Maternal Alcohol Reduction Intervention in South Africa [MaRISA]

Protocol Manual

NCT05319977; March 10, 2021

Please note: The research proposal is for a National Institute of Health grant to be funded by NIAAA. The proposal has been selected for funding. In keeping with the funding guidelines, after MRC ethics approval

CHAPTERS

CHAPTER 1: INTRODUCTION

SAMRC Investigators:

Site Principal Investigator (contact PI); Co-Investigator 1 & Co-Investigator 2

RTI International Investigators:

Principal investigator; Co-Investigator 1 & Co-Investigator 2

USA Consultants:

Consultant 1: Biostatistician

CHAPTER 2: STAFFING & OPERATIONS

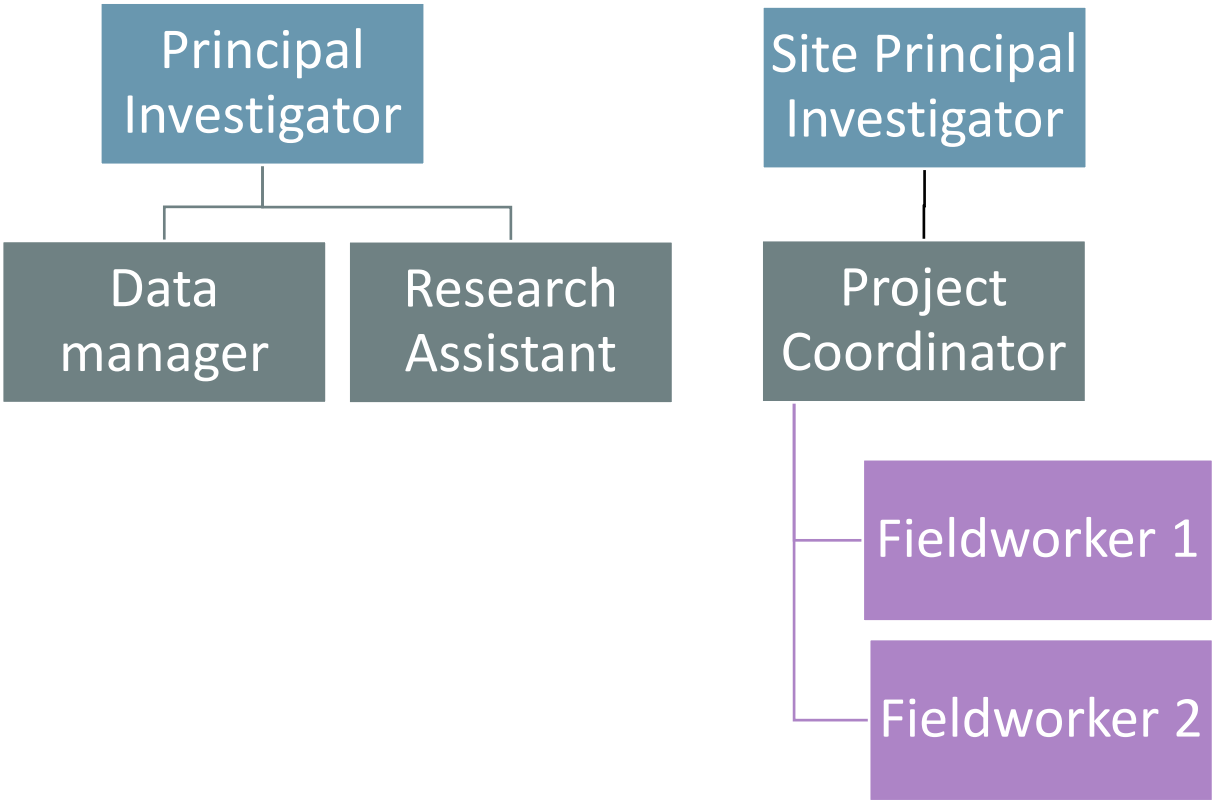
2.1. Introduction

This chapter reviews what is expected from staff working on this research study. There will be a number of activities and tasks that staff will be expected to perform. Each of these roles include specific tasks and responsibilities that must be completed to a high standard. This chapter will describe the core activities and functions of each role.

All staff, regardless of level, are expected to represent a project that cares about people by always acting as role models and be kind to participants, other patients and healthcare staff. We encourage staff to show respect and be professional at all times while working on this study. Please note, we are guests in the healthcare facilities, therefore, it is critically important that we keep good relationships with all staff we engage with at the healthcare facility.

2.2. Roles and Responsibilities of Staff

2.2.1 Organogram



2.2.2 Project Staffing

There are a variety of staff working on this project.

Project Coordinator: is responsible for assisting the Site-PI with all study related activities and co-ordination, including applications for approval to the Department of Health. They are responsible for overseeing day-to-day activities, ensuring that all study-related materials and incentives are available. They are responsible for data management and will provide support in the reproduction of study-related materials, and assist with literature searches, preparation of slides and other materials for reports, presentations, and publications. They are supervising all field workers, provide training to field workers on recruitment, data collection and tracking procedures. They will conduct quality checking to ensure all data storage SOPs and data collection SOPs are being adhered to. This will include collection of self-report and biological data. They will be responsible for maintaining regulatory (GCP and ethics) oversight, maintenance and stock control of supplies.

Fieldworkers

Will be based at the participating healthcare facilities and MOUs. They will be responsible for conducting screening to identify potential patients who are eligible to participate in the study, consenting eligible patients and enrolling them in the study, scheduling appointments, collecting contact information, conducting the baseline and follow up assessments and tracking participants for study appointments. All of these activities will require the completion of certain paperwork that will be explained in subsequent chapters of this manual. When conducting such activities, staff members must be very conscientious about checking the quality of their own work and ensuring that all interviews are completely and accurately documented using the appropriate forms. Fieldworkers will report directly to the Project Coordinator and indirectly to the Site PI.

Fieldworkers Daily Tasks:

- Maintain confidentiality at all times,
- Be flexible with scheduling appointments (e.g., late afternoon appointments or weekend follow up appointments for assessments),
- Check the quality of own work,
- Check email accounts at least once daily,
- Check project-device messages regularly throughout the day,
- Maintain appointment book
- Keep all supplies in a secure location,
- Report any missing items immediately to the Project Coordinator and
- Report all incidents to the Project Coordinator as described in the 'Incident Reporting' chapter.

