1077HS

Participant Manual

for Community Advisory Boards

PROMISE
IMPAACT 1077
Promoting Maternal and Infant Survival Everywhere

IMPAACT
International Maternal Pediatric Adolescent AIDS Clinical Trials Group

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This teaching tool was developed by the François-Xavier Bagnoud Center at the University of Medicine and Dentistry of New Jersey, with the support of the International Maternal, Pediatric and Adolescent Clinical Trials Network.

We would like to express our gratitude for the work of the CAB Members 1077HS Training Manual Working Group. Members of this group recognized the need for these training tools, invested their time, skills and experience, and provided valuable input that guided and shaped the development of all of the contents of this training manual.

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Foreword

This training manual is a resource for Community Advisory Board members at sites implementing IMPAACT 1077HS. The training manual goals are to help CABs with:

- Understanding key sections of the protocol.
- Stimulating discussion between CAB members and scientific staff on various aspects of the protocol.
- Collecting information from CAB members on various local issues that should be addressed by the local research team so as to have effective protocol implementation.
- Preparing CAB members to effectively fulfill their role of communicating research projects to their communities.

Please note: The training manual requires that the trainer and participants have a good overall understanding of the standard structure, format and content of protocols; for example, the meaning of terms such as "eligibility criteria" and "adverse event management" should be understood before undertaking protocol-specific training for 1077HS. The IMPAACT CAB curriculum is available for use if general training is necessary to prepare for 1077HS review. (The curriculum is available on the IMPAACT web site: http://www.impaactgroup.org/icab-trainer-manual).

Facilitating the group

Preparation is the key to conducting a successful training course. The trainer should be thoroughly familiar with training manual content and aware of skills necessary for facilitation.A facilitator helps participants learn through individual and group discussions; the training is not meant to be didactic (lecture-style)

We suggest that trainers complete the following before starting:

- ❑ Read the current protocol documents, which are available on the IMPAACT web site: http://www.impaactgroup.org/1077hs-protocol-specific-web-page
- ❑ Read the training manual, including case studies and suggested answers.
- ❑ Prepare for each of the exercises. Obtain and organize the materials needed.
- ❑ Be prepared to provide directions for exercises, to lead and facilitate group discussions, and to provide participants with help as needed.

Training Schedule

This training takes approximately 3 hours to teach. The course can be organized in either of the following ways, depending on Community Advisory Board members availability:

- Two sessions: 1.5 hours each on separate days. The trainer will cover interactive slides for "Six Crucial Questions" and "1077HS 1-2-3 Knowledge Game" in Session 1. The 1077HS detailed protocol explanation interactive slides, case studies and role play will be covered in Session 2.
- One session: 3 hours on one day. The trainer will cover the entire training manual and should provide a short break in between Session 1 and Session 2 topics.

A course schedule appears below, but the trainer should feel free to re-structure the course to best fit participants' schedules.

	Content
Duration	**Session 1**
30 minutes	Interactive slides "Six Crucial Questions"
60 minutes	1077HS Knowledge Game
	Session 2
45 minutes	Interactive slides "1077HS detailed protocol explanation"
45 minutes	Case studies
15 minutes	Role play

Please provide a copy of the word document "Six Crucial Questions" to all CAB members for review two weeks before the training.

Six Crucial Questions And Answers You Should Know About 1077HS

What is the purpose of the protocol?

Antiretroviral drugs are used for treating patients with HIV infection. Effective treatment requires a combination of antiretroviral drugs—usually at least three drugs. This combination therapy is called highly active antiretroviral therapy, or HAART.

Antiretroviral drugs also reduce the risk of mother-to-child transmission of HIV; as such, they are a critical component of prevention of mother-to-child transmission of HIV, particularly if provided in combination with other interventions such as safer obstetric practices and counseling and support for safer infant feeding. ARVs reduce the risk of MTCT because they reduce the viral load. Viral load refers to the amount of HIV in the blood. The viral load is very high shortly after initial infection with HIV. A high viral load leads to a higher transmission risk. Viral load falls steeply when the body develops antibodies to HIV and rises again after a number of years as the immune system weakens.

CD4 count is the number of CD4 cells in the blood. CD4 cells are the type of white blood cell that is the immune system's key infection fighter. The CD4 count reflects the "health" of the immune system and is used to decide when to start HAART in persons with HIV. A person with HIV who is receiving effective HIV treatment with HAART will usually see an increase in the number of CD4 cells.

When HIV actively multiplies, it infects and kills CD4 cells. The normal CD4 count in a healthy adult is between 500 and 1400 cells/mm^3. As the CD4 count of an adult falls below 200 cells/mm^3, the risk of opportunistic and serious HIV-related infections becomes higher.

