99. Does not know/ does not answer

7. FOOD INSECURITY EXPERIENCE SCALE		
7.1	You or others in your household worried about not having enough food to eat because of a lack of money or other resources? **1** Yes **0** No **2** Don't know **3** Refused	
7.2	Still thinking about the last 12 MONTHS, was there a time when you or others in your household were unable to eat healthy and nutritious food because of a lack of money or other resources? **1** Yes **0** No **2** Don't know **3** Refused	
7.3	Was there a time when you or others in your household ate only a few kinds of foods because of a lack of money or other resources? **1** Yes **0** No **2** Don't know **3** Refused	
7.4	Was there a time when you or others in your household had to skip a meal because there was not enough money or other resources to get food? **1** Yes **0** No **2** Don't know **3** Refused	
7.5	Still thinking about the last 12 MONTHS, was there a time when you or others in your household ate less than you thought you should because of a lack of money or other resources ? **1** Yes **0** No **2** Don't know **3** Refused	

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7.6	Was there a time when your household ran out of food because of a lack of money or other resources ? **1** Yes **0** No **2** Don't know **3** Refused	
7.7	Was there a time when you or others in your household were hungry but did not eat because there was not enough money or other resources for food? **1** Yes **0** No **2** Don't know **3** Refused	
7.8	Was there a time when you or others in your household went without eating for a whole day because of a lack of money or other resources? **1** Yes **0** No **2** Don't know **3** Refused	

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WHO Feeding Indicators

BREASTFEEDING AND COMPLEMENTARY FEEDING								
1	In his/her life, has your child ever nursed? **1** Yes **0** No • *p9.6*							
2	Is [NAME] still nursing now? **1** Yes **0** No							
3	How old was your child when he/she stopped nursing? **99** still nursing						**Months**	
4	Did [NAME] nurse yesterday during the day or at night? **1** Yes **0** No • *p9.7*							
5	How many times did your child nurse during yesterday during the day and at night?						**day**	**night**
6	In general, how many minutes does your child nurse (at each breast) every time you let him/her breastfeed?						**right**	**left**
7	How old was your child when you started giving him/her foods other than breastmilk?						**Months**	
8	Now I want to ask about some liquids that [NAME] perhaps drank yesterday during the day and at night.							
	Liquid		**1** Yes **0** No	How many times?	Liquid		**1** Yes **0** No	How many times?
	A	Water			G	Water with sugar		
	B	Milk (from a cow or another animal) or powdered milk (Nido, Delactomy...)			H	Corn flour or oat based drink such as incaparina, vitacereal, masa, mosh, corazón de trigo		
	C	Infant formula (NAN, enfamil...)			I	Sodas/soft drinks		

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<table>
<tr><td></td><td>D</td><td>Homemade soup or instant soup from the store (Mahler…)</td><td></td><td></td><td>J</td><td>Coffee, pinol, corazón de trigo, tea, maicena, tortilla water</td><td></td><td></td></tr>
<tr><td rowspan="3"></td><td>E</td><td>Natural juice or juice from the store</td><td></td><td></td><td rowspan="2">K</td><td rowspan="2">Soup broth from bean, leaf green, vegetable, beef, chicken or another kind of soup</td><td rowspan="2"></td><td rowspan="2"></td></tr>
<tr><td>F</td><td>Natural fruit drinks or from the store packets</td><td></td><td></td></tr>
<tr><td>9</td><td colspan="8"><u>A. Explain the Question:</u>

“Now I am going to ask you about what [NAME] ate yesterday. Think about yesterday morning when [NAME] woke up. Did she/he eat anything? Please tell me everything that she/he ate." (keep asking until she answers nothing else)

You can use these questions to elicit more information from the mother:

“What did she/he do after that? Did she/he eat anything? Please tell me everything that she/he ate. Anything else?” (keep repeating the question until the mother says that her child went to sleep for the night)

If the mother mentions a food that consists of different parts, like a soup, ask: “ What were the ingredients in [the food]?”

<u>B. Underline:</u> In the boxes below underline all the foods that the mother mentions while she speaks.

<u>C. Mark yes and the number of times:</u> If the mother mentions a food, mark yes for the category it belongs in and write the number of times that the child ate something in that category, adding a tally each time she mentions a food in that category.

<u>D. Review unmentioned categories:</u>

When the mother says that the child didn’t eat anything else, review the unmentioned categories. “Yesterday during the day and night did [NAME] eat [UNMENTIONED CATEGORY]?” Underline and mark yes if she mentions another food.

ATTENTION!: You should not read the categories, only solicit the record of what the child ate yesterday from when he/she woke up to when he/she went to bed. Neither should you ask about specific meals (for example you should not say “What did he/she eat for breakfast yesterday?”</td></tr>
</table>

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#	TYPES OF FOOD	**1** Yes **0** No	How many times?
A	• Bread, rice, pasta, tortillas, tamalitos, tamales, corn on the cob, Cornflakes, or any other food made from wheat or corn • Potato, cassava, plantain		
B	• Carrot, güicoy, pumpkin, squash, sweet potato • Any leafy green (chipilín, hierba mora, quilete, spinach) or dark green vegetable (broccoli) • Mango, papaya, orange, peach, bell pepper, melon (with vitamin A), tomato (if it is more than a condiment)		
C	Other fruit or vegetable (banano, green bean, strawberry, chayote, green tomato, mushroom, apple, blackberry, cucumber, pineapple, radish, cabbage, watermelon or other)		
D	• Organ meats or entrails (liver, kidney, intestine, heart, gizzard, feet...) • Chicken, beef, rabbit, pork, duck, goat • Fish, seafood (fresh)		
E	Egg		
F	Beans (any color), lentils, peas, nuts, seeds, peanuts		
G	Yogurt, cheese		
H	Oil, lard, butter, cream, or another kind of fat		
I	Any food with added sugar such as chocolate, sweets, desserts, cookies, cakes		
J	Condiments for flavor such as chili, tomato, onion, greens, dried fish		
10	*If there was not consumption of any category, ask:* "Yesterday during the day and night did [NAME] eat any solid, semi-solid or soft (like puree) food? **1** Yes..... *ask* "Like what?" *and write above* **0** No		
11	Yesterday, how many times during the day and night did [NAME] eat solid, semi-solid or soft (like puree) foods (not liquids)? *Confirm*		

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	that this number is equal to what you wrote above for the questions about yesterday's diet.	
12	Yesterday, during the day and night, did [NAME] drink anything from a bottle? **1** Yes **0** No	

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Appendix B: Anthropometrics and Hemoglobin

ANTHROPOMETRY OF THE CHILD							
Subject ID Code							
Weight (kg)			**Length/Height (cm)**			**Position**	**Code of person who measures**
		.			.	**1** Laying **2** Standing	
		.			.		
		.			.		

Hemoglobin value g/dL		
Registered value by Hemocue		

PARTNERS HUMAN RESEARCH COMMITTEE
PROTOCOL SUMMARY

Answer all questions accurately and completely in order to provide the PHRC with the relevant information to assess the risk-benefit ratio for the study. Do not leave sections blank.

PRINCIPAL/OVERALL INVESTIGATOR

Peter Rohloff

PROTOCOL TITLE

An Individualized Approach to Promote Nurturing Care in Low and Middle Income Countries: A Hybrid Effectiveness/Implementation Trial of the International Guide for Monitoring Child Development

FUNDING

NIH/NICHD

VERSION DATE

6/29/2020

SPECIFIC AIMS

Concisely state the objectives of the study and the hypothesis being tested.

The aim of this study is to conduct a hybrid effectiveness/implementation assessment of the GMCD in two LMIC settings, India and Guatemala, within established rural CHW programs. The primary objectives are (a) to evaluate the real-world effectiveness of the GMCD; (b) to use an implementation science framework to understand barriers and facilitators to effective population coverage, provider implementation, and maintenance; (c) to conduct an economic evaluation of the GMCD.

BACKGROUND AND SIGNIFICANCE

Provide a brief paragraph summarizing prior experience important for understanding the proposed study and procedures.