2.3. Staffing Operations

2.3.1 Staff Dress-code

All frontline staff for this study (including fieldworkers employed by the study) are expected to wear their MaRISA t-shirts when conducting research activities at the field site office, the healthcare facility and the communities. These t-shirts will be issued to staff. These t-shirts can preferably be worn with a pair of jeans or black pants and comfortable shoes. We expect all fieldworkers employed by the study to always look neat and professional.

2.4. Project Sites

MaRISA operational site will be based at the Delft offices. The study recruitment site will be based at two healthcare facilities, i.e., Bishop Lavis MOU, and Macassar MOU.

The Delft office is situated in Delft, and are currently being shared with staff from other affiliated research studies. This section will provide detailed information on the safety procedures which should be followed at all our project sites, both our main site and at the health facilities, as well as protocols relating to the management and monitoring of petty cash and supplies.

All research activities will be conducted at the following healthcare facilities:

Health Facility / Clinic Name	Facility Type	Site Code	Address
1. Site A	Community Health Centre	M_BL	MOU, Bishop Lavis, Cape Town
2. Site B	Community Health Clinic	M_MC	MOU, Macassar, Cape Town

The research team will initiate contact with each health facility prior to conducting any formal research related activities. The facility and/or operational managers will initially be contacted to make logistical arrangements where research activities will be conducted for the duration of all study phases.

2.5 Safety Procedures at Project Sites

2.5.1 Delft Offices (Field Site)

In order to encourage the safety of staff and all assets situated at the Delft office we would like to promote the following safety measures to be taken on a daily basis:

- Always ensure that the project site gates are kept locked.
- Never allow anyone who looks suspicious to enter the site, rather talk to them through the security gate.

- No expensive assets such as devices, computers, cameras, cell phones etc. should be left out overnight; please make sure that all assets are locked-up before leaving at the end of day.
- Also ensure that all windows are closed, and air conditioners are switched off before leaving at the end of day.

2.5.2 Health Facility Sites

At each health facility there will be a security company contracted to ensure the safety of all employees and patients, as well as keeping the building including all the assets on the premises intact. Employees are encouraged to familiarize themselves with the security personnel at the facility and establish their role at the facility. Employees should also enquire from the facility manager or operational manager at the facility what safety protocols the facility has in place so that they are aware of these protocols.

If you are concerned about a participant's mental status prior to commencing a scheduled appointment discreetly communicate the matter with the Project Coordinator, to discuss whether the participant needs to be rescheduled for another day and/or referred to the Emergency Room or Mental Health Nurse on duty.

When conducting case management activities, the following steps should be followed to ensure safety and security of assets:

1) First contact the participant telephonically a day before making a home visit.
2) During this call make an appointment with the participant for a specific day and time that you will be visiting them at their home, to ensure that they will be available.
3) **Please note: NO FIELDWORKER SHOULD CONDUCT CASE MANAGEMENT / HOME VISITS ALONE – ALWAYS BE ACCOMPANIED BY ANOTHER STAFF MEMBER.**
4) If at any time you feel uncomfortable, unsafe or threatened, communicate this with your companion and return to the health facility immediately. If this occurs prior to reaching the participant's home, then contact the participant when back at the health facility and explain the situation and try to reschedule another convenient time you can do a home visit.

5) Except for the study cell phone don't carry any other valuables with you when conducting home visits.

****Please remember to report any incident in your incident report form, which must be filled in immediately or soon after the incident, sent to the Project Coordinator and Site PI via email/electronically, and kept on file at the field site (Delft Office).**

2.5.3 Engaging with Health Facilities

After receiving an approval letter from the Department of Health indicating that you can continue with all research activities at a facility, communication should follow in a systematic manner.

- **Step 1 -** Contact senior management (Facility Manager (FM), Operational Managers (OPMs) & Fam. Physician) via email to introduce the study, provide them with the approval letter and schedule an appointment for research purposes / a visit.
- **Step 2 -** Always follow-up a day or two later telephonically if you didn't receive response via email; if you have received response the telephonic follow-up should still occur to confirm details of appointment.
- **Step 3 -** Prior to going to the facility follow-up a day before, telephonically or via email to remind management that you will be coming to the facility to conduct research activities / a visit etc.
- **Step 4 -** On the day of the appointment (depending on the visit), on arrival at the facility always first go to the FM or OPM to greet them and inform them that you are at the facility for the day and also provide them again with a hard-copy of the approval letter if it's the first day or first time you come to the facility.

2.6 Protocol for Petty Cash

The SAMRC will advance petty cash to the Project Coordinator, amounts of which will be determined by the needs of the project. Requests for petty cash must be submitted to the SAMRC through the JDE financial system at least one month in advance to ensure money will be available to reimburse participant's transport fees.

Prior to the initiation of recruitment procedures, each field worker will be issued a specific calculated amount by the Project Coordinator to reimburse participant's transport fees. The fieldworker will sign a receipt documenting they acknowledge receipt of the money and that they will be held responsible if the participant does not receive their reimbursement. It will also be the fieldworker's responsibility to make sure the participant signs the receipt book when issued with the transport fee. Transport fee will be issued only at study required appointments, i.e. when participants need to visit the healthcare facility for urine monitoring or if the baseline appointment is scheduled on a different day than the screening appointment. The petty cash received needs to be locked up in a lockable petty cash box, which will be kept in a double lockable steel cabinet, and only the fieldworker and Project Coordinator should have access in the form of keys to both the petty cash box and the cabinet. **Under no circumstances should the petty cash box be left out unlocked and unattended during the day or be left out overnight.**

2.7 Supplies

Please note: All hard-copy forms will be printed and available prior to data collection activities. All other necessary materials will be arranged as needed.

The fieldworker will be responsible for all assets and supplies issued to them at the start of the study. If for any reason they foresee there will be a shortage of documents or supplies, it is their responsibility to inform the Project Coordinator in a reasonable timeframe. If this does not occur, procurement of supplies will unfortunately take longer to obtain which will have a detrimental effect on the daily functionality of the study.

CHAPTER 3: PROTECTION OF HUMAN SUBJECTS

3 Introduction

Protecting the rights and confidentiality of the participants in the MaRISA study is of utmost importance. This chapter will briefly review participants' rights and the commitments to participants that all staff must make, data security issues, and professional ethics.