Antiretroviral medications are recommended for people living with HIV when the immune system is showing signs of damage from HIV. Immune system status is determined by 1) the clinical status of the person (whether or not they are sick with HIV-related symptoms) and 2) by the number of CD4 cells. When the immune system is weakening and the CD4 count is dropping, ARVs are recommended for treatment of HIV.

However, a pregnant woman living with HIV needs ARVs to reduce the risk of MTCT, even if her CD4 count is high and ARVs are not needed to preserve her health. In sites where IMPAACT 1077HS will be done, pregnant women with HIV infection are offered HAART for PMTCT, even if they do not yet need HAART for their own health. Then, after pregnancy, these women stop taking HAART. This is the current standard of care, but there has not yet been a research study (clinical trial) to determine if this is the best practice. We don't really know what is best: Should the woman

continue HAART once she's started it for PMTCT? Or, should she stop HAART until she needs it for her own health?

We can't know the answer to these questions without conducting a clinical trial. The safety and effectiveness of different types of treatments, medications and other interventions for prevention or management of diseases must be scientifically tested in a clinical trial.

This study aims to answer whether women's health is better served by continuing or stopping HAART after pregnancy.

In this study, there will be two treatment "arms", and women who enter the study will be randomly assigned to one of these two arms. In arm A, called the continue HAART arm, women will continue to take HAART after pregnancy. In arm B, called the stop HAART arm, women will stop HAART after pregnancy. Following the health and status of HIV disease progression in both groups of women will help determine the best way to care for women living with HIV after pregnancy.

Who is eligible for the study?

Approximately 2000 women from countries that use HAART for PMTCT will take part in this study. The study countries include Botswana, Brazil, Thailand and the United States.

In order to be eligible for the study, women be at least 18 years old and must have HIV. They must have a CD4 cell count of 400 or higher and must not have needed or taken ARVs for their own health in the past. During their current pregnancy, they must have taken HAART for PMTCT for at least 4 weeks. Importantly, women must be willing and able to provide written informed consent to take part in the study.

The study involves multiple visits for evaluation and assessments. Therefore participants' willingness to attend study visits as required and remain in their current geographical area of residence for the duration of the study is essential. Participants must be in good heath, not undergoing TB treatment, not be in a correctional facility and not planning to breastfeed the child.

What is expected of participants?

Women who may be eligible for the study will first complete the study informed consent process. This may be done at or after 36 weeks gestation. After informed consent is obtained, eligibility screening may then begin. Screening will involve medical history and review of medical records, a physical exam and lab tests to ensure eligibility for the study. Eligible participants will then be enrolled and randomized, which is like tossing a coin, to either of the two study arms. Randomization must take place within 28 days after childbirth.

Participants will also be asked to provide written informed consent for long term storage and future testing of specimens collected during 1077HS. Participants may choose not to provide this consent and still enroll in the study. For those who choose not to provide this consent, all specimens remaining after the study will be destroyed.

After enrollment, participants will have a study visit after 4 weeks. Thereafter, visits will occur every 12 weeks for the duration of the study. There will be about 7 visits during the first year of being in the study and an average of 4 study visits for subsequent years. At each visit, participants will answer questions about their medical history and the medications they are taking, have physical examinations, and blood tests.

There is a third informed consent process that may also be done as part of the study. If a participant becomes pregnant while on HAART in the study, she will be asked to consent to continue taking study medications while pregnant.

How long will participants be in the study?

Participants will take part in the study for an average of 4 years, with a range of 2 years for women enrolled late into the study, to 6 years for those enrolled at the start of the study. All participants, no matter when they enroll in the study, will be followed for 84 weeks after the last woman is randomized into the study.

It should be noted, however, that women who join the study have the right to withdraw from the study at any time, if they choose.

What are the possible risks associated with the study?

Participants taking study drugs may experience side-effects. These are unwanted effects (such as vomiting or nausea) that some people experience as a result of taking the medication. Though most side effects are mild and temporary, some side effects can be serious. During the informed consent process, the study staff will conduct a comprehensive discussion of possible side-effects and provide a list of the possible side effects. This information will continue to be reviewed with participants who enroll in the study throughout the study period. Study participants will be taught how to manage side effects, including when to seek immediate medical attention.

For patients who take ARVs, there is always a possibility that drug resistant virus will develop. .When drug resistant virus develops, the ARVs are no longer effective at reducing the viral load. The risk of developing drug resistance is especially high when adherence is poor (the drugs are not taken as prescribed). It is also possible that participants who are not on HAART after delivery (as well as participants who do not take their medicines as prescribed) could experience disease progression.