In low and middle-income countries (LMICs), over 40% of children under age five are at risk of not reaching their developmental potential, primarily due to poverty and undernutrition. The most recent 2010 estimate puts the number at risk at 249 million, minimally improved from 279 million in 2004. This has profound implications for LMICs, in terms of lost human capital and increased costs to the health and education sectors. The World Health Organization and UNICEF have launched the Nurturing Care Framework, which calls for health and other social systems to support caregivers to optimize children's development potential. Preliminary data shows this strategy can improve outcomes, and caregiver support interventions can be implemented by community health workers (CHWs). However, major evidence gaps remain for CHW- led interventions, particularly regarding how early child development (ECD) implementations can be effective and sustainable across diverse systems and contexts.

In 2016, the International Guide for Monitoring Child Development (GMCD), a monitoring and intervention package developed with NIH funding to address ECD in LMICs, became available. The GMCD intervention uses validated developmental milestones conserved across LMIC populations, tailored communication, and nurturing care guidance for caregivers to promote ECD. Recent external evaluations rate the GMCD as the highest-performing instrument for monitoring the development of individual children

in LMICs, and it has excellent sensitivity and specificity for early identification of developmental difficulties. The next phase of needed research is therefore to examine the effectiveness and costs of the GMCD deployed in the real-world settings where it is likely to have the most impact, namely community-based interventions led by CHWs.

RESEARCH DESIGN AND METHODS

Briefly describe study design and anticipated enrollment, i.e., number of subjects to be enrolled by researchers study-wide and by Partners researchers. Provide a brief summary of the eligibility criteria (for example, age range, gender, medical condition). Include any local site restrictions, for example, "Enrollment at Partners will be limited to adults although the sponsor's protocol is open to both children and adults."

This is a nonblinded, two-arm cluster randomized controlled trial of the international Guide for Monitoring Child Development (GMCD) intervention. We plan to enroll 624 child participants (312 in India and 312 in Guatemala, 13 control and 13 intervention clusters per site, 12 individuals per cluster). Subjects will be recruited from participating clusters (health centers or service delivery organizations) in rural India and Guatemala affiliated with Maya Health Alliance (Guatemala) or the Mahatma Gandhi Institute of Medical Sciences (India).

Eligibility criteria for the trial are: Age 0-24 months at the time of enrollment visit, and receiving health services from frontline health workers of Maya Health Alliance (Guatemala), Mahatma Gandhi Institute (India) or their local partners.

Exclusion criteria for the trial are: Children who are critically ill and are judged by the frontline health worker to require hospitalization or center based care; children whose caregivers do not provide informed consent for the study.

The study will also involve focus groups and in-depth interviews with 150-200 stakeholders and frontline workers involved in the implementation of the study, to gain insights into barriers and facilitators to implementation.

Briefly describe study procedures. Include any local site restrictions, for example, "Subjects enrolled at Partners will not participate in the pharmacokinetic portion of the study." Describe study endpoints.

Subjects from intervention clusters will receive the GMCD intervention, delivered in monthly visits to the home by frontline health workers. Subjects in control clusters will continue to receive usual care from their frontline health workers. After 12 months, control clusters will cross into the intervention, and all subjects in all clusters will receive the GMCD intervention for an additional 12 months. Each GMCD visit includes assessment of risk factors, open-ended exploration of caregiver concerns about development, assessment of functioning in seven developmental domains, and using mutual problem solving strategies to develop a nurturing care plan with the caregiver.

For studies involving treatment or diagnosis, provide information about standard of care at Partners (e.g., BWH, MGH) and indicate how the study procedures differ from standard care. Provide information on available alternative treatments, procedures, or methods of diagnosis.

There is considerable interest in using existing networks of frontline health workers and community health workers in low-resource settings to provide early child development interventions. However, there is no international consensus on standard of care, and in the two study sites here, there is no local standard

of care for providing early child development services. These services will be added, as part of this intervention, to existing community health worker workflows, which are mostly focused on monitoring child growth and nutrition.

Describe how risks to subjects are minimized, for example, by using procedures which are consistent with sound research design and which do not unnecessarily expose subjects to risk or by using procedures already being performed on the subject for diagnostic or treatment purposes.

This project involves a minimal risk intervention to improve nurturing care for children at risk of delayed development. Data collection in studies visits involves primarily the use of observational instruments (sociodemographic surveys, psychometric instruments), as well as the collection of noninvasive anthropometric data. The only invasive procedure will be collection of a capillary blood specimen for hemoglobin analysis. This procedure involves rare risk of infection. Proper infection prevention and control precautions will be implemented to reduce the risk of infection.

Describe explicitly the methods for ensuring the safety of subjects. Provide objective criteria for removing a subject from the study, for example, objective criteria for worsening disease/lack of improvement and/or unacceptable adverse events. The inclusion of objective drop criteria is especially important in studies designed with placebo control groups.

The trial is of not more than minimal risk and, therefore, no adverse events related to trial participation are anticipated. However, any possible adverse events, as well as complaints or perceived adverse events from participating communities or caregivers will be tracked by the investigator team and reported to IRB and granting authorities. The study will not employ stopping rules or a Data Safety Monitoring Board. A detailed description of procedures the PI and Study Team will use to monitor safety is given in the Detailed Protocol.

In addition, Linkages to Care for all participating subjects will be closely maintained by collaboration with participating health centers. Details of plans for promoting this coordination and for facility any necessary medical referrals are outlined in the Detailed Protocol.

FORESEEABLE RISKS AND DISCOMFORTS

Provide a brief description of any foreseeable risks and discomforts to subjects. Include those related to drugs/devices/procedures being studied and/or administered/performed solely for research purposes. In addition, include psychosocial risks, and risks related to privacy and confidentiality. When applicable, describe risks to a developing fetus or nursing infant.

Complications of Procedures

Common Risks: During the capillary blood sample collection for hemoglobin assessment, there is some risk of temporary discomfort to the child.
Uncommon Risks: During the capillary blood sample collection for hemoglobin assessment, there is a rare risk of infection. Proper infection prevention and control precautions will be implemented to reduce the risk of infection. Infants experiencing an infection will be immediately referred to the local health clinic or hospital for treatment.

Psychosocial risks and Risks to Privacy:

Common Risks: For caregiver participants in the intervention, a primary risk is that of lost productivity or perceived interference with domestic routines and other responsibilities. This is

because the intervention involves monthly home visits for 2 years, as well as 3 study visits. We estimate that the study visits will last 120 minutes each. Each intervention home visit will also last an estimated 60 minutes. For stakeholders and healthcare workers participating in interviews, a risk is they may feel compelled to participate because of fear of repercussions for not participating from their employer.
Uncommon Risks: These include psychological stress to caregivers, primarily from discussing with health workers matters related to any potential or observed developmental delays in their children. Finally, there is the rare risk of accidental disclosure of personal identifiable or confidential data.

EXPECTED BENEFITS

Describe both the expected benefits to individual subjects participating in the research and the importance of the knowledge that may reasonably be expected to result from the study. Provide a brief, realistic summary of potential benefits to subjects, for example, "It is hoped that the treatment will result in a partial reduction in tumor size in at least 25% of the enrolled subjects." Indicate how the results of the study will benefit future patients with the disease/condition being studied and/or society, e.g., through increased knowledge of human physiology or behavior, improved safety, or technological advances.

Stakeholder participants will benefit mostly indirectly from this project by helping to improve implementation knowledge around early child development interventions. However, they may also benefit directly from a greater sense of empowerment and job satisfaction.

Frontline workers delivering the intervention may benefit directly through a greater sense of empowerment and job satisfaction. They will also receive advanced training in the assessment and promotion of early child development hypertension, directly advancing their professional development.

Children and caregivers in the clinical trial in both control and intervention arms will benefit from access to a panel of developmental tests which they otherwise may not have access to. Results of these tests will be made available to each subject in a format that they can share with their primary care providers, directly contributing to their usual medical care. In addition, subjects with concerning incidental or abnormal findings will receive assistance from the study team in referrals to care. Subjects and caregivers in the intervention arm (and in the control/delayed-intervention arm after 12 months) will in addition receive intensive individualized support to promote early child development.

The information gained through this project will contribute measures of the clinical effectiveness and important insights into the implementation of early child development interventions by frontline workers in rural Guatemala and India. This well controlled trial will foster broader dissemination of the international Guide for Monitoring Child Development and individualized approaches to fostering nurturing care in Guatemala, India and globally.