2.1. Ensuring Participants' Rights, Privacy, and Confidentiality

3.1.1 Participants' Rights

Basic human rights must be respected and maintained by a research organization and all who are involved in its activities. The protection of rights and confidentiality has always been especially critical in studies focused on substance use, where exposure of past or current abuse or addiction can have social, economic, and legal consequences. MaRISA's research procedures are designed to protect individual rights and to comply with all applicable laws and ethical principles. Among the rights that must be protected are:

- *The right to accurate representation:*
    - Requires honesty in dealing with participants and provision of completely accurate information about the study.
- *The right of informed consent:*
    - Requires that a participant be given adequate information to make an informed decision about participation.
- *The right to refuse:*
    - Requires that an individual be fully informed of his/her right to decline to participate, to withdraw, or to refuse to answer any question.
- *The right of privacy:*
    - Requires guarantees against invasion of privacy as well as specific protection as specified in the South African Protection of Personal Information Act of 2013.

These rights are extremely important to us as individuals and as professionals engaged in applied research. All SAMRC studies must develop specific written plans for conducting research with human subjects. Research staff must also operate under the supervision of committees for the protection of human subjects to ensure that they do not violate these rights.

In research involving follow-ups and contacts, it is necessary to collect names, addresses, and other personal information from participants for future follow-ups. A great deal of information collected from participants pose a risk to participants, especially if their use of substances is not known to others. It is extremely important that the data collected be kept confidential.

3.1.2 Project Staff Commitment

The staff member collecting data directly from a participant presents perhaps the greatest risk to a participant's privacy. As in all our research, we are very concerned about this risk and take several steps to ensure that problems do not occur. All project staff are required to sign the **MaRISA Staff Agreement of Confidentiality form**, depending on their project roles and responsibilities. These pledges serve to reinforce the seriousness of this aspect of the study. The confidentiality agreement states that project staff members are prohibited from revealing information obtained from study participants. The agreement also states the consequences for staff revealing this information.

CHAPTER 4: QUALITY ASSURANCE & DATA MANAGEMENT

3. Introduction

It is really important that we collect the correct data (information), in the correct way. In this chapter, we will describe the types of data that we are collecting, give you tips on how to collect good data and also how to correct data which has been collected in error.

Data will be held in a confidential and secure manner as outlined in the Data Management Plan. All data will be entered into REDCap, a password-protected data collection and management system that will have built-in checks for consistency and completeness. Electronic data entered in REDCap will be downloaded to the internal RTI project share weekly. All data are kept on password-protected servers. The PI and Data Manager will be responsible for reviewing and cleaning the data and preparing weekly reports during data collection, with assistance and guidance from RTI Co-Is. All data, including forms with personally identifiable information (PII) such as locator forms and consent forms, will be kept on password-protected servers. South African investigators and staff will have full access to the data. All collected hard-copy data will be stored in double-locked steel cabinets only accessible by the Site-PI, Project Coordinator and the two fieldworkers. All data will be scanned and uploaded to REDCap for ease of access and data analysis purposes.

Data Quality Control (QC) and Quality Assurance (QA)

Quality assurance systems will be put in place to ensure that the data are cleaned and accurately transmitted, organized, and properly managed. With participants' permission, the Site-PI/Project Coordinator will observe remotely 20% of baseline and follow-up appointments and will document feedback.

Correction Process

Once an issue has been identified in the QA or QC findings, it will be discussed at the weekly site check-in meetings. The root cause of a recurrent problem will be identified, and follow-up actions will be taken to correct the problem based on the input from the RTI and SAMRC staff. These actions may include but are not limited to, changing a process or revisions of project forms, training, or reassignments of tasks. For more serious issues such as protocol violations and breach of project participant confidentiality, the Co-Is will be notified immediately and will work with the field staff to ensure that corrective actions are taken in a timely manner. Based on the severity of the issues identified, the PIs will immediately report the issue to the PO, DSMB Chair and institutional review board of record (SAMRC Ethics Committee), who will determine further recommendations.

Table 1: Corrective Action Reporting Process

Step	Description	Responsible Person
1	Identify the issue (protocol violation, breach of confidentiality, data issue (such as entry, missing etc.))	Project Coordinator and Fieldworkers
2	Report oversight, error or issue to PI or Co-Investigator (Co-I)	Project Coordinator
3	Recognize impact of issue	PIs
4	Investigate cause	PIs
5	Recommend corrective action	PIs
6	Implement corrective action	All staff
7	Notify PO, DSMB Chair and SAMRC Ethics Committee within 48 hours as needed.	PIs

Potential Improvements

Identifying and implementing potential improvement of project protocols will be an ongoing process that will be integrated into the routine planning, management, and implementation project processes. It is the responsibility and standard practice of all project staff to identify and appropriately communicate opportunities for quality improvement to the PIs. These improvements will be documented, and ethics approvals will be included in the yearly progress reports.

3.1. Data collection issues and solutions

Here are a few common issues that may come up during data collection or during a session:

- At the beginning of the assessment, remind the participant how long the assessment will take to complete. Make sure they can stay for that length of time it takes to complete the assessment. Do not begin the assessment if they cannot stay for the entire time it will take- rather reschedule the appointment.
- If you see that a participant is confused about a question or task, stop and ask them if they understand. If you are still not sure if they understand or not, ask them to explain the question to you in their own words.
- If a participant says one thing for one question, and then answers completely differently for another question on the same topic, stop and try to see if the person has understood you. If necessary, go back to the previous question and check their answer.
- At certain times, participants may become less willing to answer questions, or they may seem to just be giving you any answer to finish quickly. Stop the interview and ask the participant if they are alright. Sometimes this is because a participant is upset about something. Sometimes the person is in a rush to leave, or they are hungry or thirsty. Ask them if they would like a break to eat their snacks, take medication or use the bathroom. Let them know how much longer the session will be.
- If at any time you are worried that a participant is not well, alert the medical staff straight away. The participant's medical care is not your responsibility at all. Ask

for help if you are concerned. The following symptoms or signs in participants should be reported:

a. feeling faint or dizzy
b. complaining of pain, especially chest pain or a severe headache
c. sudden weakness
d. slurred speech
e. confusion and becomes unable to understand the questions.
f. any type of sudden bleeding or going into labor
g. anything else that worries you.