Drawing blood may cause discomfort, pain, dizziness or local bruising and, rarely, a local infection.

Although the study teams will do their best to ensure that participant confidentiality is maintained, absolute confidentiality cannot be guaranteed. For example, there is a possibility that participants might meet by chance with acquaintances also on the study, who as a result may reveal the status of the participant.

How are study participants protected?

Participants cannot be enrolled in the study without their consent. This means that participants must fully understand the purpose of the study, what is expected of them, the potential risks and potential benefits, their rights as study participants, etc. Though the participant signs a consent form before enrolling in the study, information-sharing with the participant is ongoing — including all new information or changes to the study. Participants should understand that they may choose to withdraw from the study at any time. They should also understand who to contact with questions about the study and their rights as study participants.

The study protocol must be reviewed and approved by the local Institutional Review Board (IRB) before enrollment is allowed. Once enrollment starts, ongoing monitoring and reporting is conducted by the IRB and by independent monitors. Another independent group of scientific experts, the Data Safety and Monitoring Board (DSMB) regularly evaluates the data collected during the trial to determine if any safety issues have developed that require a change to the protocol (or stopping the study). Additionally, the DSMB compares the study data from each arm of the study. If, for example, participants from one arm of the study are doing much better than participants in the other arm of the study, the study will be stopped. In this case, all participants are offered the more effective treatment option.

Participants randomized to stop HAART post-delivery are monitored carefully throughout the study. If the CD4 count falls and they become eligible for treatment with HAART (for their own health), HAART will be provided.

Participants on HAART who develop side-effects due to medications will be assessed and appropriate decisions made to ensure their safety. The study team may recommend changing or stopping the medicines, as clinically indicated.

Participant confidentiality will be protected through the use of coded numbers for laboratory forms, evaluation forms, reports and other records that are transferred or transmitted off-site for processing. All records will be kept in a secured area. All computer entry and networking programs will be done with coded numbers only.

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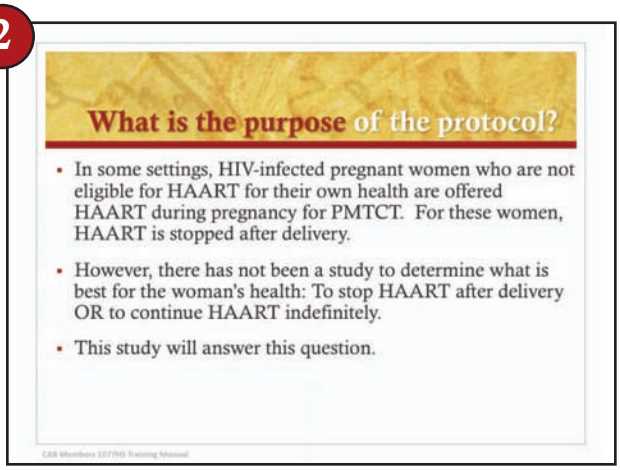

- The use of HAART during pregnancy for preventing mother-to-child transmission of HIV is known as PMTCT.
- PMTCT using HAART during pregnancy is a very effective method of reducing mother-to-child transmission of HIV.
- HIV patients are started on HAART depending on the level of their immunity. Immunity can be assessed through CD4 cells level or AIDS-related clinical signs.
- The standard practice in countries using HAART for PMTCT is to stop the medications after child birth for women who do not require HAART for their own health.
- The effects of stopping HAART after PMTCT on maternal health have not been studied systematically.
- 1077HS will provide evidence based facts to support continuous use of HAART or stopping HAART after PMTCT for women who have not reached clinical indication for HAART.

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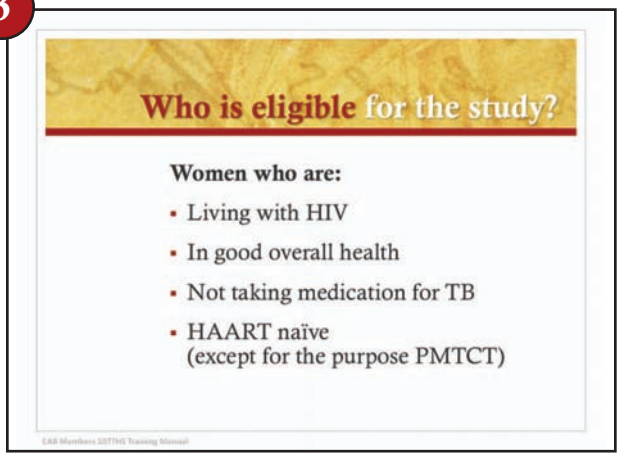

- HAART naivety is defined as not having used HAART for more than 14 days for a reason not related to pregnancy.
- No participant can be recruited for a second time if she becomes pregnant after initial enrollment.
- They should be in good general health, not on anti-Tb medication, not institutionalized and at a legal age to provide an informed consent.
- A total of 2000 participants will be recruited for the study.