EQUITABLE SELECTION OF SUBJECTS

The risks and benefits of the research must be fairly distributed among the populations that stand to benefit from it. No group of persons, for example, men, women, pregnant women, children, and minorities, should be categorically excluded from the research without a good scientific or ethical reason to do so. Please provide the basis for concluding that the study population is representative of the population that stands to potentially benefit from this research.

This study will enroll rural inhabitants of two study sites in India and Guatemala. In both sites, rural communities will be randomized to intervention or to control and then children within each will be randomly selected to participated in study procedures. Exclusion criteria are designed only to identify

those children with severe medical illness (such as acute malnutrition) for whom participation would not be appropriate. Otherwise all children within study communities are equally eligible to participate. In addition, in a cross-in phase after 12 months, control communities/children will receive access to the intervention, allowing all study participants to receive the intervention by the end of the study.

When people who do not speak English are excluded from participation in the research, provide the scientific rationale for doing so. Individuals who do not speak English should not be denied participation in research simply because it is inconvenient to translate the consent form in different languages and to have an interpreter present.

Participants in the study will be Marathi or English speakers (in India) and Spanish or Kaqchikel/K'iche' Maya speakers (in Guatemala). Study staff will all be bilingual in these languages, and no one will be excluded from the study based on preferred languages. Detailed study procedures are in place to ensure that all study procedures and instruments are equally available in the preferred language of all participants (see Detailed Protocol)

For guidance, refer to the following Partners policy:
Obtaining and Documenting Informed Consent of Subjects who do not Speak English
https://www.partners.org/Assets/Documents/Medical-Research/Clinical-Research/Non-English-Speaking-Subjects.pdf

RECRUITMENT PROCEDURES

Explain in detail the specific methodology that will be used to recruit subjects. Specifically address how, when, where and by whom subjects will be identified and approached about participation. Include any specific recruitment methods used to enhance recruitment of women and minorities.

At the beginning of the study, the 52 clusters (26 in India and 26 in Guatemala, corresponding to individual clinics or similar administrative units) will be randomly allocated in a 1:1 ratio to one of 2 study arms: immediate intervention or delayed intervention after 12 months (control). Once the clusters have been assigned to a study arm, a list of eligible children will be provided to the research team by frontline workers within each cluster. In order to retain a representative distribution of age ranges, recruitment will be stratified by age. The children will be randomly ordered on the list and the first 6 children in separate families in each age category (0-12 months and 13-24 months, n=12 per cluster in total) will be approached for enrollment. We will enroll only 1 child per family for data collection in this study. Although other eligible children in the family will receive the intervention, data on endpoints will only be collected on enrolled children. Similarly, we will include children who are twins or multiple births in the intervention, but only the enrolled twin will have endpoint data collected.

Subjects will be recruited from participating clusters (health centers or service delivery organizations) in rural India and Guatemala affiliated with Maya Health Alliance (Guatemala) or the Mahatma Gandhi Institute of Medical Sciences (India). Subjects will be recruited from lists of families and children currently engaged in usual care with participating frontline health workers, and they will continue to access this care throughout the study

For potential participants in the clinical trial, research staff will pragmatically solicit lists of eligible families/children from participating frontline workers and their institutions. Recruitment staff will consist

of full-time research study nurses in each site. Research nurses will work with frontline health workers to enroll children in the study. They will join the frontline health worker at enrollment home visits, confirm eligibility, explain the study, and solicit written informed consent. They will explain that caregivers in both intervention and control groups can continue or initiate standard care from any organizations or frontline worker throughout the study. These recruitment activities will be supplemented with phone calls or additional home visits, as needed, to resolve questions prior to obtaining consent.

Provide details of remuneration, when applicable. Even when subjects may derive medical benefit from participation, it is often the case that extra hospital visits, meals at the hospital, parking fees or other inconveniences will result in additional out-of-pocket expenses related to study participation. Investigators may wish to consider providing reimbursement for such expenses when funding is available

There will be no remuneration in this study.

For guidance, refer to the following Partners policies:

Recruitment of Research Subjects
https://www.partners.org/Assets/Documents/Medical-Research/Clinical-Research/Recruitment-Of-Research-Subjects.pdf

Guidelines for Advertisements for Recruiting Subjects
https://www.partners.org/Assets/Documents/Medical-Research/Clinical-Research/Guidelines-for-Advertisements.pdf

Remuneration for Research Subjects
https://www.partners.org/Assets/Documents/Medical-Research/Clinical-Research/Remuneration-for-Research-Subjects.pdf

CONSENT PROCEDURES

Explain in detail how, when, where, and by whom consent is obtained, and the timing of consent (i.e., how long subjects will be given to consider participation). For most studies involving more than minimal risk and all studies involving investigational drugs/devices, a licensed physician investigator must obtain informed consent. When subjects are to be enrolled from among the investigators' own patients, describe how the potential for coercion will be avoided.

Informed consent from caregivers

A detailed informed consent script will be used to obtain informed consent from caregivers of participating children. The details of obtaining consent will differ in Guatemala and India, based on guidance from each local IRB and local norms.

In Guatemala, at the informed consent visit, the study staff member will explain the study verbally, following the informed consent script, which covers all standard aspects of informed consent. Signed informed consent is generally not culturally appropriate in this study region, given a legacy of historical trauma and discrimination against indigenous populations and low levels of literacy. During the Guatemalan civil war, individuals who were not literate could be made to sign documents as an oppressive strategy for extracting land titles. This study will not replicate those potentially traumatic practices. All consent procedures will occur in the language of the participant's choosing. Research staff in Guatemala

will be natively fluent in Kaqchikel Maya, K'iche' Maya, and Spanish. However, the informed consent script text will only be produced in Spanish. This is because Mayan languages are largely spoken languages. This means that even most research staff cannot reasonably be expected to read Mayan languages, despite being fluent native speakers. In lieu of written documents in Mayan languages, extensive preparatory practice sessions will be used to ensure smooth contemporaneous translation from Spanish to Mayan languages. This is the method that the local partner Maya Health Alliance has used in the majority of its research studies for many years. Once verbal informed consent is given, the study staff member will record the date of oral consent on the informed consent script and provide a copy of the script (in Spanish) to the caregiver.

In India, at the informed consent visit, the study staff member will read the informed consent verbally, or the caregiver will be given time to read the document, according to preference. All consent procedures will occur in the language of the participant's choosing. Research staff in India will be natively fluent in Marathi and English. Informed consent documents will be available in Marathi and English. After reading the document, if the caregiver agrees to participate they will sign the consent document. A copy of the document will be given to the caregiver.

In both sites, the consent process will make it clear that informed consent to participate in the research will not in any way impact the quality or quantity of ongoing clinical services provided to the family by the local partners. Families that choose not to participate in the research study will still be eligible for other clinical services from the local partners.

After the consent script or document is reviewed, caregiver understanding of the information conveyed will be assessed using the teach-back method. The caregiver will be offered one week to consider enrollment and to discuss study participation/informed consent with other individuals that need to be involved in the decision. When appropriate based on family structure, verbal informed consent will be sought from multiple caregivers, but informed consent from one biological caregiver or legal caregiver will be considered adequate for study enrollment, as this study involves no more than minimal risk. Children in the study will be 0-24 months of age, and therefore they are not capable of providing assent.

Informed consent from healthcare workers and stakeholders

Verbal informed consent will be obtained from all stakeholders and frontline health workers participating in focus groups or interviews. This will include reading a consent script which explains the purpose of the study and specifically mentions that employment/employment review by their employer/institution or any other of the study partners is not conditional on participation in the study, and that there will be no repercussions for declining to participate. This consent discussion/script will occur in Spanish (in Guatemala all stakeholders speak Spanish natively), or in Marathi or English (in India, based on stakeholder preference)

NOTE: When subjects are unable to give consent due to age (minors) or impaired decision-making capacity, complete the forms for Research Involving Children as Subjects of Research and/or Research Involving Individuals with Impaired Decision-making Capacity, available on the New Submissions page on the PHRC website:
https://partnershealthcare.sharepoint.com/sites/phrmApply/aieipa/irb

For guidance, refer to the following Partners policy:
Informed Consent of Research Subjects:
https://www.partners.org/Assets/Documents/Medical-Research/Clinical-Research/Informed-Consent-of-Research-Subjects.pdf

DATA AND SAFETY MONITORING

Describe the plan for monitoring the data to ensure the safety of subjects. The plan should include a brief description of (1) the safety and/or efficacy data that will be reviewed; (2) the planned frequency of review; and (3) who will be responsible for this review and for determining whether the research should be altered or stopped. Include a brief description of any stopping rules for the study, when appropriate. Depending upon the risk, size and complexity of the study, the investigator, an expert group, an independent Data and Safety Monitoring Board (DSMB) or others might be assigned primary responsibility for this monitoring activity.