3.2. Entering data on REDCap and filling in paper forms

Data Entry on REDCap Mobile App

- Ensure that the project has been downloaded to the tablets prior to data collection. This may take some time and requires an internet connection.
- After downloading the project, click Collect Data. Select an instrument and click "Create Record" to create a new record or click on an existing record and enter data as usual (following questionnaire flow). Check that each record has been saved and completed. All collected data must be sent to the server at the end of the day. Uploading data requires internet connection. Click "Send Data to Server" and then click “Begin Send button” to send data.
- Before turning off the tablet, please ensure that the data upload is complete. If an error occurs, please email Data Manager for further instructions.
- To ensure that project modifications are current in the app, click "Refresh Setup and Data." This will erase all previous data from the tablet and replace it with everything from the REDCap online server. ((** THIS SHOULD ONLY BE DONE AFTER ALL DATA HAVE BEEN SENT TO THE REDCAP ONLINE SERVER, OTHERWISE ALL DATA COLLECTED ON THE TABLET WILL BE DELETED**)).

If entering data directly on REDCap database

Each fieldworker will use their own username/password or assigned username and password while utilizing REDCap. When entering data, double check Records for duplicates and ensure all forms are completed.

3.3. Submitting collected field data

Should you need to use paper forms to ask the screening questions, baseline or follow-up assessments, you should submit these to the Project Coordinator at the first opportunity. We ask that you fill in the date of the data collection, date when you submitted the forms and which data was collected (screener, baseline assessment, etc.).

3.4. Receiving data queries

Sometimes you will receive a message from the Data Manager, asking about a certain participant or a certain question. This happens in every study, so do not be worried. This may be easy for you to answer straight away, such as giving the correct spelling of a name, or you may need to contact the person (by phone or in person) to verify the information. We need to make sure that all our data are accurate.

3.5. Keeping data safe

All the data we collect for MaRISA, whether digitally (on REDCap) or on hard copies, should be kept safe at all times. Our data include participants' phone numbers, locator information, details of their physical health or that of their babies, consent forms and any other information we collect as part of the study.

3.5.1. Maintaining participant confidentiality

MaRISA data should not be shown to anyone outside of MaRISA. In the same way, none of us should talk about any of the data with anyone not involved in MaRISA, including the clinic/healthcare staff. This is called maintaining participant confidentiality. Each of us will sign a confidentiality agreement before we start the study. Should the clinic staff, a participant's family member or another participant ask you for any information on a study participant, advise them that you may not give them this information as it is confidential. Clinic staff may know that a participant is part of the study, but beyond that we will not be sharing any study details with them. Should they keep asking, please give them the telephone numbers of the Project Coordinator or Site PI to further discuss the matter with them.

3.5.2. Storing our data safely

Once we have collected the data, all the data should be stored safely.

The participant folders should be kept locked away in the filing cabinet, even if you are still busy at the clinic/healthcare facility. You should only have the folders out that you are busy with, and you should never go and have tea, or walk away, leaving any folders, supplies or valuables outside the cabinet. This also applies to any other forms or papers related to MaRISA. If you are not busy on the tablet, please also keep it in the locked cabinet and leave the tablet in the filing cabinet at the end of your shift.

Remember: Any hardcopy forms with patient names or contact details will be stored in the CONTACT folder. All other hardcopy forms will go into the EVERYDAY folder. Each of these files will be kept in separate drawers in the stainless-steel cabinets.

CHAPTER 5: STUDY PROCEDURES

4. Introduction and Expectations

Staff should keep in mind that they are patients' first contact with the project. In doing so, the team gives patients their first impression of the project.

How you approach people, your body language, dress code, attitude and what you say will leave a lasting impression on people who are screened for the study and others. These impressions can influence whether people will want to participate or not in the study. Be conscious of the impressions you make and be careful of what you say – try and make people feel comfortable and welcome.

For the pilot testing phase, we aim to recruit 60 (30 pregnant and 30 post-partum) women for the two healthcare facilities. Both the pregnant and post-partum women need to report that they are using alcohol. Fieldworkers will conduct the baseline assessment, 6-week follow-up assessment, and the 3month follow-up assessment.

5.1 Pilot: Recruitment Procedure

Much of the success of screening potential study participants will result from exercising good judgment and maintaining sensitivity toward the people you speak to. Staff members who have been chosen to work on MaRISA have two important qualities:

(1) They are capable of working in the healthcare facility and know the surrounding community, and

(2) They have good instincts as to the best ways to get a response from potential participants. Rely on these instincts but remember that a degree of assertiveness is essential to doing the job well.

It is important to recruit women into the study who seem interested and have a notable level of **readiness to change**, as perceived by the potential participant's verbal and nonverbal communication. Recruiting interested and motivated women into the study increases the likelihood that they will be engaged and committed to completing all steps of the study. **We want participants who are willing and able to come to all**

their appointments. It is therefore important to check whether they have the time and ability to commit to being in the study for the duration of the study.

If people hesitate or do not seem that interested, do not put pressure on them to take part! If we recruit people who are not committed to being in the study throughout the whole process, this will negatively affect our follow-up rate.

Additionally, during the screening and consenting process, project staff members have the opportunity to determine whether participants are mentally capable of participating in the study, particularly during the consent process (which will be further explained below).

If potential participants cannot say in their own words what the study is asking of them during the consent process, they should not be enrolled into the study.

5.2. Screening

Once introductions are made and a patient's cooperation has been secured, complete the participant ID, staff ID, site and date fields on the screener, using the tablet.

- For the pilot phase, we will be using the "Pilot Screener for Pregnant and Post-Partum Women" at the onset of the pilot phase.

Recruitment will be done via clinic referrals, posters, and flyers.

Participant IDs will be according to the following format, it will consist of ten digits with both alphabetic and numerical items, e.g., M_BL0001PR or M_BL0001PP.

Please note: the first alphabetic digit refers to the MaRISA study, an underscore sign separates it from the next 2 alphabetic digits which indicates the site, e.g., Bishop Lavis = M_BL, the next 4 digits indicates how many participants have been enrolled into the study and the last 2 digits indicates whether the participant is currently pregnant or post-partum.

There are types of potentially sensitive information that are requested on the screening questionnaire. It is important to stress the confidential nature of the screener. Reassure them that their identity will never be linked to their responses and that their responses are only used for research purposes. Always remind individuals that their answers will be kept strictly confidential.