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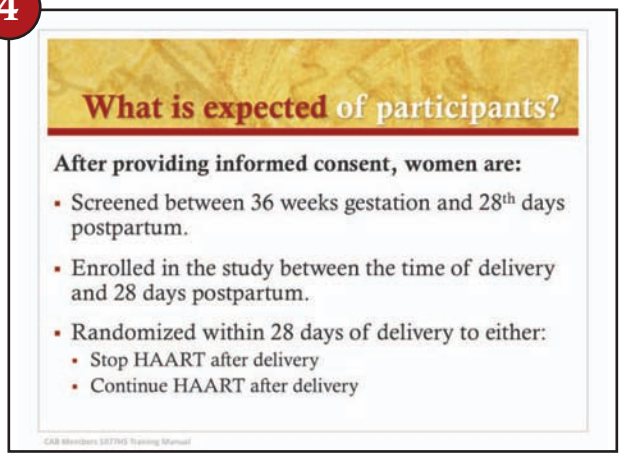

- Participants will be randomized into the study after child birth but within 28 days.
- The study visits have a flexibility of ± 14 days.
- Participants will have a screening visit, an entry visit, follow up after 4 weeks and then one study visit every 12 weeks ~3months.
- There are three informed consents:
  - Screening and enrollment: Given to all participants. Study procedures cannot be done without this consent form.
  - Specimen storage for future use: Given to all participants for a permission to store their specimens for future use. Participants who decline this consent will be recruited into the study but their samples will not be stored for future research. However, samples will not be destroyed until the conclusion of the study.
  - Consent for women who become pregnant while on study medication: Given to women only on study medications.

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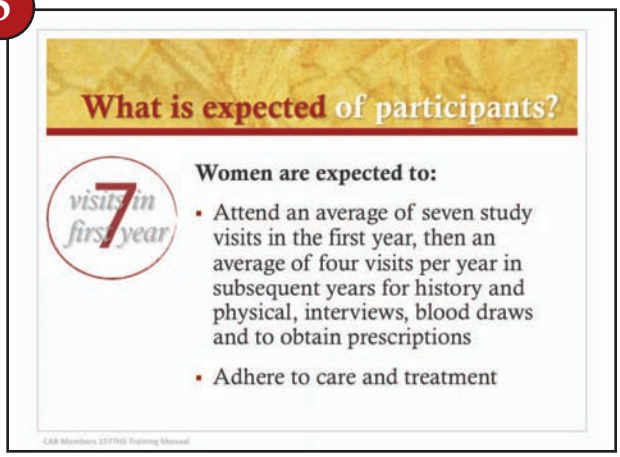

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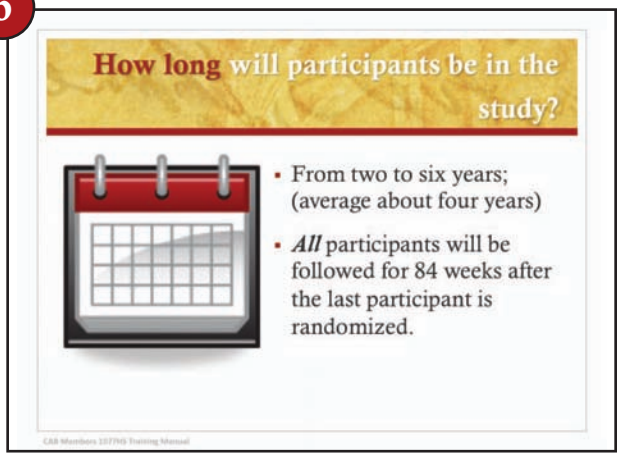

- Duration taken on the study will depend on the time when the participant is recruited.
- Important to note that all participants will be followed until 84 weeks after the last participant has been randomized into the study.
- Women who join the study have a right to withdraw from the study at any time, if they choose

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- Side effects are unwanted effects that are drug specific. Some are well known, as a causal relationship has been established, but others are not known.
- In research Toxicity effects or side effects and changes in lab values due to medications are graded in levels 1 to 4. The level determines further steps to be taken to guide safety of the participants.
- When antiretrovirals are not taken per instruction, for example, not taken on schedule or taken at smaller doses than directed, the virus may develop resistance to those antiretrovirals. Stopping antiretrovirals as it will be done in STOP HAART arm of the study may cause the virus to rebound, virus rebound means that the HIV viral load goes back up.
- Drawing blood may cause discomfort, pain, dizziness, or local bruising and rarely a local infection.
- The study staff are trained to keep all participants information confidential however, there is a possibility of meeting with acquaintances at study visits who may reveal the status of the participant.

