

MTN-016

Screening and Enrollment Visit Procedures: Women



Objectives

- Be able to appropriately apply eligibility criteria for enrollment into MTN-016.
- Be able to complete all screening and enrollment steps for eligible women.
- Understand the visit schedule for obtaining protocol-required procedures and surveys for both MTN-016 and MTN-003.

How will your site...



- Identify when a participant goes into labor?
- Collect medical record data on the mother's delivery for VOICE and MTN-016 CRFs?
- Schedule the newborn/initial visit?

Screening/Enrollment Scenario 1

Abigail enrolled in VOICE in 3 months ago and today her pregnancy test returned positive for the first time.

She reports her last menses was 42 days ago.

What do you need to consider to determine if Abigail is eligible?

MTN 016 Study

← Approximate duration of study participation for woman= 1- 40 weeks

Approximate duration of study participation for infants = 1 year →

V 01.0 SCREENING & ENROLLMENT

Eligibility: confirmed pregnancy for woman enrolled in MTN003

WOMAN INFORMED CONSENT

Locator/ Contact Information

Medical record release
Medical record Review (if delivery has occurred)

CRFs

- Demographics
 - Enrollment
 - Parent Protocol Participation
 - Medical/ Medication History
 - Pregnancy Report & History
 - Genetic Screening History
- As Indicated:
- Pregnancy Outcome
 - Schedule U/S
 - Ultrasound Results

INFANT INFORMED CONSENT

1+ hr visit

V 02.0, 03.0, 04.0 QUARTERLY VISIT

Update Contact Info

Medical record release
Medical record Review (if delivery has occurred)

CRFs

- Follow Up
 - Med History Log (updated)
 - Con Med Log History (updated)
 - Genetic Screening History (updated)
- As Indicated:
- Social Harms Assessment
 - Pregnancy Outcome
 - Schedule U/S
 - Ultrasound Results
 - Woman Missed Visit

INFANT INFORMED CONSENT

Coordinate with appropriate monthly VOICE visit
Visit Window = +/- 45 days

0.5 + hr visits

INTERIM VISIT

Update Contact Info

Medical record release
Medical record Review (if delivery has occurred)

CRFs

- Med History Log (updated)
 - Con Med Log History (updated)
 - Genetic Screening History (updated)
- As Indicated:
- Social Harms Assessment
 - Pregnancy Outcome
 - Schedule U/S
 - Ultrasound Results
 - Woman Missed Visit

INFANT INFORMED CONSENT

POST-DELIVERY

Follow Quarterly Visit or Interim Visit Processes as appropriate

INFANT INFORMED CONSENT

V 01.0 NEWBORN/ INITIAL VISIT

CRFs

- Infant Enrollment
 - Infant Visit
 - Infant Physical Exam
 - Infant Con Meds Log
 - Infant Med History Log
- As Indicated:
- Infant HIV Test Results

Visit Window = within 10 days of delivery

2+ hr visit

V 02.0 INFANT MONTH 1 VISIT

CRFs

- Infant Visit
- Infant Physical Exam
- Infant Con Meds Log
- Infant Med History Log

As Indicated:

- Social Harms Assessment
- Infant HIV Test Results
- Infant Missed Visit

Visit Window = +/- 2 weeks

V 03.0 & 04.0 INFANT MONTHS 6 & 12 VISITS

CRFs

- Infant Visit
- Infant Physical Exam
- Infant Developmental Screening
- Infant Con Meds Log
- Infant Med History Log

As Indicated:

- Social Harms Assessment
- Infant HIV Test Results
- Infant Missed Visit

Visit Window = +/- 1 month

2+ hr visit

V 01.0

SCREENING & ENROLLMENT

Eligibility: confirmed pregnancy for
woman enrolled in MTN003

WOMAN

INFORMED CONSENT

Locator/ Contact Information

Medical record release

Medical record

Review (if delivery has occurred)

CRFs

■Demographics

■Enrollment

■Parent Protocol Participation

■Medical/ Medica-tion History

■Pregnancy Report & History

■Genetic Screening History

As Indicated:

■Pregnancy Outcome

■Schedule U/S

■Ultrasound Results

INFANT

INFORMED CONSENT

Refer to your MTN-016 Cheat Sheet

MTN-016: EMBRACE

What is the main inclusion criterion for participation in 016?

