MATRIX-007 Study-Specific Procedures (SSP) Manual Section 5 – Study Procedures

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5. Introduction

This section provides information on requirements for study procedures in MATRIX-007, including enrollment and follow-up visits for pregnant participants and infants, as well as systems for participant tracking.

5.1. Study and Visit Location

The CARE PrEP study is ideally operated out associated CATALYST study sites in a country. If necessary, due to space limitations or other CATALYST site facility constraints, CARE PrEP may base a study site at another location near CATALYST associated site. Depending on the geographical spread of CATALYST sites in a country, one CARE PrEP study site may be linked with more than one CATALYST site. CARE PrEP site locations must have adequate space to complete study procedures, provide a private space for participants, and securely and methodically maintain study documentation and materials. At a minimum, sites will need to be equipped with the following:

- At least 2 separate, lockable filing cabinets for storage of study documents and equipment
- Private space to conduct maternal vitals/fetal heat tones, Point-of-Care (POC) testing, infant physical exams and collect self-reported data from participants
- A comfortable waiting space for pregnant participant and infants
- Copier/printer machine
- Space for study staff to complete administrative/operational tasks

Teams should refer to the **Study Setup Checklist,** provided by the LOG, for all supplies, materials and space considerations needed for study start.

Site facility staff should also be sensitized to the study with rapport built to enable CARE PrEP study staff access to HIV and pregnancy test result and client records to document medical information as well as facility space and equipment, per agreed upon study arrangements. Study staff will also need to setup arrangements for scheduling ultrasounds if these are to be performed at the site facility.

It is expected that all Enrollment Visits will occur on-site. When appropriate and feasible, follow-up visits may be conducted off-site at the participant's home or a location suitable to the participant provided the participant has given consent. Follow up visits may also be conducted via phone contact for designated procedures. When deciding to conduct off-site visits, study teams should consider the privacy and safety of study staff and participants, as well as the cost and logistics of having study staff leave the site to conduct the visit. Importantly, a participant's decision to permit off-site visits will not impact participant eligibility. Contact methods and off-site visit types that are permissible (or explicitly not permissible) should be outlined in SOPs along with associated procedures. See SSP Section 5.5 below for more information on the conduct of off-site study visits.

5.2. Obtaining and Updating Locator Information

To be eligible for enrollment, participants must provide adequate locator information such as a full name, phone or other means to been reached for study retention (e.g., through a community health worker or designated family/partner).

Participant locator information will be captured in a **Participant Locator Form**. Each site will determine what constitutes adequate locator information for their local context, indicate this in an SOP, and adapt a site-specific Participant Locator Form. See sample form on the MATRIX-007 website.

The Participant Locator Form is a paper-based form identifiable by participant name. It is critical that safeguards be in place to keep this information confidential and that forms identifiable by name only be stored separately from participant information identifiable by PID. The only link between the PID and a participant's identity should be on the **MATRIX-007 Name Linkage Log**, stored securely. See SSP section 1 for information on participant confidentiality and document organization.

Research staff will initially collect contact information for all study participants on the **Participant Locator Form** during the enrollment visit. This is prompted towards the end of the **Eligibility CRF** when adequate locator information is assessed as study inclusion criteria. Study staff should complete the Participant Locator Form with the participant and then finish completing the Eligibility CRF. If a participant cannot complete the screening process at a single visit, sufficient contact information should be collected on the form to be able to follow-up with the prospective participant before they leave the visit.

During the informed consent process and when collecting locator information, study participants must be informed that other locator sources provided on the form will be contacted if study staff are unable to locate the participant directly. Study staff will negotiate with the participant how they will identify themselves when locator sources are contacted. Arrangements agreed upon with the participant should be documented on the locator form.

Locator information is reviewed and updated as needed at each visit/contact. When updating locator information, site staff should confirm each source of information is still current (i.e., rather than simply asking "Has any of your information changed since your last visit?") and also probe for additional information that the participant was not able or willing to provide at previous visits. Any updated information should be done per GCP when writing on the form.

5.3. Identification and Verification

At each visit, study staff must verify the identity of the participant and confirm active enrollment in the study. This can be done by providing participants a PID card/sticker. Participants should have a copy of their PID card to present at each visit; or participants may prefer to have a photo of their PID stored on their phones which they can present. When infants enroll, the ID(s) can be added to the same card bearing the maternal PID.

Study staff should also confirm participant identity by asking to verify additional information (e.g., by asking for birth date, name, or phone number) to compare against the **MATRIX-007 Name Linkage Log** and **Participant Locator Form**.

Depending on the frequency a certain facility-based record is accessed, such as HIV test results or ANC records, teams can consider adding an inconspicuous mark to the client record next to study participants' name or on the inside of their chart to connect facility-based records to the study

participant (e.g., a sticker of a designated color). Of note, PID should *not* be written on client registers or within client charts to protect participant confidentiality.

Approaches to confirming participant identity should be outlined in SOPs.

5.4. Visit Types and Schedule

Study visits include Enrollment, Antenatal Quarterly Visits, Pregnancy Outcome Visit, and Post-natal Visits. The following sections will detail the operational aspects of these visits. Sites are expected to develop visit checklists for each visit type based on the sample **Visit Checklists** provided (available on the MATRIX-007 study website). While sites should aim to perform procedures in the order indicated in the approved site study Visit Checklists, it is acknowledged that this might not always be possible. If procedures are consistently listed out of order on the site study visit checklists, sites are encouraged to update their checklists and send to the CRM for review.

Each study visit has a date it is targeted to occur on along with a visit window. Whenever possible, visits should be completed on the target day. If the visits cannot be completed on the target day, the visit should be completed within the visit window. If a visit does not occur within the window, see SSP section 5.8 below for missed visit information and procedure make-up. See SSP section 5.18.2 below for information on a scheduling tool available in REDCap that will calculate visit target dates and windows.

Table 5-1 below describes the visit types and codes, and target dates and completion windows for each visit.

Table 5-1 Visit Types and Schedule

Visit Type	Visit #	Target	window
Enrollment	V101	N/A	Complete within 35 days from date of consent
Antenatal Quarterly 1	V102	+12wks from V101	- 12wks +6wks
Antenatal Quarterly 2	V103	+24wks from V101	-6wks/+6wks
Antenatal Quarterly 3	V104	+36 wks from V101	-6wks/+6wks
Pregnancy Outcome	V201	Within 5 days pregnancy outcome (PO)	+6wks from PO
Post-natal 3-Month	V202	+12wks from PO date	-6wks /+6wks
Post-natal 6-Month	V203	+24wks from PO date	-6wks/+12wks

Table 5-2 shows the schedule of visit procedures from the Protocol. Study staff should attempt to complete all required procedures for a given study visit. If a procedure is missed or cannot be completed, this should be indicated on the Study Visits CRF completed for that visit and a Protocol Deviation CRF filled-out (See SSP section 1 for protocol deviation reporting guidance). Also, no procedures other than those required or indicated at a visit or non-study related procedures (for which the participant did not provide written consent) should occur; a protocol deviation would also be reported in this case.