Staff ID#: Will be a staff member's Initials.
Site ID#: Bishop Lavis = M_BL; Macassar = 002

To be eligible, women must fulfil in the following criteria, i.e.:

Criterion	Participants
Age	Be ≥18
Pregnancy or Post-Partum Status	be pregnant (≤28 ges wks) or postpartum (≤3 mos)
Alcohol Use	• have reported alcohol use during the current pregnancy or lactation • test positive for alcohol use by urinalysis (i.e., EtG)
Birth Venue (linked to birth outcomes)	plan to complete antenatal care at the current clinic and remain in the area for at least 3 months
Cellphone Status	own a cell phone to receive text messages
Serious Medical Conditions and Suicidal Thoughts	women who report serious medical problems threatening their current pregnancy or report current suicidal thoughts or attempts in the past month are **NOT eligible**
Other	intend to breastfeed for 6 months

Women who participated in KIIs (the formative phase) or pretesting will not be eligible for pilot testing. Women who reported serious medical problems threatening their current pregnancy or current suicidal thoughts or attempts in the past month will not be eligible and will be provided with necessary referrals.

Table 1: Possible dispositions for not participating or not continuing with participation.

DISPOSITIONS			
	Dispositions based off screening questions		**Dispositions before or after screening**
2.01	Age <18 years old	3.01	Not interested (before screening)
2.02	ETG tested negative	3.02	No time

2.03	Refused bio-sample	3.03	eligible, but not interested or refused
2.04	Over 28 weeks preg.	3.04	no reason given
2.05	Over 3 month postpartum	3.05	other
2.06	No alcohol use in current pregnancy or postpartum		

Screening, consenting and baseline and follow-up assessments will be conducted electronically via REDCap. Following consent, we will collect detailed contact information and schedule women for a baseline assessment.

5.2.1. Alcohol Biological Testing

Please follow the next steps when collecting biological samples.

1. Provide participant with a urine cup to collect a urine sample as part of the screening process.
2. Check the expiration dates when preparing the test.
3. Make sure you have a marker to label the test with the participant's study ID before you start the testing.

Remember, willingness to be tested for alcohol is a requirement for study participation. If a participant has difficulty to pass urine, encourage them to drink some water or juice continue with explanations or completing other forms and to provide the urine sample a bit later. Giving the participant a drink before she starts the appointment will also be helpful.

TEST INSTRUCTIONS

For this study, we will be using an EtG urine test to determine if someone has alcohol in their body. EtG stands for *ethyl glucuronide*, which is a substance produced in the liver when your body processes alcohol. EtG remains present in the body for about one to five days after drinking, depending on how much alcohol a person has drank, using small strips that are dipped in urine. Please use gloves before, during and while cleaning up after the biological testing process. Please conduct the testing as per the steps indicated.

Record results on **MaRISA Specimen Collection Log.**

CLEANING AFTER TESTING

Make sure everything is thrown away appropriately after you have completed all biological testing. Everything used for the testing such as the tray must be wiped down with sanitizer or wipes after conducting biological tests.

5.3. Baseline Assessment

Remind the participant of their rights to confidentiality and privacy in answering the questions with the exception if they indicate desire to harm themselves or someone else. Refer to the Distressed Participant Procedures (see **Chapter 6**) if a patient ever indicates they will do harm to themselves or someone else. If the participant has any questions or concerns about being in the study, they can contact the Site PI. Her contact information is on the **Information and Consent Form**.

Baseline assessment questions will be conducted via CASI on a tablet. Assessment questions will cover sociodemographic factors; social determinants; recent and lifetime polysubstance and alcohol use; IPV/GBV exposure; partner drinking; stigma; coping with stress; and reproductive, sexual, physical, and mental health.

5.4. Follow-up Appointments and reimbursements

The participant will be reimbursed for their transport costs based on the following scale. Transport costs should only be reimbursed if the participant has needed to travel to come to the healthcare facility for a study appointment:

Categories of distances	Amount provided
0km – 3km	R10
4km – 10km	R30
11km +	R50

<u>Pilot Phase</u>:

In addition to monitoring participants' through urinalysis twice a week, participants will be asked to participate in the 6-week and 3-month follow-up assessments at the healthcare facility they were enrolled at.

A participant will be provided R150.00 each at baseline and follow-up assessments.

Consent will be obtained to collect participants' birthing facility information for those who were recruited during pregnancy to track birth outcomes. If a participant is already postpartum and breastfeeding, self-reported incidents of breastfeeding while using alcohol will be collected. Infants' data relating to their height, weight, and head circumference will be collected.

If a participant misses a visit, we will contact the participant following a standard protocol (i.e., phone call on the appointment day, the following day, and 1 week after the missed visit to encourage rescheduling for the missed appointment). Participant locator information will also be updated at each appointment. Staff members need to

prioritize tracking participants who have the least number of days left before their upcoming appointment so that they do not time out of the study. In other words, you should contact participants first whose next appointment is closest to the current date.

If a participant has withdrawn from the study or has reported the loss of her foetus/baby to field staff and this was reported to Project Coordinator, the participant should not be tracked any longer. These participants will also not be replaced in the study since they have been reported on.

5.6 Creating Participant Folders

The fieldworker needs to be aware of the hard-copy documents which each of these folders will consist of so that if any hard-copy forms are missing from a folder or more hard-copy forms are needed they would be able to identify which forms are left out or are needed.

The fieldworker will be required to allocate a participant ID number to each of the folders and hard-copy forms by means of a participant ID sticker.

5.6.1. Participant EVERYDAY Folders

The EVERYDAY folder will contain all non-identifying hard-copy forms, i.e.:

- ✓ Participant Screener (hard copy available in English, IsiXhosa and Afrikaans)
- ✓ Baseline Assessment (hard copy available in English, IsiXhosa and Afrikaans)
- ✓ Appointment Cards
- ✓ Follow-Up Assessments (hard copy available in English, IsiXhosa and Afrikaans)
- ✓ Fetal/Birth/Neonatal Outcomes Form

Information and materials which will be included in the EVERYDAY folder and may possibly be given to the participant at the end of the first appointment:

- ✓ Referral Guide Hand-out
- ✓ MaRISA Contacts & Rights Cards (available in English, Afrikaans and IsiXhosa)
- ✓ MaRISA Appointment Cards (one for each consecutive appointment)

5.6.2. Participant CONTACT Folders

The CONTACT folder will contain all identifying hard-copy forms, i.e.:

- ✓ Information and Consent Form (available in English, IsiXhosa and Afrikaans)
- ✓ Contact Information Form (hard copy)
- ✓ MaRISA Specimen Collection Log
- ✓ Participant Locator Form (hard copy)
- ✓ Referral Form (hard copy)
- ✓ And/or any other document containing identifying information e.g., copies of receipts for transport fee received; etc.