MTN-016: EMBRACE

Main Maternal Inclusion Criterion

- During participation in parent protocol, has/had known confirmed pregnancy 1 year ago or less.
- All eligibility criteria are determined through assessments performed outside of MTN-016, usually through the parent protocol, but possibly, with signed release, through medical charts from primary care.

MTN-016: Inclusion Criteria

Pregnancy confirmed by:

- Two consecutive monthly study visits with positive pregnancy tests OR
- One or more of the following:
 - Auscultation of fetal heart tones
 - Positive pregnancy test confirmed by clinic staff in presence of clinically confirmed enlarged uterus
 - Positive pregnancy confirmed by clinic staff in the presence of a missed menses by participant report
 - Clinical assessment of fetal movement
 - Demonstration of pregnancy by ultrasound

Missed Menses

What is the difference between

missed

and

late

menses, for this protocol?

MTN-016 definition of “missed menses”

- *Positive pregnancy test confirmed by clinic staff in the presence of **missed menses** by participant report.*
- Missed: no menses occurring at least 60 days from first day of last menses.
- For amenorrheic or irregularly cycling women, + hCG tests for 2 consecutive months will be required or use of the other criteria.

Remember:

- Every VOICE Study Visit is a potential MTN-016 Study Visit
 - Screening and Enrollment
 - Interim
 - Quarterly



Screening and Enrollment

- Any time a VOICE participant has a positive pregnancy test:
 - Introduce MTN-016
 - Did the woman miss her previous VOICE monthly visit? Has the woman missed her menses for the past 60 days? Consider MTN-016 screening/enrollment.
 - No missed menses? Plan that the next VOICE visit might be MTN-016 screening/enrollment.

Screening and Enrollment

- Any time an MTN-016 participant becomes pregnant again:
 - Confirm eligibility for this subsequent pregnancy:
 - Has the woman missed her menses for at least 60 days? Consider re-consenting for MTN-016.
 - No missed menses? Plan to re-consent for MTN-016 at next VOICE study visit.

MTN-016: S&E Visit Procedures

- Determine Eligibility
- Informed Consent
- Demographics
- Locator
- Medical/Medication History
- Pregnancy History
- Genetic Screening History
- Ultrasound Results
- As Indicated:
 - Pregnancy Outcome



Screening & Enrollment Logs

MTN-016 Women Screening and Enrollment Log

Site Name and Location:

No. (ex. 1, 2, 3)	Parent Study PTID* (ex. VOICE PTID)	Date IC signed (if not signed, specify reason and complete Staff Initials column)	016 PTID	Eligible?		Subsequent Pregnancy?		Enrollment date (dd MMM yy)	If not enrolled, specify reason	Number of Live Births	Staff initials
				Y	N	Y	N				
				Y	N	Y	N				
				Y	N	Y	N				
				Y	N	Y	N				
				Y	N	Y	N				
				Y	N	Y	N				

Screening & Enrollment Logs

	016 Infant PT ID	Date IC signed (if not signed, specify reason and complete Staff Initials column)	Infant PTID	Eligible*	Enrollment date dd-MMM-yy	If not enrolled, specify reason	Staff initials
1.				Y N			
2.				Y N			
3.				Y N			
4.				Y N			

Back to Abigail...

Abigail enrolled in VOICE in 3 months ago and today her pregnancy test returned positive for the first time and she reports last menses was 42 days ago.

What are the inclusion criteria to consider for Abigail?

- A participant in VOICE at time of conception?
- Was her last menses at least 60 days ago?