Table 5-2: Schedule of Visit Procedures

	Antenatal		Postnatal		
	Enrollment	**Quarterly Visits**	**Pregnancy Outcome Visit**	**Month 3 Visit**	**Month 6 Visit/SEV**
ADMINISTRATIVE AND REGULATORY					
Obtain written informed consent for screening and enrollment	X				
Obtain signed medical records release and ANC provider information (if required per local laws/regulations)	X				
Assign a unique PID[5]	X		X (infant)		
Collect/update/review contact/locator information	X	X	X	X	
Assess/confirm eligibility	X				
Provide reimbursement	X	X	X	X	X
Schedule obstetric ultrasound for gestational age confirmation, if adequate records not available	X				
Schedule next visit[5]	*	X	X	X	
COUNSELING					
HIV pre- and post-test counseling[2]	X	X	X	X	X
CLINICAL					
Collect/update/review maternal medical history[1]	X	X	X	X	X
Collect/update/review maternal pregnancy history	X	X	X		
Collect demographic information	X				
Ascertain pregnancy outcome			X		
Maternal depression screening			X	X	*
Blood pressure, height, weight (height only at ENR; weight only at ENR and Antenatal Quarterly visits)	X	X	* (maternal)	* (maternal)	* (maternal)
Review applicable test results/exam findings	X	X	X	X	X
Review available obstetric ultrasound results		X			
Review/confirm gestational age		X			
Detection of fetal heart tones via Doppler (if gestational age estimated at >16 weeks)	X	X			
Infant feeding assessment[5]			X	X	X
Collect/update/review infant medical history[5]			X	X	X
Infant physical exam – weight, length, surface exam[5]			X	X	X

		Antenatal		Postnatal		
		Enrollment	**Quarterly Visits**	**Pregnancy Outcome Visit**	**Month 3 Visit**	**Month 6 Visit/SEV**
POINT OF CARE TESTS						
Blood	HIV rapid test(s)[2]	X	X	X (maternal)	X (maternal)	X (maternal)
	Syphilis test(s)[3]	X	*	* (maternal)	* (maternal)	* (maternal)
Urine	Urine pregnancy test[4]	X			*	*

X = Required
* = If indicated
[1] = To include medication review, including PrEP use when applicable
[2] = HIV rapid testing will be done per local standard of testing; participants with a positive rapid HIV test will be referred back to the CATALYST study site or public sector clinic for confirmatory testing per the national testing algorithm in each study country; HIV rapid testing and pre- and post-test counseling may be omitted from study visits if HIV occurred as part of PrEP or ANC visit within 5 days of the study visit and MATRIX-007 study staff can verify the test results or if participant has initiated ART and MATRIX-007 study staff can verify the ART documentation, as outlined in the MATRIX-007 SSP section 5 and 6
[3] = Syphilis rapid testing will be done per local standard of testing; participants with a positive rapid syphilis test will be referred outside the MATRIX-007 study site for additional testing if needed and for treatment per local standard of care; syphilis testing may be omitted from this study visit if MATRIX-007 study staff can verify a documented negative result performed with a MATRIX-approved test during pregnancy and in the prior 3 months, as outlined in the MATRIX-007 SSP section 5 and 6
[4] = Pregnancy testing will be done per local standard of testing; pregnancy testing may be omitted from study visits
if pregnancy testing or ultrasound confirming pregnancy occurred as part of PrEP or ANC visit within 5 days of the study visit and MATRIX-007 study staff can verify the test results as outlined in the MATRIX-007 SSP Manual
[5] = Omit at Pregnancy Outcome Visit in cases of pregnancy loss; Omit assigning infant PID, scheduling next visit and infant physical exam at Pregnancy Outcome and Post-natal Quarterly Visits in cases of infant loss

5.4.1. Enrollment Visit (with Study Eligibility Assessment)

Once a potential pregnant CATALYST participant is referred for CARE PrEP, study staff has confirmed the person's interest in CARE PrEP, and they have passed pre-screening procedures (if done), they may be scheduled for an Enrollment visit. The study visit includes conducting study consent, study eligibility determination, and enrollment study procedures for those who are enrolled during the visit.

Required enrollment procedures and suggested order/flow are reflected in the sample Visit Checklist available on the MATRIX-007 website. After provision of written informed consent, pregnant participants will be assigned a PID and undergo a series of eligibility assessments.

5.4.1.1. Pre-Enrollment (screening):

Consent: The first step of an enrollment visit before any study procedures may be done is provision of informed consent. Study staff will first need to determine whether the participant may be consented as an adult, i.e. determine if over 18 years old or considered an emancipated/mature minor. Study staff should use the **IC coversheet** to determine whether a potential participant under the age of 18 meets emancipated status. Note: All participants under 18 must meet

emancipated/mature status to enroll in CATALYST. CARE PrEP is responsible to independently confirm emancipated/mature status to ensure all participants under 18 are properly consented for CARE PrEP. Study staff should also comply with country-specific age verification requirements as outlined in a SOP, which may include verifying a national ID or other documentation of age and/or emancipated status. Informed consent should be obtained according to SSP section 3 (Informed Consent). Once consent is completed, the outcome – whether consent obtained or not – should be documented on the **IC Coversheet.**

If consent is not obtained (no signed consent), the participant should be thanked for their time and the visit can end.

PID assignment: For those whose consent is obtained, a PID for the pregnant participant will be assigned. The infant(s) will not be assigned a PID until enrollment of the infant(s) after birth. Each site will be provided with a list of PIDs that should be assigned in the order in which participants enroll. See SSP section 7 (Data Management) for more information on PID assignment. The participant's name and PID must be added to the site's **MATRIX Name Linkage Log** and the participant can be offered a card with the PID for them to keep or to take a photo of the PID to store on their phone (if site practice).

Eligibility Assessment: Next study staff will assess study inclusion/exclusion criteria by completing the **Eligibility CRF** and any procedures to verify eligibility criteria. Source documentation for eligibility criteria is to be indicated in the **Source Document SOP** (See SSP Section 1 for Source documentation guidance). Eligibility assessment will include the following:

- Confirmation of written consent was obtained
- Administration of the **Eligibility CRF** covering the following:
    - Estimation of time of conception and gestational age on date of enrollment. See SSP section 6 for guidance.
    - HIV result record review or testing*, including providing HIV pre/post-test and risk-reduction counseling.
    - Syphilis result record review or testing (testing can be done with a combination HIV syphilis rapid.) *Positive outcome is not exclusionary.* See SSP section 6 for guidance.
    - Pregnancy hCG record/ultrasound review or testing* (Reference the **Pregnancy Dating Job Aid**)
    - Assessment of CATALYST participation and PrEP exposure for the current pregnancy
    - Behavioral assessment
    - Administration of the site-specific **Participant Locator Form** should be completed to assess adequate locator information

  Note: A signed ICF serves as adequate source documentation for the following eligibility criteria, which does NOT need to be assessed separately in the eligibility CRF:
    - Comply with all study requirements and procedures
    - Provide permission to contact participant's antenatal, intrapartum, postpartum and pediatric care provider(s) and to obtain copies of antenatal, intrapartum, postpartum and pediatric care records
    - Provide permission to access the participant's CATALYST study data

  * Repeat testing of exclusionary HIV and hCG test values at enrollment should only be conducted with specific clinical rationale for retesting. Chart notes should document decisions and rationale behind the retesting of abnormal, exclusionary results.