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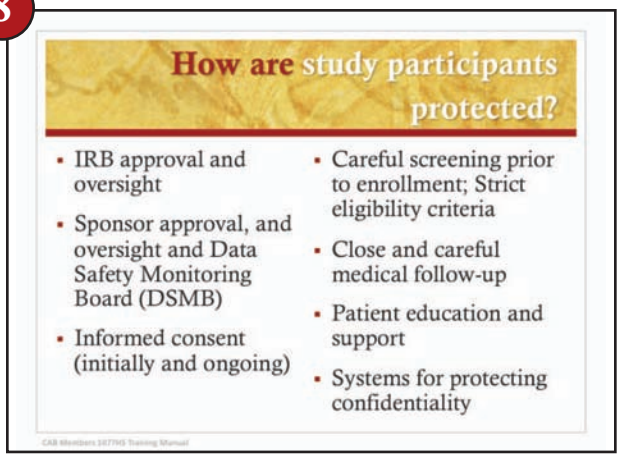

- Local IRB will review and approve the study. Any changes to be done on the protocol will need approval of IRB.
- DSMB regularly evaluates the data collected during the trial to determine if any safety issues have developed that require a change to the protocol (or stopping the study).
- Written informed consent to ensure that participants are making their own decisions voluntarily.
- Participants in the stop HAART arm of the study will be followed closely and HAART can be started if they attain criteria for HAART per local guidelines at the site.
- Coded numbers instead of names will be used for laboratory forms, evaluation forms, reports and other records that are transferred or transmitted off-site for processing.

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Knowledge Assessment Game 1077HS 1-2-3

KNOWLEDGE GAME

Part 1:

Respond with either YES or NO for the following statements and be prepared to provide an explanation to support your answers.

1. HAART refers to the use of one antiretroviral medication for preventing mother-to-child transmission of HIV.
2. Research clearly shows that it is beneficial to stop antiretrovirals (ARVs) in HIV-infected women who are otherwise healthy after using them for preventing mother-to-child transmission of HIV.
3. Number of CD4 cells is one of the indicators used to show if an HIV-infected person requires HAART.
4. Can someone who has been on ARVs for 21 days, and then stopped prior to becoming pregnant, be eligible for 1077HS?
5. Sites may start screening pregnant women at a gestation age of 3 months so as to increase the number of subjects screened for possible enrollment.
6. Can an investigator at site X change the protocol on his own after approval by the IRB, so as to answer a question he thinks is of critical scientific importance at his site?
7. Participants in stop HAART arm of the study are not supposed to use HAART for the entire duration of the study.

Part 2:

Discuss the questions and provide a short answer for each.

1. What is the minimum CD4 cell count a participant can have at the initiation of HAART for PMTCT to be eligible for 1077HS?
2. For how long do eligible participants for 1077HS need to have been on HAART for PMTCT to qualify for the study?
3. How many times can a participant be enrolled into 1077HS?
4. How many participants are expected to take part in the study?
5. How long after the last participant has been randomized into the study will follow up take place?
6. What is the estimated number of visits a participant is expected to make in the first year? How about in subsequent years?
7. What are the possible disadvantages associated with continuing HAART for a woman who used HAART solemnly for PMTCT and not her own health?

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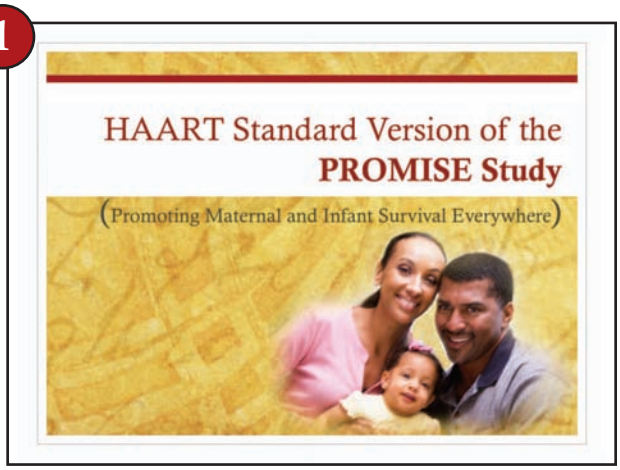

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- The protocol is geared towards promoting maternal and infant survival.
- The efforts of addressing different issues on maternal and infant survival are being done all over the world "everywhere".