MTN-016: Inclusion Criteria

Pregnancy confirmed by:

- Two consecutive monthly study visits with positive pregnancy tests OR
- One or more of the following:
 - Auscultation of fetal heart tones
 - Positive pregnancy test confirmed by clinic staff in presence of clinically confirmed enlarged uterus
 - Positive pregnancy confirmed by clinic staff in the presence of a missed menses by participant report
 - Clinical assessment of fetal movement
 - Demonstration of pregnancy by ultrasound

Screening/Enrollment Scenario 1

Abigail:



- VOICE participant at the time of conception,
- but has not missed her menses for at least 60 days.
- Be prepared to consent and enroll Abigail into 016 at her next VOICE visit, or if she returns for an interim visit after 18 more days.

Screening/Enrollment Scenario 2

Miriam had previously been enrolled in MTN 003 but has missed her last 3 monthly VOICE visits.

Now she returns to the clinic and states she is pregnant. She heard about MTN-016 from a friend and would like to know more about it and possibly take part in it.

Screening-Enrollment Scenario 2

Pregnancy confirmed by:

- Two consecutive monthly study visits with positive pregnancy tests OR
- One or more of the following:
 1. Auscultation of fetal heart tones
 2. Positive pregnancy test confirmed by clinic staff in presence of clinically confirmed enlarged uterus
 3. Positive pregnancy confirmed by clinic staff in the presence of a missed menses (of at least 60 days) by participant report
 4. Clinical assessment of fetal movement
 5. Demonstration of pregnancy by ultrasound

Screening/Enrollment Scenario 2

- Is Miriam eligible for 016 enrollment?
- Will you approach her about rejoining 003?

Screening/Enrollment Scenario 2

Miriam:



- At least 60 days since her last menses.
- Will she return to VOICE?
 - If her urine pregnancy test is positive, she is eligible immediately.

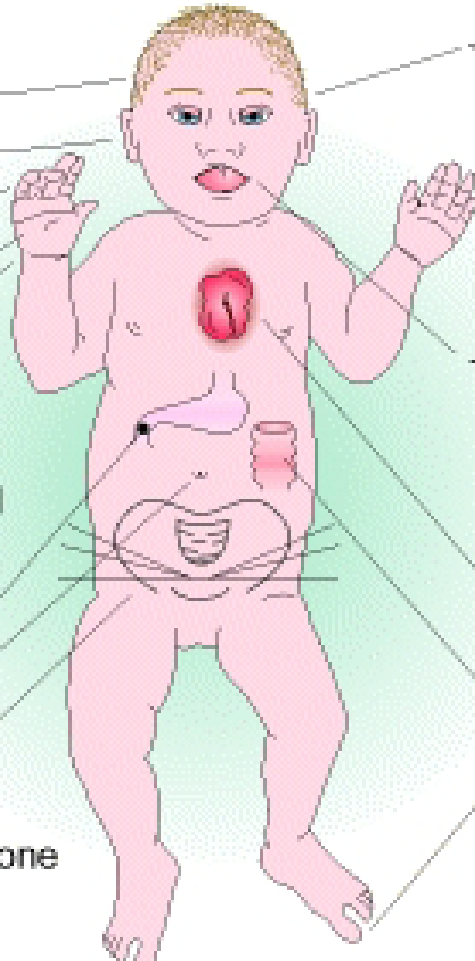
Genetic Screening History Tool

- Tool will be posted on the MTN-016 website.
- Staff may use this tool to aid in discussions with participants while in the clinic.