CHAPTER 6: DISTRESSED RESPONDENTS

6.1 Introduction

Given the nature of this study, there may be instances, where you are faced with a distressed participant who you are concerned needs additional mental health support. For the most part, you can address this by talking to the participant and providing them with a referral to see the mental health nurse or for additional substance abuse services.

6.1. What is a distressed participant?

By “distressed” we mean that a participant shows signs of experiencing negative emotions and by her words, expressions, or other nonverbal behaviors or body language indicates that she is emotionally upset.

Possible signs or indications of distress:

- A participant who is tearful and/or reports that she feels badly or is sad.
- A participant who shows signs of being considerably more nervous or anxious (e.g., very nervous speech, increased sweating, difficulty sitting still during the appointment) than would be expected during an appointment.
- A participant who seems agitated or aggressive and that you cannot easily calm down.

6.1.1. Steps to follow with mildly distressed participants who need additional services.

In most cases of distress, participants may talk about feeling badly but you will be able to manage or contain these feelings and continue with the appointment. They may, however, need additional services or support once all study appointments have been completed.

In these cases, complete the following steps at the end of the study appointment:

- Indicate to the person that they seem upset or anxious.
- Discuss with the participant the importance of additional support.
- Ask if they would like to receive additional services to talk more about feelings that came up during the course of the study.

- If the participant indicates she would like to talk with someone further, ask if they would like you to refer them to an organization.
- Complete the referral and release form.
- With the patient's permission, call the agency or the mental health nurse to make an appointment.
- Provide the patient with a copy of the referral letter in an envelope and keep one in the CONTACTS folder.
- Provide the patient with a copy of our resource guide for additional services.
- If the participant indicates that she does not want you to make a direct referral, suggest various organizations for her to contact on her own and give them a copy of the resource guide.

These steps should only be followed if the participant shows signs of distress or expresses a need for further support - but ***no suicidal intent or imminent harm is disclosed or suspected***.

If the person expresses any desire to end their life or hurt themselves or others, follow the steps described in 6.2.

6.1.2. Steps to follow with very distressed participants.

There may be instances where participants are so distressed that you are concerned for their safety and may not be able to continue with the appointment. Remember that we have made it clear in the consent form that there are exceptions to our promise of confidentiality. If participants express the intent to harm themselves or others, or ongoing abuse and/or neglect of children, then we have a duty to report this matter to the proper authorities, e.g., the police, courts or social workers. Field staff will provide information on toll-free hotlines that people can call to talk to someone and seek assistance, as well as local resource information.

If during the study you are concerned that a participant intends to harm herself or others, then mandatory reporting procedures need to be followed on completion of the appointment. Immediately inform the Project Coordinator and the Site PI, who will report the mandatory reporting incidents to the ethics committee and our project officer within 72 hours.

In these instances, please follow the following steps:

- As far as possible, complete the study appointment.
- Indicate to the person that they seem upset or anxious.
- If they are expressing a desire to end their life (suicide), explore further whether this is an expression of distress or whether they have a) had previous attempts, b) have a plan to end their life.
- If there is immediacy and a plan for suicide, remind the person of the limits of confidentiality as expressed in the consent form, and your duty to report.
- Follow the mandatory reporting procedures described below.
- Complete the referral and release form
- Call the the mental health nurse to make an immediate appointment or accompany the participant to the ER section of the healthcare facility.
- Provide the patients with a copy of the referral letter in an envelope and keep one in the CONTACTS folder.
- Provide the patient with a copy of our resource guide for additional services.
- Follow the reporting procedures in Chapter 7- complete an incident report form and immediately send to the Project Coordinator and Site PI who will both keep copies on file.

6.2. Mandatory reporting procedures

It is possible that a participant will indicate during the course of a discussion that she is in immediate danger of harm or poses a threat to the safety of others. We want you to feel that you can handle this situation with confidence.

There are essentially three situations in which there may be immediate danger of harm:

1) **Suicidal Intent:** The participant expresses a desire to hurt or kill themselves.

2) **Hurtful Intent to Others:** The participant expresses an interest in hurting or killing someone else (not necessarily someone living in the household).

3) **Child Abuse and Neglect:** Ongoing abuse and/or neglect of children.

For each of these cases, you must follow compulsory or mandatory reporting procedures.

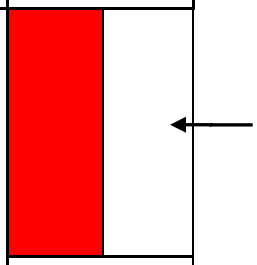
These procedures are important to follow because they take away the responsibility of you having to decide what to do. These procedures are in your best interest and in the best interest of the participant- they are there to keep the participant safe and unharmed.

6.2.1. Suicidal Intent

If a participant expresses an interest in harming or killing herself, assess whether the risk is immediate or not immediate.

Assessing immediacy of risk for suicide: Assessing risk for suicide involves exploring whether the person has current suicidal thoughts, a plan for suicide and access to means. Assess the risk asking the following questions:

	In The Past Month	
Answer Questions 1 and 2	**YES**	**NO**
1) *Have you wished you were dead or wished you could go to sleep and not wake up?*		
2) *Have you actually had any thoughts about killing yourself?*		
If **YES** to 2, answer questions 3, 4, 5, and 6. If **NO** to 2, go directly to question 6		
3) *Have you thought about how you might do this?*		
4) *Have you had any intention of acting on these thoughts of killing yourself, as opposed to you have the thoughts but you definitely would not act on them?*		
5) *Have you started to work out or worked out the details of how to kill yourself?* *Do you intend to carry out this plan?*		

	In The Past Month
	In the Past 3 Months
6) ***Have you done anything, started to do anything, or prepared to do anything to end your life?*** Examples: Collected pills, obtained a gun, gave away valuables, wrote a will or suicide note, took out pills but didn't swallow any, held a gun but changed your mind or it was grabbed from your hand, went to the roof but didn't jump; or actually took pills, tried to shoot yourself, cut yourself, tried to hang yourself, etc. ***In your entire lifetime, how many times have you done any of these things?***	

If the person answers YES to either questions 4, 5, or 6, this is a red flag, and you should consider them at high risk for suicide. Risk is not immediate if the person is expressing some suicidal thoughts to describe how badly they feel but they do not have a plan.