Study staff should complete a QC of the **Eligibility CRF** for accuracy and completion prior to submitting in REDCap. If at any point an eligibility criterion is not met, the visit can be stopped and the participant thanked for their time (with reimbursement per site SOP). In this instance, submit the **Eligibility CRF** with 'not eligible' indicated and a screen fail code selected. Any criteria not assessed before the visit was discontinued can be left blank. The **Participant Tracker** should be completed to record information about the enrollment visit's outcome. See section 5.18 below for details on the Participant Tracker. Any pre-screening form, IC coversheet and/or consent form for a non-enrolled person must be kept on file and filed securely. See SSP section 1 for document organization guidance.

Once the participant signs the consent form, has a PID assigned, and meets eligibility criteria, the **Eligibility CRF** will be completed with 'enrolled' specified and submitted to REDCap, at which point the participant is considered 'enrolled' In the study

5.4.1.2. Post-Enrollment

Once the above procedures are completed and the participant is enrolled, the remaining enrollment visit procedures should be completed as specified on the sample Visit Checklists and as outlined in Table 5-2 above.

5.4.1.3. Incomplete and Split Enrollment Visit

Ideally the Enrollment visit should be completed on the same day as consent is signed, however there may be circumstances where the Enrollment Visit must be completed over more than one day - called a 'split' visit. See SSP section 5.6 below for more details on split visits during study follow-up. Examples of why the Enrollment visit might be split include: the participant is unable to stay for the entire visit, an aspect of study eligibility cannot be confirmed at the time of the first visit date, or the participant has not yet met the PrEP exposure eligibility criteria for PrEP ring or oral PrEP. For example, the participant reports only having access to the ring for the last two weeks and needs more time to achieve the reported 21 days of PrEP use in the last 28 days. Completion of the enrollment visit can be scheduled for a time after which minimum PrEP ring/oral PrEP use (at least 21/28 days) has been achieved. In this case, any CRFs started on the first day of the split visit should be saved. The participant does not need to reconsent at the next visit, however all eligibility criteria needs to be reverified before the participant can proceed to be 'enrolled' and finish the Enrollment visit. Reverifying includes going through the Eligibility CRF again and confirming all eligibility criteria are met as of that date of completion. All screening procedures (consent and study eligibility determination) must be completed within a 35-day window or the person will be considered a screen fail. Participants may re-screen one time for the current pregnancy if study staff deem appropriate and the re-screen is likely to result in an enrollment.

If the participant's eligibility was confirmed and they 'enrolled' but cannot finish the remining study procedures that day, the visit can be completed on another day (as part of a split visit). Pre-enrollment procedures (screening) do not need to be repeated when the participant returns to finish the remaining Enrollment Visit procedures.'

5.4.2. Antenatal quarterly Visits

Following enrollment, the pregnant participant will complete Antenatal Quarterly Visits until a pregnancy outcome occurs. Up to three of these visits are possible, targeted for every 12 weeks from the time a pregnant participant enrolls in the study. See Table 5.1 above for visit windows. Visits should try to be kept near the visit target date to have appropriate spacing between quarterly visits. However, for convenience to the participant, these visits can be scheduled following an ANC

or PrEP appointment on the same day. It is ideal to have the CARE PrEP visit after the other appointment to be able to access the most recent medical and testing results. If a participant has a pregnancy outcome prior to a scheduled antenatal quarterly visit, the remaining visits would be discontinued (no longer expected). The participant would transition to complete the Pregnancy Outcome Visit.

See Sample Visit Checklists for full visit procedure instructions.

5.4.3. Pregnancy Outcome Visit

The Pregnancy Outcome Visit should occur as soon as possible after the participant's pregnancy outcome occurs to maximize the ability to capture accurate and complete data collection – ideally within 5 days. The Pregnancy Outcome visit window closes 6 weeks after the pregnancy outcome date. If allowable by the IRB, study teams may consider an additional reimbursement amount for the extra time and effort to complete the visit within 5 days of the outcome. Study staff should encourage participants to contact study staff as soon as they have an outcome for their pregnancy. Study staff should also track expected due dates (can be done in the Participant Tracker) and contact the participant around that time. Once the participant's pregnancy outcome is confirmed, such as by phone, through a participant-approved community health worker, or notification from the delivery ward, the participant should be scheduled for the Pregnancy Outcome Visit. If the pregnancy results in a live birth, the infant(s) should be present for the visit. Study staff may arrange to complete the Pregnancy Outcome Visit at an off-site location such as the facility where the participant is admitted for delivery, the participant's home, or other location agreed upon by the participant and per off-site visit consent. See SSP section 5.5 below for off-site visit guidance.

For study sites that have a delivery ward within the same facility, study staff should sensitize care providers in the ward about the study and make arrangements for study staff to be alerted if a participant is admitted for labor. Study staff can attempt to complete the visit while the participant is still at the facility – either by conducting the visit within the ward if permissible or escorting the participant to the study area upon discharge from the delivery ward. Any system and communication plans should be outlined in SOPs.

A Pregnancy Outcome Visit may be split in order to complete all study procedures. For example, the participant may provide some information over the phone if they are not able to present for an in-person visit right away or the participant may come for the visit but not be able to bring the infant(s) until a later point. If some study procedures need to be completed on a separate date as a split visit, it is ideal to complete this split visit as soon as possible.

When the participant does not present for the Pregnancy Outcome visit within the 6 week window, efforts should continue to bring in the participant to obtain the pregnancy outcome according to the following:

- The Postnatal 3- or 6-Month Visit is expected (infant is alive) and the visit window has opened: the participant and infant can complete procedures for both the Pregnancy Outcome Visit and the Postnatal Visit merged in the Post-natal Visit.
    - For a merged visit, use the Pregnancy Outcome Visit Checklist (as a guide of needed pregnancy outcome procedures) to ensure the Pregnancy Outcome CRF, Infant Outcome CRF (if first time seeing an infant born alive), and EPDS CRF (if the 6-month Post-natal Visit) are completed. However, record all CRFs in REDCap under the Post-natal Visit being conducted. Also complete a Protocol Deviation for 'Visit conducted outside of window;" see SSP section 1 for protocol deviation guidance.

- Pregnancy Outcome resulted in a loss: The maternal participant can complete pregnancy outcome procedures at an interim visit. Use the Pregnancy Outcome Visit Checklist. This visit would also be considered the study exit visit for the participant(s).

Infant enrollment: Infants born alive with consent on file are automatically enrolled into the study upon birth (DOB is the enrollment date). There are no set study eligibility criteria. At the PO visit, infants are formally entered into the REDCap. A mother can withdraw consent for the infant at any time. If this occurs prior to birth, the infant will NOT be enrolled into the study. If this occurs after birth, even at the PO visit, the infant was considered enrolled for the time of birth until the point of withdrawal. See SSP section 5.16 below for study exit procedures. For pregnancies that result in a loss (miscarriage or still birth), the infant is not enrolled. Only enrolled infants receive a PID. CRFs for non-enrolled infants (including fetal losses), such as the Infant Outcome CRF, and Medical Conditions/Events CRF should be recorded under the maternal record in REDCap; if there is more than one non-enrolled infant in a pregnancy, identify each by the fetal ID from the Ultrasound Results CRF.

See Sample Visit Checklists for full procedure instructions.