TERM	EXPLANATION/DEFINITION	NOTES
Cleft Lip or Palate	A child with cleft lip is born with part or the entire upper lip split or missing. In cleft palate, part or the entire roof (top) of the baby's mouth (inside) is missing at the time of birth.	
Heart Defect	The shape of the heart or connections of the blood vessels to the heart are not normal, and thus the heart does not move blood properly. The baby may look normal on the outside, but may also look blue, grey or pale all of the time or just with activity or feeding.	This can sometimes be seen on ultrasound, especially a special ultrasound called echocardiogram. It is not diagnosed just by looking at a baby or listening to the heart, although a heart murmur may be heard with some defects. Heart defects may cause severe weakness, turning blue while feeding or death.
Spina Bifida	A baby with spina bifida (also known as open spine) may have a sac sticking out of the middle or lower part of the back or the affected area may just be open with no skin or covering. The baby be unable to feel things normally (abnormal sensation) and to move the legs.	There may also be weakness or inability to move, or abnormal feet or legs.
Muscle Disease/ Muscular Dystrophy	The muscles are very weak and may get weaker over time. Sometimes, this may occur with other problems in the body, such as stomach problems, learning problems, etc.	This is diagnosed by a doctor getting a small sample of muscle out of the body for laboratory tests. In severe muscle disease, the person cannot walk.
Mental Retardation	The child does not learn like typical children. They learn slowly, may be unable to learn some things, and have difficulty doing things that are normal for children their age.	In severe mental retardation, the person may not be able to speak or control their bladder/bowels.
Down Syndrome	A child is born with a very small chin, weak muscles, a tongue that may rest outside of the mouth, a short neck, a very round face, and mental retardation (see above).	This is also called Trisomy 21. The child may also have difficulties with their digestion and heart defects.
Cystic Fibrosis	This disease causes difficulty breathing and frequent infections of the lungs. Children may have other problems in the body especially blockage of the bowels from thick mucus and not grow properly.	This is also sometimes called CF. Children may pass away at a young age. This disease can pass through families.
Kidney Disease	The body needs kidneys to help clean the blood and make urine. A person born with kidney disease may have problems growing, vomit often, have side or back pain, or may have no symptoms.	The first sign of a kidney problem in children may be high blood pressure; a low number of red blood cells, called anemia; or abnormal urine, including blood in the urine.
Sickle Cell Anaemia	This is a disease of the blood that causes people to have episodes of very severe pain, due to their blood not flowing properly through small veins. These painful episodes can be triggered by an infection.	The pain may be so bad that people need to go to the hospital for medicine. These children may be prescribed antibiotics and folic acid to take every day. This disease can pass through families.
Haemophilia	The body has difficulty controlling bleeding inside and from the skin. Even a small cut or minor surgery may cause a lot of bleeding. People with haemophilia may have cuts that will start bleeding badly again after stopping at first.	Some people call this Bleeder's Disease. Sometimes, this is not diagnosed until a child has an accident of some sort. Many bruises may be on the skin. This disease can pass through families.
Thalassaemia	This is a disease of the blood that can cause fatigue. It is a type of anemia that can be mild or severe. It is not the common kind of anemia seen in pregnancy or in people who lack iron in their diet. The liver and spleen may be enlarged.	This is also sometimes called Mediterranean or Cooley's Anemia. It may be treated with blood transfusion. It can pass through families. It is more common in families that are Italian, Greek, Middle Eastern, Asian, or North African.

Down Syndrome

Growth failure
Mental retardation
Flat back of head
Abnormal ears
Many "loops" on finger tips
Palm crease
Special skin ridge patterns
Unilateral or bilateral absence of one rib
Intestinal blockage
Umbilical hernia
Abnormal pelvis
Diminished muscle tone