Note: A suicide plan or preparation for death, such as saying goodbyes and putting affairs in order, indicates serious suicidal intent!

6.2.1.1. Procedure: NO IMMEDIATE RISK

If it is clear to you that the participant poses **no immediate risk** to herself (i.e., the participant is not currently suicidal, but alluded to self-harm for some other reason, for example, to express how difficult their life circumstances are), then you should do the following:

a) Complete the appointment,

b) Remind participant of limits to confidentiality from the "Participant Information and Consent Form" and discuss seeking help by contacting LifeLine, SADAG or the Mental Health Nurse,

c) After following these steps, you should complete an incident report form and report the incident to the Project Coordinator. Chapter 7 describes the reporting process in more detail.

6.2.1.2. Procedure: IMMEDIATE RISK

If you assess that the participant is at **immediate risk** to herself, read the following script to the participant:

Script: Risk of participant suicide or self-injury (immediate danger of harm)
Team member reads:
"When you agreed to participate in this study, I promised that I would tell someone what you told me only if it was necessary to protect you or other people. You told me earlier that you were thinking of harming yourself. I suggest we contact an organization called LifeLine or SADAG and let them know so they can talk to you about how you feel. LifeLine and SADAG offers counseling. You can discuss your problem with one of their counsellors and they may be able to help you. Do you want to call them, or should I call them for you?"

Willing participant:

- If the participant agrees to contact Lifeline or SADAG, use the project phone to make the call for the participant, hand them the phone and go to another room to give them privacy during the call.
- If the participant asks you to make the call on their behalf, use the project phone to make the call for the participant, hand the phone to the participant and go to another room to give them privacy in the call.

Unwilling participant

- If the participant is unwilling to contact the crisis hotline and doesn't want you to contact them, then you should immediately contact the Project Coordinator/Site PI, who can assess the situation (e.g., determine reasons why the participant is unwilling to contact the hotline so these issues can be addressed) and who can contact one of the psychologists in the investigative team for further inputs.

- You can also contact the family physician and/or mental health nurse at the facility for their guidance.
- In the meantime, do not leave the participant by herself nor let them leave on their own, as they pose a risk to themselves.
- Ask the participant if she has a close family member or friend who can come to sit with them until you receive clear instructions about what to do.
- If the participant remains unwilling to contact the hotline, provide the participant with the referral guide as well as the counselling hotline numbers.
- Make sure you document who you spoke to, and the advice provided on the incident form (see Chapter 7)

6.2.2. Hurtful Intent to Others

It is extremely unlikely, but someone may spontaneously tell you that they are planning to seriously hurt or kill someone else. If a participant expresses an interest in harming or killing someone else, you should take the following steps.

- As far as possible, complete the study appointment.
- Indicate to the person that they seem upset.
- If they are expressing a desire to hurt someone else, explore whether there is an immediate risk (i.e., they have a plan and the means to do it).
- If there is immediacy and a plan, remind the person of the limits of confidentiality as expressed in the consent form, and your duty to report.
- Follow the mandatory reporting procedures described in Chapter 7.
- Complete an incident report form and immediately send to the Project Coordinator and Site PI who will both keep copies on file.

6.2.2.1. NO IMMEDIATE RISK

If no immediate danger is perceived, advise the Project Coordinator and the Site PI immediately who will evaluate the seriousness of the issue and give advice on what to do. If the danger of harm is definitely credible, then the authorities will be called to report the incident. If the danger of harm is believed to definitely be credible, you may be advised to contact the police.

6.2.2.2. IMMEDIATE RISK

If immediate danger is perceived, please alert the Project Coordinator and the Site PI immediately and they will report the incident to the authorities. Do not let the participant leave before you have instructions from the police as to the next steps to take. Please follow each of these steps. If you feel in danger, please follow the safety procedures outlined in the manual and ask for the assistance of the clinic's security personnel.

It is highly unlikely that you will be faced with this situation!

6.2.3. Child Abuse/Neglect

It is extremely unlikely, but someone may tell you that s/he has abused or neglected a child. If a participant reports this, you must report the incident to the police (if sexual abuse), or Childline (if any other type of abuse) after completing the appointment.

Follow these steps:

- As far as possible, complete the study appointment.
- Indicate to the person that they seem upset.
- If they are reported abusing a child, remind the person of the limits of confidentiality as expressed in the consent form, and your duty to report.
- Follow the reporting procedures in Chapter 7- complete an incident report form and immediately send to the Project Coordinator and Site PI who will both keep copies on file.

CHAPTER 7: INCIDENT REPORTING

7. Introduction

This chapter will outline the various types of reporting that may take place, and under which circumstances they should occur.

Although the proposed study presents no greater than minimal risk to participants, adequate provisions to mitigate these risks will be outlined further in this chapter. The potential risks to participants include:

1) lack of comprehension and acknowledgement of informed consent, study purpose, and rights of participants;
2) exposure to psychological or physical coercion by clinical staff and others;
3) possible disclosure of confidential information;
4) the possible mental discomfort associated with some of the sensitive issues raised during assessments and biological specimen collection and results; and
5) social ramifications of participation in the study.

7.1. Incident Reporting

Incidents are defined as untoward events that occur during conduct of research projects and that affect research participants or staff or may affect study progress.

It is the responsibility of study staff who becomes aware of incidents to report them promptly so that they can be evaluated, reported and responded to appropriately by the study management. Depending on what has occurred, a reported incident may also qualify as an adverse event (AE) or serious adverse event (SAE), social harm, protocol deviation, and/or require reporting to civil authorities.

Examples of incidents that might occur during the study and should be reported include:

- a participant becomes violent towards a staff member.

- a participant reports to a fieldworker that she has suffered abuse from her husband because of her participation in the study or intervention.
- a staff member learns of distrust or rumours spreading about the study in the community,
- a staff member commits or becomes aware of a breach of confidentiality or a lapse in ethical conduct by staff,
- protests / strikes / riots in the community that affect the work of fieldworkers.
- occupational health hazards such as occupational TB,
- a staff member becomes aware of child abuse in the home

These and other incidents should be reported to the study management who will collate and triage all reports, and, depending on the category of incident, report to the study PIs, funders and regulatory bodies.