5.4.4. Post-natal Visits

Post-natal visits targeted at 3-months and 6-months are expected following a pregnancy outcome of a live birth. These visits should be attended by both the maternal participant and infant(s). Study staff should remind the participant of this requirement and attempt to schedule the visit within the visit window. However, for convenience to the participant, these visits can be scheduled following a post-natal/well baby or PrEP appointment on the same day. It is ideal to have the CARE PrEP visit after the other appointment to be able to access most recent medical and HIV testing results. The Postnatal 6-Month Visit will be the final study visit where all participants will exit if not exited earlier for another reason (pregnancy loss, infant death, withdraw). In case of an infant participant death after the PO Visit is completed, the maternal participant will be asked to complete the post-natal visit they are in the window for as their study exit visit, omitting any infant procedures that cannot be completed.

See Sample Visit Checklists for full procedure instructions.

5.5. Off-site visits

The MATRIX-007 protocol Section 7 specifies that visit procedures may be conducted off-site with participant consent. Off-site visit procedures are distinct from participant contacts made for the purposes of retention/tracing; these procedures are described separately in SSP Section 3 (Accrual Retention), and also separate from phone contacts to perform some procedures in lieu of or as part of a slit in-person visit; these procedures are described in SSP section 5.6 below.

This section describes requirements which must be met prior to implementation of off-site visits, as well as situations which may warrant an off-site visit and what visit procedures will be permitted. Sites should define a set of circumstances to conduct off-site visits and procedures that can be performed based on staff capacity in an SOP.

Off-site visit procedures (excluding site procedures for retention efforts) may only be conducted if the participant has provided written consent for herself and/or her infant to be visited by study staff outside of the study site. Sample text for off-site visit consent is included within the sample enrollment informed consent form. Should local IRB/ECs require a separate informed consent to conduct off-site visits; sites may develop the consent in conjunction with the MATRIX CRM.

If participant consents to off-site visits, study staff should discuss issues that may jeopardize participant confidentiality and/or safety, such as living situation, and whether they have disclosed participation in the study to family, neighbors, or others who may learn of these off-site visits. Where participation has not been disclosed, maximal effort should be made to avoid inadvertent disclosure because of the off-site visit.

Each time an off-site visit is warranted, clinic staff must verify written consent for off-site visits is on file. When communicating with participants ahead of off-site visits, the rationale and the procedures to be conducted for the visit should be clearly explained to her as well as the approximate time that will be needed to complete the required procedures. Every effort should be made to ensure that the time and location is convenient for the participant.

5.5.1. Reasons for off-site visits

Site staff should use good clinical judgment and discretion when determining that an off-site visit is needed for a particular participant. Examples of situations for off-site visits for MATRIX-007 include, but are not limited to:

- Participant does not have time or is unable to come to the site for the visit
- In effort to capture pregnancy outcome information within 5 days of the outcome, when the participant is unable to present to the site
- Follow-up on a SAE or SH
- Follow-up on a participant who has voluntarily withdrawn from the study, but is willing to have study exit procedures conducted

5.5.2. Permitted Locations, Visit Types, and Procedures

Off-site visits may occur at a participant's home or at other appropriate venues (such as delivery wards), provided that both participant and staff are comfortable with the venue and provided that safety and confidentiality can be maintained.

Any type of follow-up visit may be conducted off-site, except the Enrollment Visit must occur on-site. Generally, the required visit procedures should remain largely the same as they would for an on-site visit. However, it is recognized that some procedures may need to be modified or omitted due to limited capacity to conduct them off-site, especially if equipment is needed to conduct a procedure (i.e. vitals, infant growth measures, POC testing). Site staff should document within participant chart notes and the **Study Visit CRF** which visits were conducted off-site and what procedures were omitted or modified as a consequence (if any). As with any visit (on-site or off-site), participants have the right to decline/refuse completing any study procedures; site staff should clearly document refusals in the participant chart and Study Visit CRF. Effort should be made to finish required visit procedures that are not conducted during an off-site visit as part of a split visit within the visit window. A Protocol Deviation should also be completed for any missed procedures.

5.5.3. Off-site Visit Requirements for SOP

Sites are required to have SOPs in place prior to implementation of off-site visits. Considerations that should be addressed in the SOP:

- Procedures for contacting and scheduling participants for off-site visits.
- Procedures for verifying participants' consent prior to conducting off-site visits.

- Procedures to protect the safety of study staff, participants and any family members present during off-site visits, as well as confidentiality of participants.
- Outline of any procedures for:
  - Management of symptoms/illness requiring medical attention. Specifically, procedures for management of positive pregnancy tests, positive HIV rapids, as well as provision of any necessary referrals should be described.
  - Generally, if any issues requiring further follow-up arise at an off-site visit, the participant should be referred (or brought) to the site as soon as possible for further evaluation. Depending on the severity of the issue, site staff may need to transport participant immediately from the off-site visit to the clinic or nearest healthcare facility.
- Description of how routine participant identification procedures will be modified for off-site visits.
- List of materials and supplies that will be needed for an off-site visit

5.5.4. Source Document considerations

- Sites should ideally take the tablet/laptop off site and capture data directly into and be able to reference data from REDCap. Discretion can be used if taking equipment to an off-site visit is not feasible/advisable. Note: that offline data entry into REDCap is only possible on a tablet (not the web-based version on a laptop. See SSP Section 7.)
- If a tablet/laptop is not taken off-site:
  - CRFs that are considered source documents must be completed during the visit in real time on paper. *Updates* to log-style CRFs in REDCap (e.g. medical events/conditions, Medications) or other site-specific trackers can be made upon return to the study site based upon chart notes taken during the visit, but documentation of the off-site visit should never rely on memory.
  - Staff notes (summarizing source documents in the chart) may be necessary to follow up on medical events/conditions/medication use, etc. documented at previous visits. These may be *transcribed* from source documents in the participant binder or within REDCap and brought off-site. No *completed* paper CRFs or other paper source documents should leave the study clinic.
  - Blank paper CRFs and blank chart note pages should be taken off-site to allow visit documentation to occur in real time. They should not be updated or completed after the visit based upon visit notes or memory.
  - It is recommended that paper CRFs be used in these instances and data-entered electronically upon return to the study site.
- All documentation from the off-site visit should be filed in the participant chart and no documentation from the off-site visit should ever be destroyed (for instance, no notes should be jotted on scrap paper that is later thrown away at the study site).
- Source Documentation SOPs apply to off-site visit documentation and data collection/management just as they do for on-site visits.

5.6. Visits Conducted Over Multiple Days: Split Visits

All procedures specified by the protocol to be performed at a follow-up visit, ideally, will be completed at a single visit on a single day. If all required follow-up procedures cannot be completed on a single day (e.g., because the participant must leave the study site before all required procedures are performed), the remaining procedures may be completed on a separate day but within the visit window, if possible. When this happens, it is referred to as a "split visit." Split visits are permitted for any type of visit in MATRIX-007. See SSP section 5.4.1.3 for specific guidance on

split enrollment visits. There are no specific guidelines regarding what procedures must be completed on the same day. If study staff are physically with the participant (onsite or off-site visit) it is ideal to complete all procedures that require in person contact, such as HIV testing, vitals, infant exams, etc. Procedures that do not require being in-person such as collected self-reported data may be done over the phone at another time within the visit window if returning to the site to complete the visit is not possible. See details about phone contacts in section 5.7.