NOTE: Regardless of data and safety monitoring plans by the sponsor or others, the principal investigator is ultimately responsible for protecting the rights, safety, and welfare of subjects under his/her care.

The trial is of not more than minimal risk and, therefore, no adverse events related to trial participation are anticipated. However, any complaints or perceived adverse events from participating communities or caregivers will be tracked by the investigator team and reported to IRB and granting authorities using the above schedule. The study will not employ stopping rules or a Data Safety Monitoring Board.

Research staff in each participating recruitment site as well as frontline workers in both intervention and control clusters will be instructed to report in person or by telephone all complaints, protocol deviations, or unanticipated problems to the Primary Study Coordinator for each site on the same day that they are discovered. The Primary Study Coordinator will be charged with gathering necessary information from this initial report and contacting the Primary Site Co-Investigators and Principal Investigator.

As an unblinded trial of minimal risk, the PI will be the individual primarily charged with reviewing study progress and safety. The PI will review these data monthly together with the primary site Co-investigators and will provide reports to the reviewing IRBs every 12 months, which will include the report of any complaints or minor protocol deviations. Reports will provide additional information of reasons for trial dropout, adherences to eligibility criteria, reassessment of level of risk occasioned by participation in trial, and justification for study continuation versus early termination.

Describe the plan to be followed by the Principal Investigator/study staff for review of adverse events experienced by subjects under his/her care, and when applicable, for review of sponsor safety reports and DSMB reports. Describe the plan for reporting adverse events to the sponsor and the Partners' IRB and, when applicable, for submitting sponsor safety reports and DSMB reports to the Partners' IRBs. When the investigator is also the sponsor of the IND/IDE, include the plan for reporting of adverse events to the FDA and, when applicable, to investigators at other sites.

NOTE: In addition to the adverse event reporting requirements of the sponsor, the principal investigator must follow the Partners Human Research Committee guidelines for Adverse Event Reporting

As a not more than minimal risk study of a behavioral intervention, no AEs are anticipated and no planned

reporting schema other than logging and reporting of complaints, unanticipated problems, minor and major protocol deviations (as outlined in detailed protocol) are planned.

MONITORING AND QUALITY ASSURANCE

Describe the plan to be followed by the principal investigator/study staff to monitor and assure the validity and integrity of the data and adherence to the IRB-approved protocol. Specify who will be responsible for monitoring, and the planned frequency of monitoring. For example, specify who will review the accuracy and completeness of case report form entries, source documents, and informed consent.

NOTE: Regardless of monitoring plans by the sponsor or others, the principal investigator is ultimately responsible for ensuring that the study is conducted at his/her investigative site in accordance with the IRB-approved protocol, and applicable regulations and requirements of the IRB.

The PI will be assisted in review and reporting activities by the Primary Study Coordinators and primary site Co-Investigators. A summary of review/reporting activities is outlined below. Furthermore review of the rate of subject accrual and compliance with inclusion/exclusion criteria will occur monthly during the recruitment phase, to ensure sufficient enrolment and that they meet eligibility criteria. The PI will be responsible for conducting this review, with assistance from the Primary Study Coordinator and primary Site Coinvestigators in each site.

Data type	**Frequency of review**	**Reviewer**
Subject accrual, compliance with consent and enrolment protocols	Monthly	PI
	Every 12 months	IRBs
Status of all enrolled subjects	Monthly	PI
	Every 12 months	IRBs
Data entry and quality control checks on 10% of study visits and other study data/subject charts	Weekly	Primary Study Coordinator
Adherence data: study visits and intervention	Monthly	PI
	Every 12 months	IRBs
Complaints or Other Feedback from Study Participants and Communities; Minor Protocol Deviations	Per Occurrence	PI
	Every 12 months	PI
Major Protocol Deviations	Per Occurrence	PI, IRBs, NIH
Unanticipated Problems	Per Occurrence	PI, IRBs, NIH

For guidance, refer to the following Partners policies:
Data and Safety Monitoring Plans and Quality Assurance
https://www.partners.org/Assets/Documents/Medical-Research/Clinical-Research/DSMP-in-Human-Subjects-Research.pdf

Reporting Unanticipated Problems (including Adverse Events)
https://www.partners.org/Assets/Documents/Medical-Research/Clinical-Research/Reporting-Unanticipated-Problems-including-Adverse-Events.pdf

PRIVACY AND CONFIDENTIALITY

Describe methods used to protect the privacy of subjects and maintain confidentiality of data collected. This typically includes such practices as substituting codes for names and/or medical record numbers; removing face sheets or other identifiers from completed surveys/questionnaires; proper disposal of printed computer data; limited access to study data; use of password-protected computer databases; training for research staff on the importance of confidentiality of data, and storing research records in a secure location.

NOTE: Additional measures, such as obtaining a Certificate of Confidentiality, should be considered and are strongly encouraged when the research involves the collection of sensitive data, such as sexual, criminal or illegal behaviors.

To protect confidentiality, the following steps will be taken: All paper research forms from research visits will be kept in locked file cabinets and will be available only to research staff directly involved in this project. Consent forms will be stored separately. All research forms will have a cover sheet that codes identifying information to a unique number. This number will be transcribed to an electronic spreadsheet, and the cover sheet will then be removed and destroyed.

The electronic spreadsheet will be maintained on a secure, cloud server (Dropbox) at Brigham and Women's Hospital, and only the PI and Principal Study Coordinators will have access to the key directly. Most data from study visits will be entered directly online into the REDCap database (hosted at Brigham and Women's Hospital). When necessary to use, data from paper forms will be double-entered into REDCap. All REDCap entries will be linked only to subject identifying numbers, and these will be stored separately from the key that identifies subjects. Once data extraction and cleaning has been completed, this key will be destroyed, and data in the analysis phase will be completely de-identified. Laptop computers and mobile devices used for data entry will be routinely backed-up and will be password-protected and full-disk encrypted.

All research staff will complete and provide proof of completion of appropriate human subjects protection training approved by their home institution.

SENDING SPECIMENS/DATA TO RESEARCH COLLABORATORS OUTSIDE PARTNERS

Specimens or data collected by Partners investigators will be sent to research collaborators outside Partners, indicate to whom specimens/data will be sent, what information will be sent,

and whether the specimens/data will contain identifiers that could be used by the outside collaborators to link the specimens/data to individual subjects.

During the data collection and early analysis phases, potentially identifiable research data will be shared between research collaborators at BWH, at Harvard Medical School, and the two local implementing organizations, Mahatma Gandhi Institute of Medical Sciences (India) and Maya Health Alliance (Guatemala). All data will be shared through access to Partners/BWH Enterprise Dropbox and Redcap applications only.

After data collection is complete and data cleaning has been completed, data will be deidentified with linked to unique study IDs, and access to identifiable data will be removed. Research collaborators at three additional institutions (Ankara University, Ummeed Child Development Center, University of Washington) will have access only to deidentified data.

Specifically address whether specimens/data will be stored at collaborating sites outside Partners for future use not described in the protocol. Include whether subjects can withdraw their specimens/data, and how they would do so. When appropriate, submit documentation of IRB approval from the recipient institution.

Identifiable paper data (including consent forms) will be maintained at the local partners in India and Guatemala through the publication of primary study reports and manuscripts, and for potential future follow-up analyses for at least 7 years. Electronic data will be maintained in Partners Applications (Redcap, Dropbox) for at least 7 years.

Individuals can request removal of their data from the subject by making a formal request either in writing or by phone/in person conversation to the local site Principal Investigator. This procedure is detailed in the informed consent document.