Broad flat face
Slanting eyes
Epicanthic eyefold
Short nose

Short and broad hands

Small and arched palate
Big, wrinkled tongue
Dental anomalies

Congenital heart disease

Enlarged colon

Big toes widely spaced

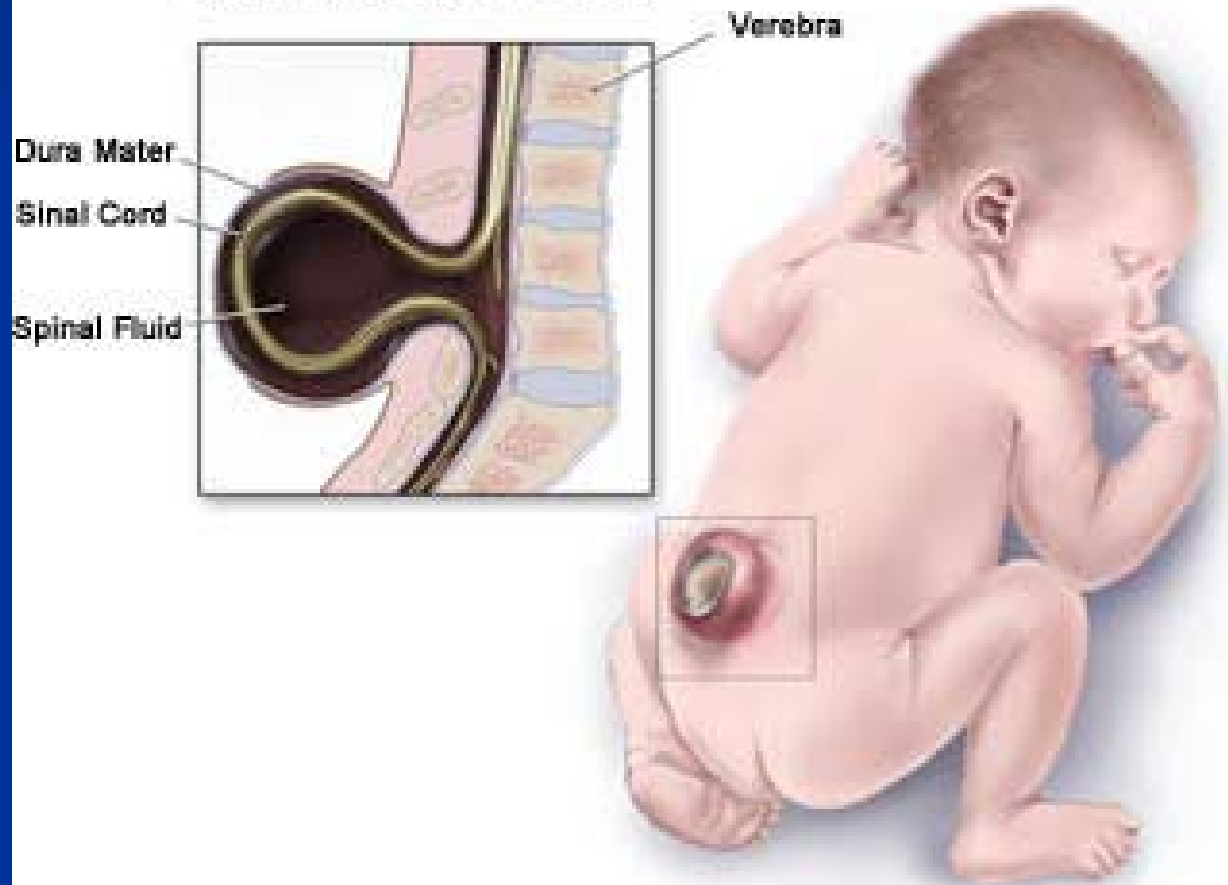


Genetic Screening History Tool

Cleft palate



Spina Bifida (Open Defect)



MTN-016

Quarterly Visit Procedures



Objectives

- Learn the MTN-016 quarterly visit procedures.
- Consider how to coordinate MTN-016 quarterly visits with VOICE visits.
- Identify woman MTN-016 primary and secondary endpoints.

Refer to your MTN-016 Cheat Sheet

* Note the visit windows at the bottom

V 02.0, 03.0, 04.0 QUARTERLY VISIT

Update Contact Info

Medical record release

Medical record

Review (if delivery has occurred)

CRFs

■ Follow Up

■ Med History Log (*updated*)

■ Con Med Log History (*updated*)

■ Genetic Screening History (*updated*)

As Indicated:

■ Social Harms Assessment

■ Pregnancy Outcome

■ Schedule U/S

■ Ultrasound Results

■ Woman Missed Visit

INFANT

INFORMED CONSENT

Quarterly Visit Scenario

- Sarah, a VOICE participant, has been co-enrolled on MTN-016 for about 5 months. She has not had her second quarterly MTN-016 visit.
- During a monthly VOICE visit, she reports that she has felt “different” lately and that she had a day or two of spotting and cramping.
- Her pregnancy test is negative.