Everyone time a portion of a visit is completed a new **Study Visit CRF** should be completed. For example, if the Pregnancy Outcome Visit was started over a phone contact, complete a Study Visit CRF marking 'Pregnancy Outcome Visit,' 'Over the Phone,' and 'Incomplete.' Then when the participant comes to complete the visit at the site as part of a split visit (must be within the pregnancy outcome visit window), complete a new Study Visit CRF as 'Pregnancy Outcome Visit,' 'onsite,' and 'complete.'

Medical record abstraction done at health facility (without the participant) as part of a specific study visit is considered part of the main study visit. A Study Visit CRF should NOT be completed. Any data abstracted can be incorporated into the study visit CRFs and chart notes associated with the record review.

5.7. Phone Contacts

Study staff may contact participants over the phone for retention purposes (visit reminder or missed visit follow-ups) or to check if a pregnancy outcome has occurred. Study visits are expected to occur in-person either on-site or off-site. There are situations when some study procedures may be conducted over the phone if the participant is able and willing. Reasons may include:

- Participant is unable to come for a visit within the window but is willing go through some procedures over the phone
- The participant started a visit in-person but could not complete all procedures and is unable to return again in-person within the visit window.
- Participant calls to report previously unreported or new study data as an interim visit, such as a Social Harm new information related to a pregnancy outcome.
- A participant reports a pregnancy outcome over the phone and is able to provide some information about the outcome before being able to complete and in-person visit.
- Follow-up on the outcome of confirmatory HIV testing

In these circumstances, study staff may ask if the participant is willing to complete some study procedures over the phone for the visit, omitting any in-person clinical procedures such as vitals, infant exam, HIV/syphilis testing, or pregnancy testing. Study staff will need to weigh the benefit of conducting procedures over the phone to capture data when reviewing hand-held records would not be feasible, and when participant's attention and privacy to thoroughly provide information could be compromised. Due to participant confidentiality concerns, transmitting any participant data over What'sApp text or SMS is NOT permitted. Study staff should never ask for such information in this format. If a participant starts to provide responses in this format, study staff should immediately tell the participant to stop and arrange a time to discuss over the phone or in-person.

When study staff are attempting to reach a participant for a phone contact, they should obtain the contact information and preferences (e.g., method, best time to call, language) from the **Participant Locator Form**. Care should be taken to not write the participant phone number down on any logs, consent or data collection forms, nor store it as a contact in a phone. No direct

mention of the study should be disclosed by research staff until the participant confirms their identity, acknowledges the reason for the call, and is in a comfortable place to continue the conversation. Research staff will need to then verify the participant's identity and PID. It is suggested that research staff have a script or talking points to follow when calling participants. The approach to contacting participants should be outlined in SOPs.

Calls (including failed attempts) should be documented in chart notes. If the call was to conduct visit procedures, study CRFs related to the procedures should be completed and a **Study Visit CRF** completed at the end of the phone contact to indicate the visit was done over the phone and if it was a complete visit and what procedures were missed (it is expected that clinical procedures and testing would be omitted for a phone contact). Visit checklists, chart notes, and any other applicable source documentation should still be completed to denote procedure completion for the visit type being conducted over the phone. Participation in MATRIX-007 is completely voluntary and while there is no maximum number of call attempts to reach a participant, the study team should use their best judgement with respect to frequency of call attempts. Teams may determine their own process to handle call attempts and outline in SOPs.

5.8. Missed visits

To the extent possible maternal and infant participants together should complete their PO Visit and Postnatal Visits. However, if the maternal participant presents for the visit but cannot bring her baby for the infant procedures until another day within the visit window (or vise versa) this can be completed at a split visit if all study procedures are done within window. In this situation, sites will need to clearly delineate the dates at which procedures were done on the visit checklist for each participant (maternal and infant) and explain in chart notes. If visit procedures are not completed within window, the visit should be marked at 'incomplete' on the **Study Visit CRF** and the missed procedures indicated in the notes section of that CRF. Missed procedures must also be documented as Protocol Deviations.

If no procedures of a scheduled visit are conducted within the visit window, the **Study Visit CRF** should be completed after the window closes to indicate the visit was 'missed.'

Missed Antenatal and Post-natal Visits should not be made-up; instead, the visit will be skipped and the study staff should attempt to bring the participant in for the next scheduled visit. Pregnancy Outcome visits that are missed should have procedures made-up at the next Post-natal Visit the participant is able to attend. If merged with the Postnatal Visit, all PO visit procedures should be completed and additionally any other procedures specific to the postnatal visit also being completed (See SSP section 5.4.3 above for guidance).

5.9. Interim visits

Interim visits are visits/contacts with a participant that take place as needed between scheduled visits where any type of study data collection is done. These visits may take place at the discretion of study staff, with study procedures conducted as indicated based on the visit reason. Examples of interim visits expected for this study are reporting a social harm or SAE, reporting HIV confirmatory testing done outside of the study, having new information following a completed visit to report related to the pregnancy, outcome, or post-natal health that is ideally captured in real time instead of waiting until the next visit window opens. The contact/visit should be identified as an interim visit in the participants study records and CRFs. Data abstraction from a medical record from a health facility (participant is not present) is NOT considered an interim visit. See SSP section 7 (Data Management) for more details on documenting interim visits and determining visit codes.

5.10. Participants Who Experience a Pregnancy Loss

If a participant experiences a pregnancy loss after enrolling, study staff should attempt to have them complete the Pregnancy Outcome Visit and exit them from the study at that visit. Post-natal Visits are no longer expected. Whenever possible, pregnancy outcomes should be collected from medical records or other written documentation from a licensed health care practitioner. When medical records cannot be obtained, outcomes may be based on participant report. Participants should receive counseling and referral for medical care, if needed, and support to help them cope with their loss.

Should additional data need to be collected on the pregnancy outcome that was not available at the initial PO visit, for example, delivery or ANC records need to be obtained for abstraction or the participant needs to provide additional information on another day (split visit), study exit can be deferred until data collection is complete. If the participant is not able to complete a full visit PO Visit (missed or incomplete), the **Pregnancy Outcome CRF** should be completed at the least, in absentia if necessary to capture outcome data, and the **Study Exit CRF, marking** 'Scheduled exit visit/end of study,' to end study participation. See section 5.16 below for study exit procedures. All CRFs should be completed under the maternal REDCap record because there is no enrolled infant.

5.11. Infant loss

Infants born alive are considered 'enrolled' on the day of birth. In the event of an infant death, study staff should attempt to compete a final visit with the maternal participant and then both the maternal and infant participants will be exited from the study. This may be the Pregnancy Outcome Visit if not already completed before the infant's death or whichever Post-natal Visit is currently expected (window is open). If the maternal participant is willing to complete a final visit, the infant exam can be omitted. The infant medical history and feeding assessment should be completed if relevant to capture information leading up to or related to the death. Whenever possible, infant death information and relevant medical information should be collected from medical records or other written documentation from a licensed health care practitioner, and recorded in the infant's **Medical Event/Conditions CRF.** When medical records cannot be obtained, outcomes may be based on maternal participant report. Participants should receive counseling, if needed, and support to help them cope with their loss.