RECEIVING SPECIMENS/DATA FROM RESEARCH COLLABORATORS OUTSIDE PARTNERS

When specimens or data collected by research collaborators outside Partners will be sent to Partners investigators, indicate from where the specimens/data will be obtained and whether the specimens/data will contain identifiers that could be used by Partners investigators to link the specimens/data to individual subjects. When appropriate, submit documentation of IRB approval and a copy of the IRB-approved consent form from the institution where the specimens/data were collected.

All research data will be collected at the two local implementing organizations, Mahatma Gandhi Institute of Medical Sciences (India) and Maya Health Alliance (Guatemala). Identifiable data from these sites will be shared with Partners Investigators through upload to Partners Redcap or Dropbox. Redcap data forms will use unique subject study IDs. A key that identifies subjects through linking to subject IDs will be stored separately with access restricted to the study PI, site PI, or their research coordinator delegate

An Individualized Approach to Promote Nurturing Care in Low- and Middle-Income Countries: A Hybrid Effectiveness/Implementation Trial of the International Guide for Monitoring Child Development
DETAILED PROTOCOL: VERSION 1.1, 6/29/2020

BACKGROUND AND SIGNIFICANCE

In low and middle-income countries (LMICs), over 40% of children under age five are at risk of not reaching their developmental potential, primarily due to poverty and undernutrition. The most recent 2010 estimate puts the number at risk at 249 million, minimally improved from 279 million in 2004. This has profound implications for LMICs, in terms of lost human capital and increased costs to the health and education sectors. The World Health Organization and UNICEF have launched the Nurturing Care Framework, which calls for health and other social systems to support caregivers to optimize children's development potential. Preliminary data shows this strategy can improve outcomes, and caregiver support interventions can be implemented by community health workers (CHWs). However, major evidence gaps remain for CHW- led interventions, particularly regarding how early child development (ECD) implementations can be effective and sustainable across diverse systems and contexts.

In 2016, the International Guide for Monitoring Child Development (GMCD), a monitoring and intervention package developed with NIH funding to address ECD in LMICs, became available (1-2). The GMCD intervention uses validated developmental milestones conserved across LMIC populations, tailored communication, and nurturing care guidance for caregivers to promote ECD. Recent external evaluations rate the GMCD as the highest-performing instrument for monitoring the development of individual children in LMICs, and it has excellent sensitivity and specificity for early identification of developmental difficulties. The next phase of needed research is therefore to examine the effectiveness and costs of the GMCD deployed in the real-world settings where it is likely to have the most impact, namely community-based interventions led by CHWs.

In this study, we will conduct a hybrid effectiveness/implementation assessment of the GMCD in two LMIC settings, India and Guatemala, within established rural CHW programs. The primary objectives are (a) to evaluate the real-world effectiveness of the GMCD; (b) to use an implementation science framework to understand barriers and facilitators to effective population coverage, provider implementation, and maintenance; (c) to conduct an economic evaluation of the GMCD. The work will occur in collaboration with principal international partners who originally developed the GMCD and in two clinical sites, one in rural India and one in rural Guatemala.

SPECIFIC AIMS

Specific Aim 1: Assess the effectiveness of the GMCD intervention to improve developmental outcomes and nurturing care in India and Guatemala. We will conduct a parallel-arm cluster randomized trial within rural CHW programs. In the primary effectiveness phase, children under 2 years old will receive the GMCD intervention or control for 12 months. Subsequently, control clusters will cross into the intervention, and continue an additional 12 months (total 24 study months). The primary developmental effectiveness outcome will be change in age-adjusted scores at 12 months on the Bayley Scales of Infant Development, 3rd Edition BSID3) (3). The secondary nurturing care effectiveness outcome will be change in mean Home Observation for Measurement of the Environment (HOME) score at 12 months (4).

Specific Aim 2: Assess barriers and facilitators to GMCD implementation using the RE-AIM evaluation framework (5). RE-AIM domains will be assessed as: (a) Reach: participation rates, comparison of participant/non-participant characteristics, attendance/drop-out; (b) Effectiveness: impact on development (BSID3) and nurturing environment (HOME) [in Aim 1]; (c) Adoption: proportion of workers/facilities participating, CHW characteristics; (d) Implementation: contact hours/visit completion, fidelity to delivery protocols; (e) Maintenance: patient outcomes and cost effectiveness analysis at 12-24 months [in Aim 3]; intent by decision makers and implementers to continue intervention. In addition, we will conduct a sequential quantitative-->qualitative explanatory analysis, using interviews and focus groups with implementers from clusters with highest/lowest impact outcomes (BSID3/HOME) to explore institutional inner and outer setting and implementation processes associated with intervention success, using the Consolidated Framework for Implementation Research (CFIR).

Specific Aim 3: Conduct an economic evaluation of the GMCD intervention. Evaluation will assess (a) costs of the interventions at 12 and 24 months; and (b) cost-effectiveness of the intervention (dollar per unit increase in BSID or HOME scores) at 12 months. This analysis will provide cost information to policymakers to help guide resource allocation decisions for ECD interventions.

SUBJECT SELECTION

a. Inclusion/Exclusion Criteria

Eligibility criteria for the trial are: Age 0-24 months at the time of enrollment visit, and receiving health services from frontline health workers of Maya Health Alliance (Guatemala), Mahatma Gandhi Institute (India) or their local partners.

Exclusion criteria for the trial are: Children who are critically ill and are judged by the frontline health worker to require hospitalization or center-based care; children whose caregivers do not provide informed consent for the study.

b. Source of Subjects and Recruitment Methods

We plan to enroll 624 child participants (312 in India and 312 in Guatemala, 13 control and 13 intervention clusters per site, 12 individuals per cluster). Subjects will be recruited from participating clusters (health centers or service delivery organizations) in rural India and Guatemala affiliated with Maya Health Alliance (Guatemala) or the Mahatma Gandhi Institute of Medical Sciences (India). Subjects will be recruited from lists of families and children currently engaged in usual care with participating frontline health workers, and they will continue to access this care throughout the study

For potential participants in the clinical trial, research staff will pragmatically solicit lists of eligible families/children from participating frontline workers and their institutions. Recruitment staff will consist of full-time research study nurses in each site. Research nurses will work with frontline health workers to enroll children in the study. They will join the frontline health worker at enrollment home visits, confirm eligibility, explain the study, and solicit written informed consent. They will explain that caregivers in both intervention and control groups can continue or initiate standard care from any organizations or frontline worker throughout the study. These recruitment activities will be supplemented with phone calls or additional home visits, as needed, to resolve questions prior to obtaining consent.

In addition to these primary study activities, implementation assessments throughout the study will involve focus groups and in-depth interviews with key stakeholders, leadership and frontline health workers delivering the intervention. We anticipate that approximately 150-200 workers and stakeholders will participate in these activities. Recruitment for these activities will be by word of mouth and purposive referrals in each clinical site from local leadership. After ascertaining willingness for participation in interviews, a research staff member will then approach each potential participant in a neutral, confidential setting to explain the details of this portion of the study, including the nature of their requested involvement in the study, the possible risks and benefits of participation, and the individual capacity to withdraw from the study or decline participation at any time without consequence, and to answer any questions the potential participant may have. Specific mention will be made of the fact that employment/employment review is not conditional on participation in the study, and that there will be no repercussions for declining to participate.

SUBJECT ENROLLMENT

a. Enrolment and Randomization Procedures

At the beginning of the study, the 52 clusters (26 in India and 26 in Guatemala, corresponding to individual clinics or similar administrative units) will be randomly allocated in a 1:1 ratio to one of 2 study arms: immediate intervention or delayed intervention after 12 months (control). Once the clusters have been assigned to a study arm, a list of eligible children will be provided to the research team by frontline workers within each cluster. In order to retain a representative distribution of age ranges, recruitment will be stratified by age. The children will be randomly ordered on the list and the first 6 children in separate families in each age category (0-12 months and 13-24 months, n=12 per cluster in total) will be approached for enrollment. We will enroll only 1 child per family for data collection in this study. Although other eligible children in the family will receive the intervention, data on endpoints will only be collected on enrolled children. Similarly, we will include children who are twins or multiple births in the intervention, but only the enrolled twin will have endpoint data collected.

b. Informed Consent

Informed consent from caregivers

A detailed informed consent script will be used to obtain informed consent from caregivers of participating children. The details of obtaining consent will differ in Guatemala and India.