Remember:

- Every VOICE Study Visit is a potential MTN-016 Study Visit
 - Screening and Enrollment
 - Interim
 - Quarterly
- Visit Window = 45 days



Quarterly Visit

- During VOICE monthly follow-up, if a pregnant MTN-016 participant has a subsequent negative pregnancy test, consider:
 - Is she within the 45-day visit window for her scheduled MTN-016 quarterly visit?
 - If yes, treat the visit as a Quarterly Visit.
 - Collect Pregnancy Outcome Data.
 - **Pregnancy loss is a MTN-016 primary endpoint.**

Quarterly Visit

- During VOICE monthly follow-up, if a pregnant MTN-016 participant has meaningful updates to her pregnancy history, consider:
 - Is she within the 45-day visit window for her scheduled MTN-016 quarterly visit?
 - Capture the data now rather than waiting for the scheduled visit.
 - **Monitoring adverse pregnancy outcomes is a secondary objective of MTN-016.**

Quarterly Visit Procedures

- Locator
- Medical/Medication History (update)
- Pregnancy Report & History (update)
- Genetic Screening History (update)
- As Indicated:
 - Ultrasound at some point between 20-28 weeks ideally
 - Pregnancy Outcome
 - Social Harms Assessment



Back to Sarah...

- Sarah is a VOICE participant.
- Co-enrolled on MTN-016 for 5 months.
- She has not had her second quarterly MTN-016 visit.
- During a monthly VOICE visit, she reports that she has felt “different” lately and that she had a day or two of spotting and cramping.
- Her pregnancy test is negative.

Quarterly Visit Scenario

- Do you conduct an MTN-016 visit?
- If so, what MTN-016 procedures are required?
- If so, what MTN-016 CRFs are required?

Quarterly Visit Scenario

- Do you conduct an MTN-016 visit?
 - If possible, yes!
 - If within the 45 day window, Quarterly Visit.
 - If not, Interim Visit.
- What MTN-016 forms are required?
 - Update: Locator, Pregnancy History, Medical/Medication History, Genetic Screening History
 - Woman Follow-up Visit, Ultrasound Result, Pregnancy Outcome

MTN-016

Interim Visit Procedures



Objectives

- Understand under which conditions a co-enrolled participant may require an interim visit for EMBRACE.

Remember:

- Every VOICE Study Visit is a potential MTN-016 Study Visit
 - Screening and Enrollment
 - Interim
 - Quarterly



Interim Visit Scenario

Clara is a pregnant woman successfully enrolled in MTN-016 from VOICE. However, she misses her next VOICE visits and does not appear as scheduled for the first MTN-016 quarterly visit. A visit to the woman's home – recorded on the locator form – reveals that she's returned to her home village.

Six months later, Clara reappears at the MTN-016 clinic with her 3 month old baby girl.

Interim Visit

- During VOICE monthly follow-up, any time a pregnant MTN-016 participant has a subsequent negative pregnancy test:
 - Is she outside of the 45-day visit window for her scheduled MTN-016 quarterly visit?
 - Treat the visit as an MTN-016 Interim Visit.
 - Collect Pregnancy Outcome Data.
 - Pregnancy loss is a primary endpoint for MTN-016.

Interim Visit

- During VOICE monthly follow-up, any time a pregnant MTN-016 participant has meaningful medical updates to her pregnancy history:
 - Is she outside of the 45-day visit window for her scheduled MTN-016 quarterly visit?
 - While it's okay to wait for the next scheduled quarterly visit, consider capturing the data closer to real-time as an MTN-016 Interim Visit.
 - Monitoring adverse pregnancy outcomes is a secondary objective of MTN-016.

Interim Visit

- The first time an MTN-016 participant returns to VOICE with a newborn:
 - Has Pregnancy Outcome data already been collected and reported for MTN-016?
 - If not and if it is outside of the 45-day visit window for her scheduled MTN-016 quarterly visit:
 - Consider this an MTN-016 interim visit and collect pregnancy outcome data.
 - Don't forget that this should also be the Newborn/Initial Visit.