If this is the PO visit, the infant should still be 'enrolled' by assigning a PID and completing the **Infant Outcome CRF** and then also exited in absentia, by completing a **Study Exit CRF**, marking 'death' as the reason. The maternal participant can also be exited at this point, marking the **Study Exit CRF** reason as 'Scheduled exit visit/end of study.' If additional data needs to be collected that was not available at the initial PO visit, such as obtaining postpartum or infant health records or the participant needs to provide additional information on another day (split visit), study exit can be deferred until data collection is complete, and completed in absentia if necessary. See section 5.16 below for study exit procedures.

5.12. Maternal Death

In the event of a maternal death, study staff should attempt to ascertain information about the circumstances of the death. This is particularly important if the death was caused by a pregnancy complication. Study staff should use discretion when communicating with family members, based on approved contacts as indicated on the Participant Locator Form or if a family member/partner approaches the study team with information. Study staff may also attempt to abstract data from medical records they have access to in order to capture medical information on CRFs, such as the

Medical Events/Conditions and **Pregnancy Outcome CRF**. Once final data on the participant is captured, study staff should exit the participant from the study in absentia, marking the reason as 'death.'

If the maternal participant died and has a surviving infant, the legal caretaker/guardian for the infant (per site SOP) should be responsible for the remainder of infant follow-up to the extent possible. Please seek guidance from the LOG in such cases. Reconsent from the legal caretaker/guardian will be required.

5.13. Positive Rapid and/or Confirmed Seroconversion

At each visit, HIV testing or review of recent HIV test results is required for the maternal participants. An HIV test can be omitted if study staff are able to access sufficient HIV test result records from testing completed within 5 days prior to the visit date. *Note: A certified copy of the HIV test results must be filed in the participant's study chart. See the MATRIX GDP Policy for how to create a certified copy.* If HIV testing is done by study staff at the visit and the outcome is positive, the participant will need to be referred for confirmatory testing. If the participant is willing, study staff should complete the study visit and at the conclusion of the visit do a warm referral to a health facility that can conduct the confirmatory testing and (if applicable) test the infant per national PMTCT guidelines. Ideally, this can happen within the HIV Testing Service (HTS) point at the health facility where the CARE PrEP site operates. CARE PrEP staff should sensitize facility in-charges and CATALYST research staff of this arrangement.

Confirmatory testing results will need to be communicated back to CARE PrEP study staff – this can be done by study staff checking with the participant following the confirmatory testing and reviewing their test result records. If the participant has confirmatory testing done at another facility due to preference or the site-based HTS cannot complete the confirmatory testing, study staff will need to follow-up with the participant to ascertain their outcomes, ideally by reviewing any records the participant has on hand. Results must be documented on the **Test Results CRF,** and any test results or ART initiation documentation filed as certified copies in the participant's chart. For participants who report that the confirmatory testing status is inconclusive, this outcome can be documented on the Test Results CRF as they await for additional test results. Once the confirmatory testing is conclusive, a new Test Results CRF should be completed.

If a participant presents for a visit and recent HIV test result records indicate or the participant self-reports a seroconversion, the Test Results CRF should be completed. In the absence of confirmation testing results, ART initiation documentation can be used to confirm a seroconversion. Certified copies of documentation should be filed in the participant's binder. If no ART or confirmatory test result is available, study staff should conduct a rapid test.

Participants who seroconvert and have discontinued PrEP should still remain in the study and complete follow-up as expected. However, the participant always has the option to withdraw from the study at any time. If the confirmatory testing was not done through CATALYST, CARE PrEP study staff should encourage participants who seroconvert to inform CATALYST study staff. CARE PrEP study staff are not permitted to disclose information about participants to CATALYST, as this would be a breach of confidentiality.

A seroconversion should also be documented on the participant's **Medical Events/Conditions CRF** and ART on the **Medications CRF,** if applicable.

5.14. Subsequent Pregnancy

If a participant has completed their study participation, but then becomes pregnant again while still presumptively meeting the PrEP exposure inclusion criteria, they may be eligible to enroll again in MATRIX-007 for the subsequent pregnancy. Re-enrollment in the study will require completion of all screening and enrollment procedures again, including obtaining a new consent for the pregnant participant and the infant(s) from this new pregnancy. A new PID will also be assigned to the participant as if they were a new participant to allow the new pregnancy and outcomes to be differentiated from the previous pregnancy. To streamline some redundant data collection and maintain consistency between data collected between the two enrollments, study staff may refer to data collected from the previous pregnancy. This can be done at the time of data collection with the participant present by opening previous CRFs and verifying the data is correct before entering it into CRFs recorded under the current pregnancy. This approach would apply to documenting new data for the **Obstetric Care and History CRF, Demographics CRF, Medical Events and Conditions CRF, Medications CRF**. This would also apply for completing a new **Participant Locator Form** and **Health Care Provider Form**.

A participant could become pregnant again within the post-natal follow-up period. In this case, the maternal participant may enroll the subsequent pregnancy in the study if eligible. If the participant desires to screen for MATRIX-007 for this new pregnancy, the participant should have a new ICF completed to consent to study procedures for themselves and the infant(s) from this new pregnancy at the visit in which they will 'enroll' for the new pregnancy. New PID assignment and data collection for the subsequent pregnancy would follow the guidance described in the above paragraph for re-enrolled participants. See guidance from the MATRIX CRM if this scenario occurs. The participant should complete study procedures for the previous pregnancy in addition to procedures related to the new pregnancy. Such participants would attend visits under both pregnancies until their study participation for the first pregnancy ends i.e. infant completed the Post-natal 6-month visit. If the participant becomes pregnant again during current study participation but declines to consent for the new pregnancy, only procedures related to the previous pregnancy may be conducted.

Submit a Safety Sub-Committee (SCC) query if subsequent pregnancies occur. See SSP Section 6 for guidance.

5.15. Transfers to another site/country

During study participation, participants may leave the area in which they enrolled in the study and re-locate to another area/site where the study is taking place. To maximize participant retention, participants who re-locate from one study location to another should be encouraged to continue their study participation at their new location. To accomplish this, study staff at both the original site (called the "transferring" site) and the new site (called the "receiving" site) will complete the process of a participant transfer. Due to the physical documentation needed at a site to conduct study procedures for a participant, such as documentation for identify verification, locator, consenting information, as well as the participant charts, a participant must be based at one site at a time. Switching back and forth between sites, even when in close proximity, is not practical.

Before initiating the transfer process, the transferring site should confirm that the participant is willing and able to provide consent and complete other study assessments in English or the local language of the receiving site. The maternal and/or infant record and certified copies of all associated source documents will need to be transferred, either by study staff (if close by) or courier.