In Guatemala, at the informed consent visit, the study staff member will explain the study verbally, following the informed consent script, which covers all standard aspects of informed consent. Signed informed consent is generally not culturally appropriate in this study region, given a legacy of historical trauma and discrimination against indigenous populations and low levels of literacy. During the Guatemalan civil war, individuals who were not literate could be made to sign documents as an oppressive strategy for extracting land titles. This study will not replicate those potentially traumatic practices. All consent procedures will occur in the language of the participant's choosing. Research staff in Guatemala will be natively fluent in Kaqchikel Maya, K'iche' Maya, and Spanish. However, the informed consent script text will only be produced in Spanish. This is because Mayan languages are largely spoken languages. This means that even most research staff cannot reasonably be expected to read Mayan languages, despite being fluent native speakers. In lieu of written documents in Mayan languages, extensive preparatory practice sessions will be used to ensure smooth contemporaneous translation from Spanish to Mayan languages. This is the method that the local partner Maya Health Alliance has used in the majority of its research studies for many years. Once verbal informed consent is given, the study staff member will record the date of oral consent on the informed consent script and provide a copy of the script (in Spanish) to the caregiver.

In India, at the informed consent visit, the study staff member will read the informed consent verbally, or the caregiver will be given time to read the document, according to preference. All consent procedures will occur in the language of the participant's choosing. Research staff in India will be natively fluent in Marathi and English. Informed consent documents will be available in Marathi and English. After reading the document, if the caregiver agrees to participate, they will sign the consent document. A copy of the document will be given to the caregiver.

In both sites, the consent process will make it clear that informed consent to participate in the research will not in any way impact the quality or quantity of ongoing clinical services provided to the family by the local partners. Families that choose not to participate in the research study will still be eligible for other clinical services from the local partners.

After the consent script or document is reviewed, caregiver understanding of the information conveyed will be assessed using the teach-back method. The caregiver will be offered one week to consider enrollment and to discuss study participation/informed consent with other individuals that need to be involved in the decision. When appropriate based on family structure, verbal informed consent will be sought from multiple caregivers, but informed consent from one biological caregiver or legal caregiver will be considered adequate for study enrollment, as this study involves no more than minimal risk. Children in the study will be 0-24 months of age, and therefore they are not capable of providing assent.

Informed consent from healthcare workers and stakeholders

Verbal informed consent will be obtained from all stakeholders and frontline health workers participating in focus groups or interviews. This will include reading a consent script which explains the purpose of the study and specifically mentions that employment/employment review by their employer/institution or any other of the study partners is not conditional on participation in the study, and that there will be no repercussions for declining to participate. This consent discussion/script will occur in Spanish (in Guatemala all stakeholders speak Spanish natively), or in Marathi or English (in India, based on stakeholder preference)

c. Treatment Assignment and Randomization

See above, **Subject Enrollment (a)** for randomization procedures into intervention and control clusters. Subjects from intervention clusters will receive the GMCD intervention (1-2), delivered in monthly visits to the home by frontline health workers. Subjects in control clusters will continue to receive usual care from their frontline health workers. After 12 months, control clusters will cross into the intervention, and all subjects in all clusters will receive the GMCD intervention for an additional 12 months. Each GMCD visit includes assessment of risk factors, open-

ended exploration of caregiver concerns about development, assessment of functioning in seven developmental domains, and using mutual problem-solving strategies to develop a nurturing care plan with the caregiver.

STUDY PROCEDURES

a. Study visits and measurements

A study schema is given in Figure 1. The study will involve 3 study visits, each of approximately 2 hours in length. 2 of these visits will be conducted in the effectiveness phase of the study (0 and 12 enrollment months), and a third visit will be conducted in the extended implementation phase (24 enrollment months).

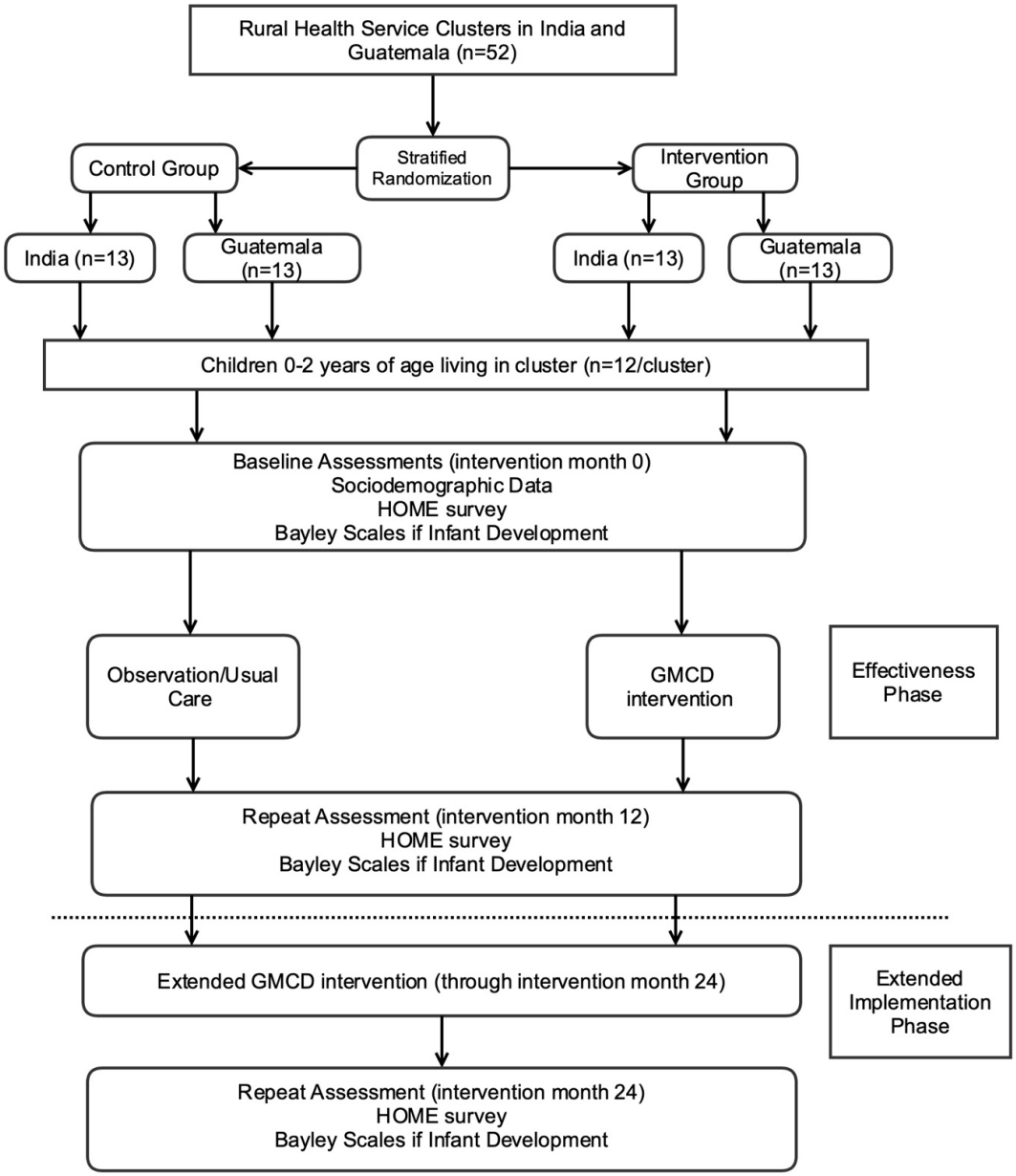

Figure 1: Study Schema/Flow Diagram

b. Drugs

Not applicable

c. Devices

The study will include collection of a capillary blood specimen for hemoglobin analysis using a point of care device. The device used will be the Hemocue Hb 201 device (https://www.hemocue.us/en-us/solutions/hematology/hemocue-hb-201plus-system) which will be acquired and owned by each of the participating field sites in Guatemala and India.

d. Study Procedures

The study intervention is application of the GMCD by frontline health workers. The GMCD is a noninvasive, minimal risk behavioral tool used to assess child development and provide counseling to caregivers.