7.1.1. Adverse Events (AE)

Adverse Events (AEs) will be defined as: report of coercion to participate in the study; or significant hesitance, concern or emotional distress from answering research, such that the participant decides to stop their participation; and harm resulting from breach of confidentiality. Medical events for postpartum health, psychiatric issues including suicidal ideation, or substance abuse that do not require urgent medical attention, emergency care, and/or hospitalization will be also treated as AEs. We will monitor attrition rates for participants but drop out from the study will not be reported as an AE unless it is decided to be related to an untoward event from study participation. Clinically insignificant events are not considered AE's. Examples of clinically insignificant events include mild viral illness (e.g., colds, flu, and runny nose), common headaches, minor scratches, and mild symptoms or problems associated with medical conditions not related to the postpartum periods. As per the definition of AEs, only significant worsening of baseline medical or psychiatric status or new problems will be reported as AEs.

7.1.2. Serious Adverse Events (SAE)

According to the *South African Good Clinical Practice Guidelines* (Department of Health; 2006), SAE is defined as "an event that is associated with death, admission to

hospital, prolongation of a hospital stays, persistent or significant disability or incapacity, or is otherwise life-threatening in connection…" with the research study. For this study, an SAE includes neonatal deaths such as still born babies or miscarriages or any life-threatening events that requires urgent medical attention, emergency care, and/or hospitalization due to early labor. A SAE can also be regarded as any undesirable experience associated with the use of a medical product in a patient or any life-threatening occurrence which could lead to disability / permanent damage, death or other serious medical events (including outcomes that may jeopardize a participant or which may require medical or surgical intervention). Participants in this study are individuals at risk for postpartum depression and other psychosocial issues, and are thus, as a population, at risk for clinical worsening. Although we do not believe the study procedures or intervention places clients at increased risk for clinical worsening, we will review and report events of clinical worsening that leads to hospitalization. These events are not anticipated to occur on a regular basis.

7.2. Identification and Initial Reporting of Incidents

The study depends upon staff to identify and report incidents promptly so that management can know about issues and respond appropriately. When study staff believe they have witnessed, experienced or learned of an event that fits the definition of an incident (AE or SAE), they should verbally report it immediately to the Project Coordinator. The staff member and the Project Coordinator will discuss the incident and if they agree it meets the definition of an incident, the Project Coordinator will provide guidance to the staff member, if needed, to complete, sign and submit the **Incident Report Form**.

In the case that an incident poses a threat to a staff member, the staff member should remove themselves from the threat according to safety procedures. If participants experience any adverse reactions to the intervention part of the study, the staff member will contact the Project Coordinator and/or Site PI immediately for additional support. Based on advice from senior project staff, the field staff will make recommendations for appropriate referrals to medical, counselling and/or other health services.

SAEs (e.g., death or hospitalization) will be reported within 24 - 48 hours of their occurrence by the Site PI, the PI, the SAMRC Research Ethics Committee, and our NIAAA project officer. SAEs will be reported regardless of whether they are considered to be study related. SAEs will be systematically assessed by staff at each participant contact as well as at each scheduled follow-up. At each follow-up, all research participants will be asked whether they had been hospitalized overnight in the past 30 days. In the event that a participant either withdraws from the study or the investigator decides to discontinue a participant due to an SAE, the participant will be monitored by the investigator via ongoing status assessment until (1) a resolution is reached (the problem requiring hospitalization has resolved or stabilized with no further changes expected), (2) the SAE is determined to be clearly unrelated to the study intervention, or (3) the SAE results in death. The PI will review the study protocol with other senior research staff and/or the ethics committee and determine what further action to take based on the best interests of the participants and of the research. With input from the PI, the SAMRC Research Ethics Committee may recommend continuation of the study, modifications to the study, or termination of the study if unacceptable.

Event	Description	Example	Reporting Requirements/Actions
Community/ Environmental Report	Any incident in which events in the community/study environment directly or indirectly have a time/cost/quality effect on the study progress. These incidents are either observed, reported in the media or information obtained from community members	Fires/Floods, natural disasters, taxi violence, service delivery strikes, development of RDP housing (temporary zone restructure resulting in community member migration), political activity, study team excluded from a community due to protest against the study	Reporting to: Project Coordinator Senior Management: PI & Site PI
Staff Safety Incident	Incidents in which staff or any other person are threatened	A participant or any other individual	Reporting to: Project Coordinator

		becomes violent towards a staff	Senior Management: PI & Site PI
Participant Harms			
Social Harm	1) Any untoward social occurrences that happen to a participant as a result of their participation in the study, or 2) any untoward social occurrences that happen to a community, or groups or individuals within a community, as a result of implementation of the study intervention	Participants provide confidential information and if this information is leaked it can have detrimental effects	Reporting to: Project Coordinator Senior Management: PI & Site PI
Protocol Deviation	Protocol non-adherence/violations (the research project's processes not being followed) leading to individual incidents, trends or omissions that result in significant added risk to the participant, non-adherence to significant protocol requirements and significant non-adherence to GCP.	-Enrollment of an ineligible patient. -Informed consent not obtained prior to performing protocol-specified procedures. -Protocol-specified procedures not followed. -Breach of participant confidentiality	Reporting to: Project Coordinator Senior Management: PI & Site PI All Co-Investigators SAMRC Research Ethics Committee NIH Project Officer
Critical Events			
Unanticipated Problems	Any incident, experience or outcomes that is unexpected, has reasonable possibility of being related to a subject's participation in the research and suggests that the research places participants or others at	-Loss of a computer/tablet that contains participants' private identifiable information. -Participant experiences physical violence (e.g., domestic) as a result	Reporting to: Project Coordinator Senior Management: PI & Site PI

	greater risk of harm than previously known or recognized.	of participating in a research study. -Unintentional disclosure of family member's or partner's health status due to participation in the research	
Suspected Research Misconduct	Suspected fabrication, falsification, or plagiarism in proposing, performing, or reviewing research, or in reporting research results.	-Study staff make up data to make it look like household visits were conducted that actually were not. -Staff falsify data on a questionnaire.	-Study staff will report allegations of research misconduct to the PI and/or designee within 24 hours of becoming aware of the incident. -In instances when the study staff cannot notify the PI and/or designee for fear of punishment or another reason, the study staff will notify an appropriate person within their institution. -The PI and/or designee will notify the appropriate person within the institution (e.g., SAMRC REC), and the funding representative, of all applicable known facts about the allegation.
Incidents Reportable to Civil Authorities	Incidents reportable to civil authorities include: Child abuse	Child abuse is observed during a household visit or whilst in the field	