Upon identifying the need for a participant transfer to another site, the transferring site will notify the receiving site as well as the MATRIX-007 LOG. After the logistical details of the transfer have been discussed and agreed upon by the two sites, following steps to complete the transfer:

- Transferring site:
  - Confirm the participant is able to consent and complete study assessments in **English or the receiving site's local language.**
    - Transfers within country: Reconsenting only needs to happen at the receiving site if the participant's original consent was NOT in a language offered by the receiving site.
    - Transfers to another country: Reconsenting MUST occur for any participant who relocates to a new country using the receiving country's ICF(s). Consent can happen in English or one of the receiving site's local languages if the participant is comfortable in that language.
  - Explain the transfer arrangements to the participant and obtain written permission to provide copies of their study records to the receiving site for both maternal and infant records to be transferred (if infant is enrolled). Even in the case only the infant is being transferred, there may be some maternal information that may be relevant to include with the infant case file on a case-by-case basis (e.g., certified copies of delivery records). If the participant has already moved and cannot return to provide written permission to release their records, the transferring site sends the release to the receiving site for completion by the participant.
  - Certified copies of all associated source documents will need to be transferred. Provide to receiving site either by study staff delivery/pick-up or courier service (overnight preferred). *Note: all original source documents but must be retained on file by the original site.*
  - Complete the **Participant Transfer CRF(s)** in the maternal and/or infant casebook, as applicable, to document completion of the transfer.
- Receiving site
  - Receive participant certified copies of source documents.
  - The participant's original PID and follow-up visit schedule remain unchanged.
  - Complete the **Participant Transfer CRF(s)** in the maternal and/or infant record, as applicable, to document the receipt of the participant(s).
    - Upon receipt of the Participant Transfer CRF in REDCap, the MATRIX-007 Data Manager makes the appropriate database updates to reflect the transfer (i.e. move record to new site). The participant's original PID and follow-up visit schedule remain unchanged.
  - When participant(s) are present:
    - Confirm intentions to deliver at a health center or hospital where adequate records may be obtained.
    - Complete reconsent for the participant as needed (see above)
    - Complete new or update **Participant Locator Form, Health Care Provider Form**, and add participant to the site's **MATRIX-007 Name-Linkage Log**

5.16. Study Exit

In cases in which the maternal participant experiences a live birth, the expectation is that both participants (maternal and infant) will complete visits through the Post-natal 6-Month Visit and be

exited at that visit. Maternal participants who experience a pregnancy loss may exit the study upon completing the visit where this outcome is documented. Maternal participants who experience an infant loss will also exit the study upon completing the visit where this infant death is documented; the infant will be exited in absentia. See sections 5.10 and 5.11 above for details around pregnancy losses and infant losses respectively.

Study participants may also withdraw from the study at any time. See section 5.16.1 below for guidance.

For all study exits, the **Study Exit Guide** should be used to complete study exit procedures. The **Study Exit CRF** should be completed at the end of the final visit completed to indicate that the participant has exited the study and the reason. Whether the participant agrees to be contacted for future studies or to receive study results should be recorded on the site's **Permission to Contact Log**

5.16.1. Early Termination/Voluntary Withdraw

Mothers may voluntarily withdraw themselves and/or their infants from the study (withdraw consent) and terminate their study participation for any reason at any time. At the time of a maternal withdrawal, site staff should confirm if the mother wishes to withdraw consent for both herself and her infant or herself alone. Infant participation should be encouraged and is permitted so long as the mother was ever enrolled in the study and consent for the infant remains on file.

In cases of a withdrawal, site staff should ask the mother if she would be willing to complete one final study visit for herself and infant (if applicable), which would count as the early termination visit. If the participant is willing, early termination procedures will be done per the study visit the participant is in window to complete. At the minimum, staff should:

- Perform a final HIV test for maternal participant, including HIV pre-and post-test counseling.
- Complete the **Study Exit CRF**, mark "Withdrawal of Consent By Participant" and specify the reason the participant has refused further study participation.
- Record the reason(s) for the withdrawal in participants' chart notes.
- Update **Participant Locator form**.
- Ensure all referrals are provided to participant as needed

The PI may withdraw participants from the study to protect their safety and/or if they are unwilling or unable to comply with required study procedures, in consultation with the Safety Sub-committee. Safety sub-committee consultation is not required for voluntary withdrawals. It is recommended that PIs use their discretion with regard to terminating participants who relocate and can no longer complete visits and are unlikely to resume study visits after counseling efforts and discussions with appropriate study staff. If a participant is known to have relocated but has not contacted the site to explicitly withdraw consent, the participant can be terminated early in absentia with the primary reason for completion/discontinuation indicated as "lost to follow-up' on the **Study Exit CRF**. Participants who relocate but agree to continue phone contacts to provide self-reported information, especially through the pregnancy outcome, can be maintained in the study per PI discretion; the rationale being that limited self-reported data is still better than no data at all.

All discussions, counseling, and decisions about early termination should be adequately documented in the participant's chart notes.

5.17. Rejoining After a Withdraw

The protocol allows for participants who voluntarily withdraw from the study to reverse their decision and re-join the study during their planned follow-up period, per their original visit schedule. The resumption of study procedures and follow-up are subject to the PIs discretion, pending safety sub-committee consultation. If such cases arise, study staff are advised to contact the MATRIX LOG for additional guidance on how to manage various aspects of protocol implementation and data collection as the participant resumes participation in the study. In general, however, the following instructions and requirements should be adhered to:

- The participant's original PID and follow-up visit schedule will remain unchanged.
- Prior to performing any study procedure, the participant must re-consent to document that they voluntarily rejoined the study. Site staff should thoroughly document in the participant's chart notes their resumption of study follow-up
- An interval (since the last visit) medical and medication history should be taken when the participant resumes study participation.

5.18. Participant Tracking and Communications with CATALYST

5.18.1. Participant tracking

Sites are instructed to main a **MATRIX-007 Participant Tracker** in excel that includes the following participant status information:

Variable	Options	Instructions/Definitions
PID	XX-XXX-XX	When infants are enrolled, insert a new row under the maternal entry to add the infant(s)
Study Statu	In screening	Select for MATERNAL participants when PID is assigned but eligibility status (enroll/screen fail) is still pending
	Screen fail	Select for MATERNAL participants when screening attempt is complete and outcome is not enrolled.
	Enrolled	Select for maternal participants when enrollment is confirmed form the Enrollment Visits; for infant participants when enrollment is confirmed following pregnancy outcome documentation.
	Exited	Select for maternal participant when study participation has ended due to: pregnancy loss, infant loss, maternal loss, PI withdraw, completion of all expected study visits. *If infant exits independent to the maternal participant, indicate this in the notes section with the exit date*
	Withdrew consent	Select for MATERNAL participants when the maternal participant has withdrawn consent for herself and/or infant. *If infant consent is withdrawn independent to the maternal participant, indicate this in the notes section with the exit date*
Screen fail reason (per attempt 1 or 2)	Code (drop-down)	Enter the inclusion/exclusion criteria code associated with the screen fail reason for Maternal participant. See 'Definitions' sheet of tracker for listing

Expected Due Date	Date	Enter the working EDD initially and update to Final EDD once known
Pregnancy outcome	Pending	Select for maternal participants who have not yet had a pregnancy outcome recorded
	Loss	Select for maternal participants who had a pregnancy loss, with no live births
	Live birth (≥1)	Select for maternal participants who at least 1 live birth from the pregnancy
# Enrolled Infants	Enter #	Enter number of enrolled infants for maternal participants
Notes	Open field text	Indicate salient information about study status, scheduling preferences, or issues with contacting/missing visits

This tool will be saved as a living document on the CARE PrEP data SharePoint in each site folder. Site study staff are expected to update this tool daily and reconcile with REDCap CRFs regularly.