3

- Although IMPAACT protocols are abbreviated as P, PROMISE protocols do not have P but are abbreviated as 1077BF, 1077FF and 1077HS.
- The three studies are designed to answer questions about PMTCT based on standard of care of PMTCT and the primary infant feeding methods in different regions of the world.
- The Breast feeding components will answer questions related to PMTCT at sites where HAART is not provided during pregnancy for PMTCT and infants are breastfed. The Formula feeding components will answer questions for settings where HAART is not provided during pregnancy for PMTCT and formula is available. The HAART Standard component is being conducted in areas where HAART is provided to HIV-infected women to prevent MTCT of HIV and the infants have access to replacement feeding.
- This training will focus on 1077HS because HAART is the standard of care for PMTCT in this setting for all pregnant women with HIV.
- Resource-limited countries generally do not provide HAART to pregnant HIV-infected women for PMTCT.

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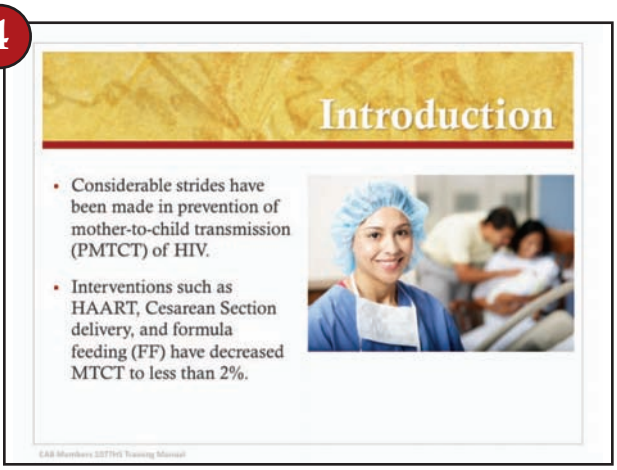

- During the early days of the epidemic there was no antiretroviral drugs.
- ACTG 076 Study showed that antiretroviral can reduce mother to child transmission of HIV, that was the starting point of PMTCT.
- MTCT of HIV was lowered even further by adopting practices that prevent transmission from mother to the baby at all the three stages during pregnancy, delivery and breast feeding.
- Resource-advantaged settings such as US and Europe have succeeded in lowering transmission to less than 2%.
- The challenges they are facing now is ensuring detection of all HIV-infected women prior to conception and early enough during pregnancy so that appropriate counseling and appropriate ART can be provided.

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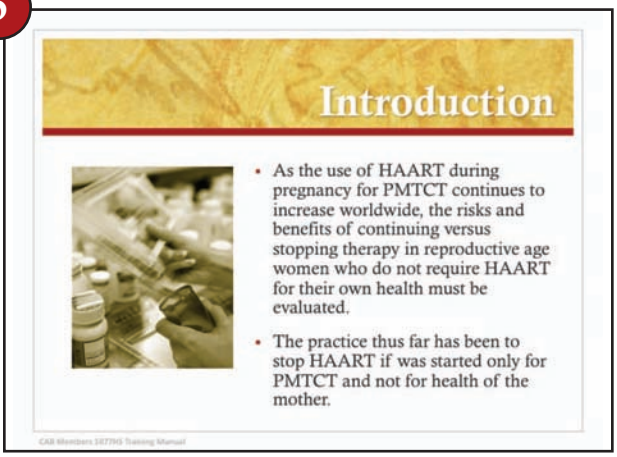

- Currently in the US and other countries where HAART is routinely used for PMTCT treatment is discontinued after delivery in women who did not require HAART for their own health at initiation although the safety of this approach has not been evaluated.
- If women who receive HAART for PMTCT incur some penalty in terms of their own health, then this may offset any benefits of a maternal HAART strategy for PMTCT.

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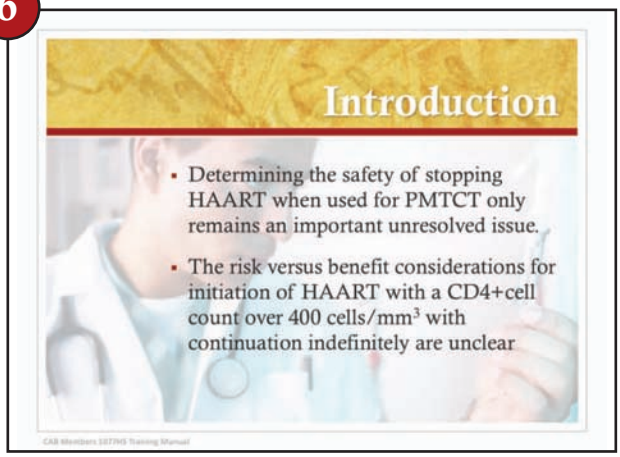