Interim Visits

Reasons for visit:

- Report pregnancy outcome
- Perform U/S assessment
- Follow up on or perform infant HIV testing
- Discuss social harm issue
- Follow up on ongoing issue(s)

Interim Visit Procedures

- Update Locator information
- As Indicated:
 - Medical/Medication History
 - Pregnancy History
 - Pregnancy Outcome
 - Social Harms Assessment



Interim Visit Scenario

Clara is enrolled in both VOICE and EMBRACE.

- She missed several VOICE visits and didn't appear as scheduled for the first quarterly visit.
- A visit to the woman's home reveals that she's returned to her home village.
- Several months later, Clara reappears at the MTN-016 clinic with her 3 month old baby girl.

What study procedures for the woman should you consider now?

Interim Visit Scenario

- Forms to Complete for the mother:
 - Interim Visit form
 - Pregnancy Outcome form
 - Updates to:
 - locator form
 - Genetic Screening History form
 - con meds log/ social harms log/ medical history log
 - inquire if U/S results are available
 - Medical record release form to obtain labor & delivery records
 - Change in HIV status?

MTN-016

Pregnancy Outcome Procedures



Objectives

- Understand the procedures for obtaining pregnancy outcome data in MTN-016.
- Consider how you will be made aware of labor and delivery in a timely fashion.
- Recognize infant data collected as part of maternal consent.

Pregnancy Outcome Scenario

- Rebecca is enrolled in MTN-016 and VOICE, and is approximately 32 weeks pregnant.
- During her second MTN-016 quarterly visit, she confirmed her intention to deliver at the local hospital.

How will you ensure you are made aware of her delivery?

How will you prepare for the upcoming infant visits?

Pregnancy Outcome

- During what type of MTN-016 visit will you collect pregnancy outcome data?

Pregnancy Outcome

- During what type of MTN-016 visit will you collect pregnancy outcome data?
 - Any type!
 - No visit is called the “Pregnancy Outcome Visit”
- Pregnancy outcome is always reported in the context of another Woman EMBRACE visit:
 - Screening and Enrollment
 - Quarterly
 - Interim
- You may learn of it during a monthly VOICE visit.

Pregnancy Outcome Procedures

- Complete Screening and Enrollment, Quarterly, or Interim visit procedures as indicated on the appropriate checklist.
- Additionally, obtain pregnancy outcome data:
 - Type and number of pregnancy outcome(s).
 - Gestational age based on obstetric assessment at pregnancy outcome.
 - If live birth, method of delivery.
 - Complications related to pregnancy outcome.
 - Baseline infant information.



Back to Rebecca...

- Rebecca is enrolled in MTN-016 and VOICE, and is approximately 32 weeks pregnant.
- During her second MTN-016 quarterly visit, she confirms her intention to deliver at the local hospital.

What procedures do you have in place at your site for ensuring timely capture of her labor and delivery data?

After learning of her delivery, what steps must you now take?

Pregnancy Outcome Scenario

- Answer Slide...

to be provided by each site this afternoon!

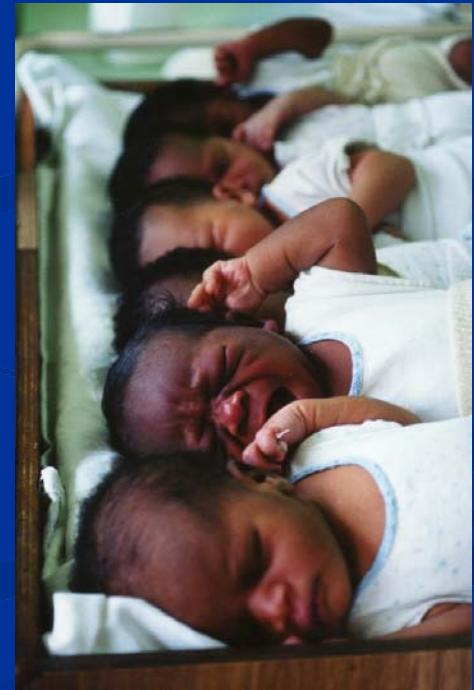
Pregnancy Outcome Scenario

- Rebecca contacts the clinic to inform them of her delivery; when asked about scheduling a newborn exam she indicates she does not want to enroll her infant on MTN-016.