The tool also includes a section to document scheduled next and future visits, that is sortable by visit type and date. This scheduling function is optional to use. REDCap also has a scheduling tool, described in the next section.

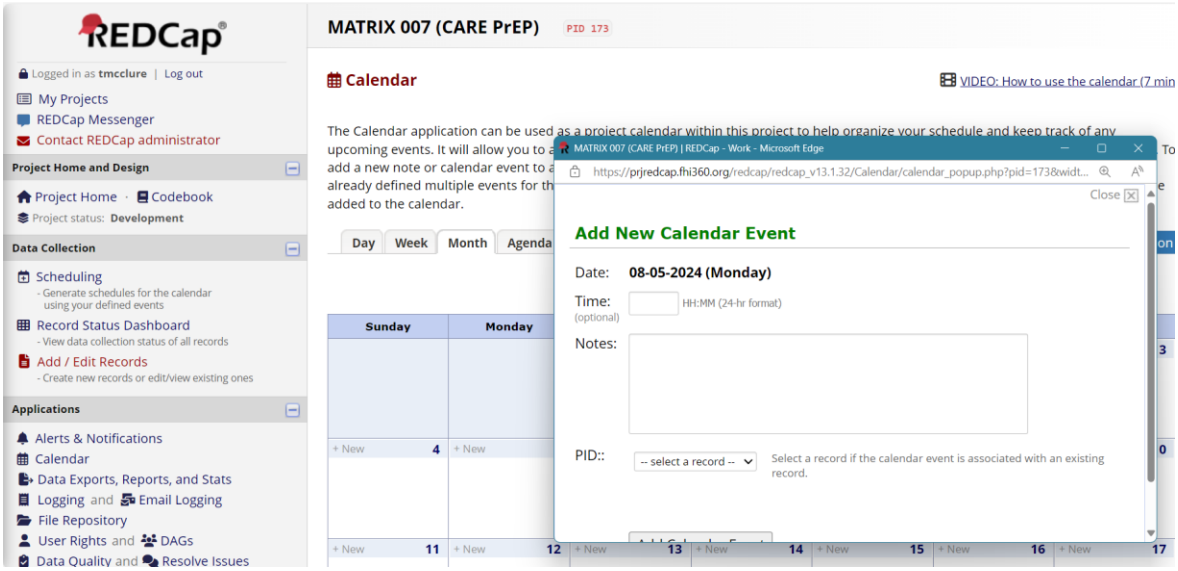
See **Appendix 1** for Participant Tracker example.

5.18.2. Visit Scheduling

Participant visit schedules can be generated in REDCap using the **Participant Scheduling (CRF)**. At the Enrollment visits, the maternal participant's enrollment date, trimester range will be completed to generate the target date and windows for the Antenatal Visits. Once the pregnancy outcome date is known, that date can be entered into the CRF to generate the Pregnancy Outcome Visit window and the Post-natal Visit targets dates and windows.

Study staff can then use the visit target dates and windows to schedule visits. Scheduled visits can be recorded in the Participant Tracker and/or REDCap's scheduling tool, per study staff preference.

- **Participant Tracker:** Allows entry of the visit type, date and notes for the 'next visit' and up to 2 'future visits.' Once the 'next visit' is complete replace the visit type and date with the next visit scheduled (can move over the content from the next 'future visit' section if applicable. Visit dates can be updated as needed for rescheduled visits. See **Appendix 1** for example of how to schedule using the Participant Tracker.
- **REDCap Calendar:** REDCap offers a feature where participant visits can be added to a calendar within REDCap. The Calendar feature is on the left-side menu of the REDCap interface. When logged into see the 'How to use calendar' video link at the top of the calendar webpage.



5.18.3. Data and information sharing

CARE PrEP and CATALYST are inherently linked studies due to individuals participating in both studies, often concurrently. However, the two studies are to operate autonomously. The MATRIX-007 protocol outlines specific considerations for communications and data sharing between the two studies.

Per protocol, MATRIX-007 will request a defined set of data from CATALYST participants be shared from CATALYST per the MATRIX-007/CATALYST Data Sharing Agreement. See SSP Section 7 (Data Management) for details on the requesting and sharing of data sets. The CATALYST participant datasets will be transferred to MATRIX-007 for analysis purposes only. No data from will be available to CARE PrEP study staff for reference during study implementation. CARE PrEP study staff may NOT access any CATALYST data nor complete any CARE PrEP data capture based on information provided by CATALYST study staff. All data recorded must be according the **Source documentation SOP**. The only information that CATALYST study staff may provide to CARE PrEP is referral information for MATRIX-007 recruitment as defined in SSP section 3 (Accrual and Recruitment).

Study staff trying to verify HIV or pregnancy testing results must defer to information available in the health facility records but not directly from CATALYST source documentation. To confirm participation in CATALYST for study eligibility assessment, study staff can do so through a Permission to Contact form or other documentation approach where CATALYST staff attest to a prospective participant's participation in CATALYST when the participant is referred from CATALYST. Another approach is that study staff can look for the CATALYST study participation notation (usually a specific-colored sticker) in the health facility's client file/register. Study staff should have CATALYST staff explain the notation system.

Because the CARE PrEP and CATALYST sites are linked together in relation to dual-enrolled participants, and may also operate out of the same or nearby spaces, communication between the study staff of the two studies is inevitable. However, it is important that the studies do not share any data or personal information about a participant. Talking between study staff even to alert the opposite study of a pregnancy outcome, seroconversion, death or other notable information about a participant is NOT permitted. If a participant has information that the other team would be interested to know, the participant should be encouraged by study staff to inform the other study directly. CATALYST should NOT be relying on information from CARE PrEP (nor vis versa) for study

data collection purposes; all information must be verified independently with the participant or defined source documentation.

CARE PrEP staff must document contacts with CATALYST in a chart note.

Appendix 1: Participant Tracker Sample Completion

SAMPLE

									Next Scheduled Visit			Future Scheduled Visit		
PID	Study Statu	Enrollment/ Screen Fail Date	Screen Fail Reason (Attempt 1)	Screen Fail Reason (Attempt 2)	Expected Due Date	Pregnancy outcome	# Enrolled Infant	Notes	Study Visit Type	Scheduled Visit Date	Notes4	Study Visit Type2	Scheduled Visit Date	Notes2
Z1-001-01	Enrolled	30-May-24			5-Nov-24	Pending			AN V104	16-Oct-24			2-Nov-24	
Z1-002-01	Screen Fail	2-Jun-24	I-2d	N-2										
Z1-003-01	Enrolled	24-Jun-24			5-Oct-24	Live birth (≥ 1)	1	Mother reported birth; will come for PO visit	PO V201	26-Oct-24				
Z1-004-01	Exited	30-Jun-24			3-Mar-25	Loss	0	Exited after POV complete						
Z1-005-01	Enrolled	24-Jul-24			1-Sep-24	Live birth (≥ 1)	2		PN 3M V20:	6-Nov-24				
Z1-006-01	In Screening							resume screening to reassess ring use	ENR V101		to complete screening			
Z1-007	Enrolled	1-Aug-24			28-Feb-25				Ultrasound	5-Sep-24		AN V102	2-Nov-24	