- The main issues addressed by 1077HS are the risks and benefits of stopping versus continuing HAART after completion of pregnancy for women who received HAART solely to prevent MTCT.
- Factors that might support initiating therapy as early as possible include the potential negative impact of uncontrolled HIV replication on renal, hepatic, neurologic, cognitive and immunological functions.
- Earlier treatment of HIV infection may have public health implications, as it may reduce HIV transmission, may have significant implication among individuals in discordant relationships (HIV infected individuals with HIV-uninfected sexual partners)
- Arguments against early treatment:
  I. Although there are several reasonably safe and well-tolerated options for first line regimens, the long-term toxicities remain unknown.
  II. ART requires life-long adherence to therapy. Some patient may find that the need to take daily medications decreases quality of life, even without side effects.
  III. Non adherence may increase development of resistance, limiting future treatment options (For effective treatment adherence should be more than 95%) For example if you are to take medication 100 times you can not miss more than 5 times for the medicines to be effective.

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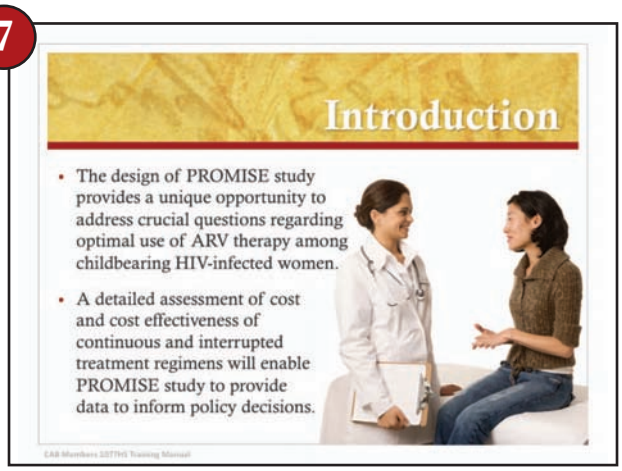

- Treatment interruption refers to the current practice among women who are given antiretrovirals for PMTCT and not their own health. After delivery the medicines are stopped/interrupted to be started again when she has criteria for treatment.
- Policy makers use research findings to decide on the standard of care.

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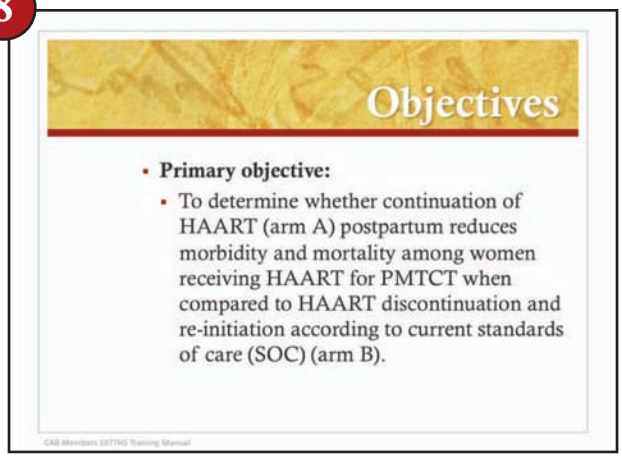

- Arm A and B represents the two study groups.
- Morbidity is an incidence of ill health. As HIV infection advances the patient develops AIDS. With low immunity level the patient tend to get sick even by organisms that would not have developed symptoms if the immunity was high.
- Mortality is death.

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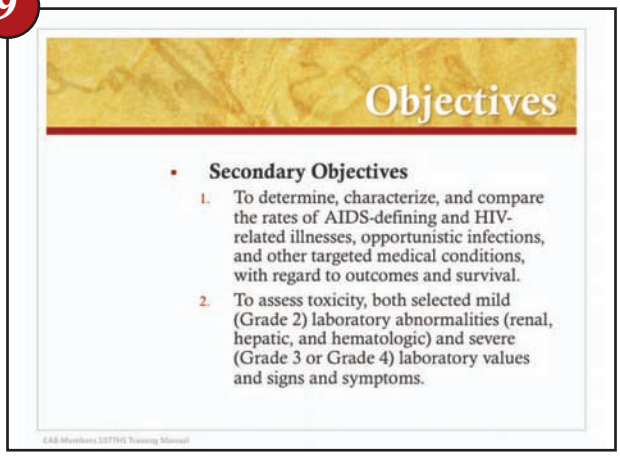

- ARVs like any other medications have side effects.
- Toxicity can be graded using laboratory methods, report from the patient (history) and physical examination.
- Symptoms refers to a report from a patient while signs are identified by a clinician during examination.
- Study clinicians are provided with clear instructions on how to grade toxicity levels. Study clinicians have instructions on actions to be taken at various toxicity levels.