Can you collect any infant data for MTN-016?

Capturing Infant Data

- Maternal consent allows for collection of infant data that are recorded on the L&D notes such as:
 - Infant Gender
 - APGAR scores
 - Length and Weight
 - Head and Abdominal circumference
 - Gestational Age



Pregnancy Outcome Scenario

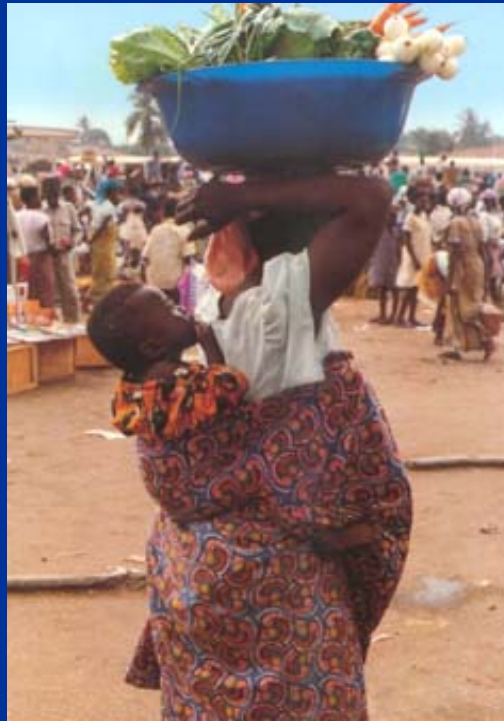
- What steps should be taken if Rebecca instead were willing to enroll her infant?

Pregnancy Outcome Scenario

- Remember Informed Consent for infant enrollment prior to any infant visit procedures.
- Schedule Initial Infant Visit within 10 days of birth.
- At which visit is pregnancy outcome data collected?

MTN-016

Subsequent Pregnancy Procedures



Objectives

- Understand the procedures for subsequent pregnancies in MTN-016.

Subsequent Pregnancy Scenario

- Emily and her infant come to clinic for the infant's 12 month visit.
- She stopped breastfeeding 4 months ago and has resumed her VOICE study product.
- She confides that she has missed her menses and thinks that she may be pregnant again.

Subsequent Pregnancy

- HPTN-035 N=551
- How many multiple pregnancies do you think there were in HPTN-035?
 - 551 women had 613 pregnancies
 - 57 instances of 2 pregnancies
 - 3 instances of 3 pregnancies



Subsequent Pregnancy

- Any time an MTN-016 participant becomes pregnant again:
 - Confirm eligibility
 - Has she had one positive pregnancy test?
 - Has the woman missed her menses for at least 60 days?
 - Consider re-consenting for MTN-016.
 - No missed menses?
 - Plan to re-consent at next VOICE study visit.

Subsequent Pregnancy

- Maternal inclusion and exclusion criteria are the same for subsequent pregnancies as for first time participants.
- Participants will maintain the same PTID for all subsequent pregnancies.
- Requires separate informed consent.
- Note: Think about binder organization for subsequent pregnancies.

Subsequent Pregnancy

- Each subsequent pregnancy represents a new and unique mother/infant pair
 - Informed Consents
 - Pregnancy History
 - Genetic History
 - Father may be different
 - May want to use genetic history from first pregnancy as a prompt, but not to copy

Back to Emily...

- Emily and her infant come to clinic for the infant's 12 month visit.
- She stopped breastfeeding 4 months ago and has resumed her VOICE study product.
- She confides that she has missed her menses and thinks that she may be pregnant again.

Subsequent Pregnancy Scenario

What might your next steps be for Emily in regards to MTN-016?

What might your next steps be in regards to VOICE?

Next steps?

- Missed menses:
 - MTN-016 screening and enrollment visit
 - Remember: new consent, same PTID
- Late menses, but not missed yet:
 - Schedule next VOICE monthly visit, wait for second positive pregnancy test
- VOICE: product hold