In terms of study data collection procedures, the following data will be collected:

From Caregivers or Participating Children:

- sociodemographic interview data (e.g., age, sex, education, employment, race/ethnicity, wealth data);
- assessment of the home care environment with the HOME survey (4);
- developmental data using the Bayley Scales of Infant Development, Version 3 (3)
- child anthropometric data (height, weight) and capillary hemoglobin data (point-of-care)
- data on time spent participating in the intervention (for cost analysis)

From Stakeholders, Intervention Leadership and Healthcare Workers:

- focus groups and in-depth interviews, which will be recorded and transcribed for further analysis.
- Data on costs to health systems of implementing the intervention (for cost analysis)
- Data on costs/time to healthcare workers for participating in the intervention (for cost analysis)

e. Summary of Data to Be Collected

The following Table summarizes all data elements to be collected and when they will be collected.

Variable	Method	Baseline (0 months)	Intermediate (Monthly)	End of Effectiveness Phase (12 months)	End of Extended Implementation (24 months)	Study Personnel	Comments
Socio demographic data	Basic health history and demographics survey	X				Study nurse	See appended study instrument
Development (*primary outcome*)	Bayley Scales of Infant Development, Version 3 (3)	X		X	X	Study psychologist or pediatrician	Commercial instrument
Development (*intervention*)	Global development score tool (GMCD) (1-2)		X			Frontline workers	The study intervention, will be delivered in monthly home visits, see appended study instrument
Home environment	Home Observation for Measurement of the Environment (4)	X		X	X	Study nurse	Commercial instrument

Anthropometrics	Weight (kg), length (cm),	X	X	X	Study nurse	WHO growth standards will be used to convert to z-scores
Diet quality	Minimum dietary diversity, minimum meal frequency and minimum acceptable diet	X	X	X	Study nurse	WHO Infant and Young Child Feeding indicators (6), see appended study instrument
Hemoglobin	Hemocue Hb 201+	X	X	X	Study nurse	Using manufacturer's protocol
Focus groups/interviews with stakeholders	Focus groups and interview guides to be developed in year 1 of the project	X	X	X	Qualitative research staff	Instruments under development during first 1 year of project
Cost to caregivers/families	Survey	X			Frontline workers	Instruments under development during first 1 year of project
Cost to frontline workers	Survey	X			Research coordinator	Instruments under development during first 1 year of project
Costs to health system	Survey	X			Research coordinator	Instruments under development during first 1 year of project

The following Table summarizes all data collection forms by language of interest and their state of development or planned use. In general, English tools will be used by study staff in India and Spanish tools by study staff in Guatemala. Intervention tools (for use by frontline workers) will be available in Marathi (India) or Spanish (Guatemala)

Variable	English	Marathi	Spanish	Intended User	Comments
Socio demographic data	Available	Under development by India team	Available	Research staff	This data collection form is available in English and Spanish for use by study staff. Study staff will be native speakers of Spanish/Maya (Guatemala) and English/Marathi (India) and will provide contemporaneous translation of question items to Maya/Marathi per subject preference
Bayley Scales of Infant Development, Version 3	Commercially Available (Pearson)	N/A	Commercially Available (Pearson)	Research staff	This tool is commercially available in English and Spanish. Study staff will be native speakers of Spanish/Maya (Guatemala) and English/Marathi (India) or utilize interpreters. As we have done in previous studies, the Bayley Scales instruments will be in English and Spanish (commercial versions) with contemporaneous translation of question items to Maya/Marathi per subject preference
Global development score tool (GMCD)	Available	Available	Available	Frontline health workers	This tool was developed in English and has been adapted to Spanish and Marathi by the study team for use by frontline workers. Given the fact that frontline workers in Guatemala are not literate in Maya (despite being native speakers), in that site contemporaneous translation after extensive roleplaying/practice from Spanish to Maya by frontline workers will be used.

Home Observation for Measurement of the Environment	Commercially Available	Under development by India team	Available	Research staff	This tool is commercially available in English and has been adapted to Spanish by the research team. Study staff will be native speakers of Spanish/Maya (Guatemala) and English/Marathi (India) and will provide contemporaneous translation of question items to Maya/Marathi per subject preference
WHO Infant and Young Child Feeding Indicators Recall Tool	Available	Under development by India team	Available	Research staff	This tool is commercially available in English and has been adapted to Spanish by the research team. Study staff will be native speakers of Spanish/Maya (Guatemala) and English/Marathi (India) and will provide contemporaneous translation of question items to Maya/Marathi per subject preference
Focus groups/interviews guides for use with stakeholders	To be developed	To be developed	To be developed	Research staff	Study staff will be native speakers of Spanish/Maya (Guatemala) and English/Marathi (India) and will conduct interviews in the participants' preferred language
Cost data collection surveys forms	To be developed	To be developed	To be developed	Research staff	Study staff will be native speakers of Spanish/Maya (Guatemala) and English/Marathi (India) and will conduct surveys in the participants' preferred language

BIOSTATISTICAL ANALYSIS

a. Specific Data Variables

Variables in this study are outlined in summary form (data collection instruments) in the preceding Table. In addition, all instruments are included as file attachments to the IRB protocol, with the exception of the Bayley Scales of Infant Development and the Home Observation for Measurement of the Environment. These are commercial instruments which will be purchased and used as-is from the respective vendors (Pearson, Arizona State University). Several instruments (qualitative instruments, cost instruments) are under development (during first funded year of project). In addition, adaptation of English language instruments to local languages is ongoing and under review by local IRBs in each country. Once these are finalized, versions will be provided to the Partners IRB.

b. Study Endpoints

Our primary outcome measure is the Bayley Scales of Infant Development, 3rd Edition (BSID3) (3). Since the tool includes several developmental subscales and composite scores (language, cognitive, motor), an important question is which should be the primary outcome. Based on our preliminary work with populations in both study site, we expect to observe strongest improvements in the language domains. Therefore, we will use the language composite score of the BSID3 as our primary developmental outcome. Our secondary outcome is improvement in nurturing care. To assess this, we will measure changes in the Home Observation for Measurement of the Environment Scale (HOME). (4)

c. Statistical Methods

Our main analysis will assess the mean differences between control vs. intervention arms in the primary endpoint at 12 months using t-tests or Wilcoxon-Mann-Whitney tests (as appropriate) and regression modeling BSID scaled scores using a mixed-effects model as follows:

$$Yij = \beta 0 + \delta Xij + ui + eij$$

where Y_{ij} is the BSID3 composite scaled score of participant j in cluster i;, δ= treatment effect of interest (difference between group mean BSID3 composite scores); X= cluster assignment, and u and e are random intercepts at cluster and participant levels, respectively. We will conduct sensitivity analyses controlling for any remaining baseline

imbalances at participant or cluster level, and will conduct the same analysis for 12 to 24 months in each site to assess overall effect including maintenance phase. We will also, as an exploratory analysis, report all of these estimates separately for male and female children.

d. Power Analysis

The sample size has been calculated to test the hypothesis of no difference in mean change in BSID3 score between study arms using means, variances and correlation data from literature using BSID3 scores in parenting intervention studies in similar geographic and age-distributed populations. Based on these studies, we assume hypothesized differences between study arms of 0.3 SD on the BSID3 composite scores with an intracluster correlation coefficient of up to 0.2. With the anticipated 156 children in 13 clusters in each study arm per site (312 in 26 clusters each in India and Guatemala), we will have 80% power to detect a difference of 0.3 SD and 90% power to detect a difference of 0.46 SD between intervention and control arms in BSID standardized scores at an alpha of 0.05. This includes allowance for 25% attrition and refusal with no loss of power. The sample size is also powered sufficiently to allow independent analysis of a difference of 0.4 SD with 80% power or 0.53 SD with 90% power in the India and Guatemala sites separately. With this sample size, we can also detect between-group differences of 3 points overall and 5 points by site with 80% power for our secondary outcome, the HOME score. Based on studies of parenting interventions in similar settings, a 3-5-point difference in HOME scores is a reasonable expectation.

e. Cost Analysis

Cost data sources and instrument are briefly described in the preceding Tables. We will measure the costs of the interventions which include costs incurred at the health facilities (system-level costs), costs incurred by frontline community health workers and individual households for participating the interventions using instruments under development but following the framework previously published by members of our group (7). System-level cost data will be collected by study coordinators at the monthly basis. Follow-up calls/visits will be needed to clarify ambiguous or missing data as necessary. CHW-level cost data will be collected in each training session by research and clinical staff conducting training and evaluation sessions. Household-level cost data will be documented by the community health workers in each visit paid to the household.

Incremental costs of the interventions compared to control will be generated using multilevel regression analysis with generalized linear models (for skewed cost data and clustering effects), with costs per beneficiary as the outcome variable, and a dichotomous variable indicating GMCD intervention or control as an exposure variable. Other covariates will include time and interaction terms for treatment and time. To provide mean and 95% confidence intervals for incremental costs, we will use non-parametric methods based on bootstrapped estimates of mean costs. A discount rate of 3% will be applied to costs and adjusted between 0%-6% for sensitivity tests. The same strategy will be used to obtain incremental effectiveness (score gained for HOME, BSID, and Vineland respectively) and cost-effectiveness ratios ($ per unit increase in each score). To examine the robustness of findings, we will generate cost-effectiveness acceptability curves with different thresholds on willingness to pay (at the health system or societal level).

RISKS AND DISCOMFORTS

This project involves a minimal risk intervention to improve nurturing care for children at risk of delayed development. It is not anticipated that participation in the intervention will lead to any adverse outcomes. All individuals will continue to receive usual care from the participating cluster institution and frontline health worker in which they are recruited.

a. Complications of Procedures

Common Risks: During the capillary blood sample collection for hemoglobin assessment, there is some risk of temporary discomfort to the child.
Uncommon Risks: During the capillary blood sample collection for hemoglobin assessment, there is a rare risk of infection. Proper infection prevention and control precautions will be implemented to reduce the risk of infection. Infants experiencing an infection will be immediately referred to the local health clinic or hospital for treatment.

b. Drug side effects: Not applicable

c. Device complications: Not applicable

d. Psychosocial risks:

Common Risks: For caregiver participants in the intervention, a primary risk is that of lost productivity or perceived interference with domestic routines and other responsibilities. This is because the intervention involves monthly home visits for 2 years, as well as 3 study visits. We estimate that the study visits will last 120 minutes each. Each intervention home visit will also last an estimated 60 minutes. For stakeholders and healthcare workers participating in interviews, a risk is they may feel compelled to participate because of fear of repercussions for not participating from their employer.
Uncommon Risks: These include psychological stress to caregivers, primarily from discussing with health workers matters related to any potential or observed developmental delays in their children. Finally, there is the rare risk of accidental disclosure of personal identifiable or confidential data.

e. Radiation risks: Not applicable

POTENTIAL BENEFITS

a. Potential Benefits to Participants

Stakeholder participants will benefit mostly indirectly from this project by helping to improve implementation knowledge around early child development interventions. However, they may also benefit directly from a greater sense of empowerment and job satisfaction.

Frontline workers delivering the intervention may benefit directly through a greater sense of empowerment and job satisfaction. They will also receive advanced training in the assessment and promotion of early child development hypertension, directly advancing their professional development.

Children and caregivers in the clinical trial in both control and intervention arms will benefit from access to a panel of developmental tests which they otherwise may not have access to. Results of these tests will be made available to each subject in a format that they can share with their primary care providers, directly contributing to their usual medical care. In addition, subjects with concerning incidental or abnormal findings will receive assistance from the study team in referrals to care. Subjects and caregivers in the intervention arm (and in the control/delayed-intervention arm after 12 months) will in addition receive intensive individualized support to promote early child development.

b. Potential Benefits to Society

The information gained through this project will contribute measures of the clinical effectiveness and important insights into the implementation of early child development interventions by frontline workers in rural Guatemala and India. This well controlled trial will foster broader dissemination of the international Guide for Monitoring Child Development and individualized approaches to fostering nurturing care in Guatemala, India and globally.

MONITORING AND QUALITY ASSURANCE

a. Monitoring of Source Data

As an unblinded trial of minimal risk, the PI will be the individual primarily charged with reviewing study progress and safety. The PI will review these data monthly together with the primary site Co-investigators and will provide reports to the reviewing IRBs every 12 months, which will include the report of any complaints or minor protocol deviations. Reports will provide additional information of reasons for trial dropout, adherences to eligibility criteria, reassessment of level of risk occasioned by participation in trial, and justification for study continuation versus early termination.

Furthermore, review of the rate of subject accrual and compliance with inclusion/exclusion criteria will occur monthly during the recruitment phase, to ensure sufficient enrolment and that they meet eligibility criteria as outlined in the Targeted/Planned Enrolment Table from this proposal. The PI will be responsible for conducting this review, with assistance from the Primary Study Coordinator and primary Site Coinvestigators in each site.

The PI will be assisted in review and reporting activities by the Primary Study Coordinators and primary site Co-Investigators. A summary of review/reporting activities is outlined here:

Data type	Frequency of review	Reviewer
Subject accrual, compliance with consent and enrolment protocols	Monthly	PI
	Every 12 months	IRBs
Status of all enrolled subjects	Monthly	PI
	Every 12 months	IRBs
Data entry and quality control checks on 10% of study visits and other study data/subject charts	Weekly	Primary Study Coordinator
Adherence data: study visits and intervention	Monthly	PI
	Every 12 months	IRBs
Complaints or Other Feedback from Study Participants and Communities; Minor Protocol Deviations	Per Occurrence	PI
	Every 12 months	PI
Major Protocol Deviations	Per Occurrence	PI, IRBs, NIH
Unanticipated Problems	Per Occurrence	PI, IRBs, NIH

b. Safety Monitoring

The trial is of not more than minimal risk and, therefore, no adverse events related to trial participation are anticipated. However, any complaints or perceived adverse events from participating communities or caregivers will be tracked by the investigator team and reported to IRB and granting authorities using the above schedule. The study will not employ stopping rules or a Data Safety Monitoring Board.

Research staff in each participating recruitment site as well as frontline workers in both intervention and control clusters will be instructed to report in person or by telephone all complaints, protocol deviations, or unanticipated problems to the Primary Study Coordinator for each site on the same day that they are discovered. The Primary Study Coordinator will be charged with gathering necessary information from this initial report and contacting the Primary Site Co-Investigators and Principal Investigator.

Linkages to Care. The intervention described in this study is of not more than minimal risk. However, it is important to ensure that subjects remained linked to medical care throughout the study and that appropriate referral plans are in place for any abnormal or incidental findings that occur within the study. The recruitment mechanism for the study ensures that such a plan is feasible. All subjects will be recruited from health centers or health services institutions affiliated with Maya Health Alliance (Guatemala) or the Mahatma Gandhi Institute of Medical Sciences (India). Recruited subjects will already be engaged in usual care services from frontline health workers at each site at the time of recruitment. They will be encouraged to continue receiving this care throughout the study.

In addition, coordination will occur between the study team and the participating referring centers and institutions in several other ways. First all relevant study clinical data performed (e.g., anthropometric data) will be provided in written form both (1) to the caregiver directly as (2) to the referring health center/treating provider, if the participant agrees to share this data, so that this data can contribute to their ongoing care.

Research staff and frontline workers in this study can be expected to occasionally encounter research participants with new important clinical symptoms or findings, such as malnutrition or significant developmental abnormalities require center-based care. In order to address this possibility, we will meet with clinical leadership from the participating centers and institutions prior to beginning the study in each site. At this meeting, we will develop a consensus protocol of criteria by which the intervention staff will coordinate referral to appropriate center-based care. Once a criterion for referral is triggered, study staff will arrange an urgent clinical evaluation as defined in the consensus protocol, and will personally accompany the subject/caregiver to this evaluation to ensure completion. We will document all details of these urgent / emergent referrals and their outcomes. To ensure that these referral processes and linkages to care continue to be safe and expeditious, the primary study coordinators will meet with representatives of the participating institutions every 3 months to review referrals and referral outcomes and to discuss any needed changes to the referral plan.

c. Outcomes Monitoring

As a minimal risk behavioral intervention, we do not anticipate any serious harms, and we do not plan any stopping rule or any interim analysis of study outcomes.

d. Adverse Event Reporting Guidelines

As a not more than minimal risk study of a behavioral intervention, no AEs are anticipated and no planned reporting schema other than usual logging and reporting of complaints, unanticipated problems, minor and major protocol deviations (outlined above) are planned.

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