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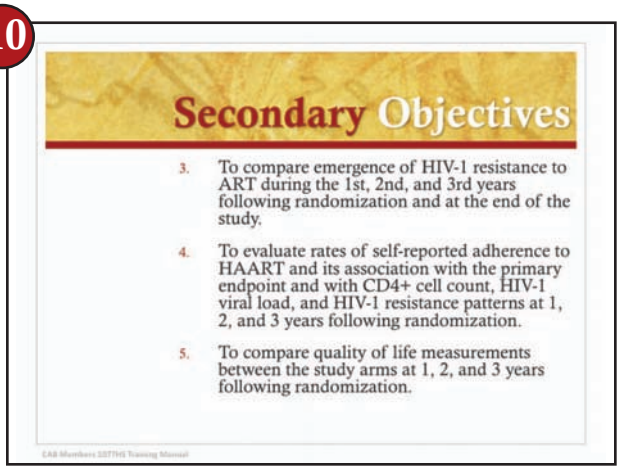

- Resistance might vary among the research arms because of adherence or treatment interruption. This study will provide a clue on resistance development patterns.
- Quality of life (QOL) will be measured based on AIDS related illnesses, Opportunistic infections, mortality, Years of life saved, medications side effects among other parameters. There is a QOL questionnaire form that participants will complete.

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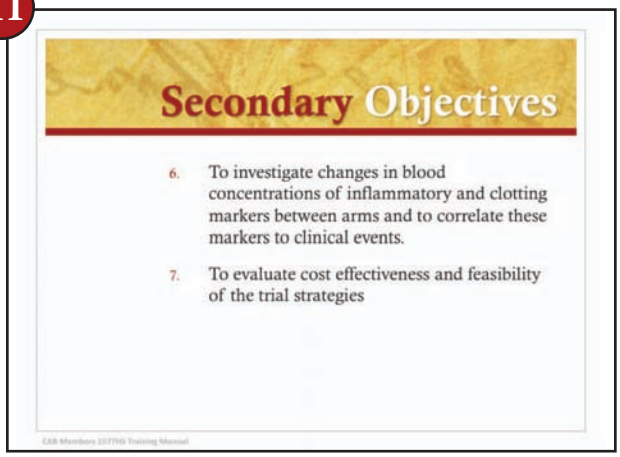
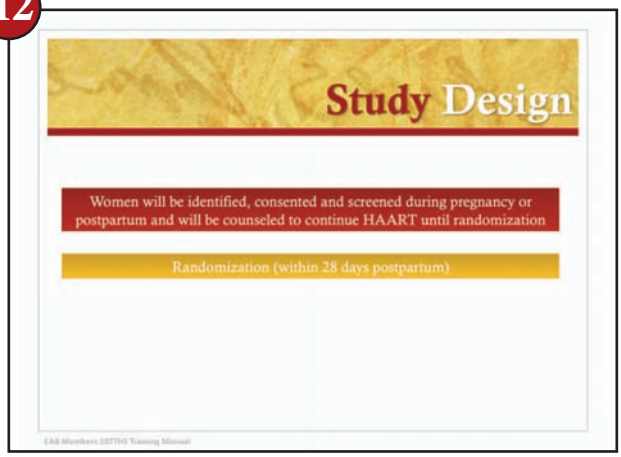


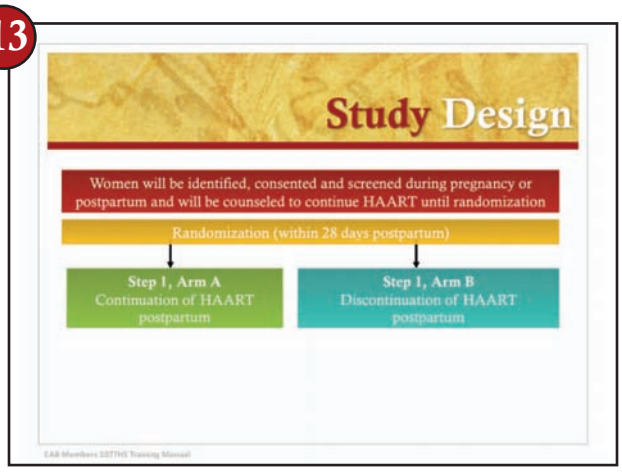
- Previous studies have shown that interruption of HAART is associated with changes in inflammatory and coagulation markers, factors that may influence the risk of organ damage.
- Cost effective analysis will guide policy decisions regarding use of the current interrupted HAART after PMTCT or continuous use even when the CD4+ are above 350 cells/mm^3.

12



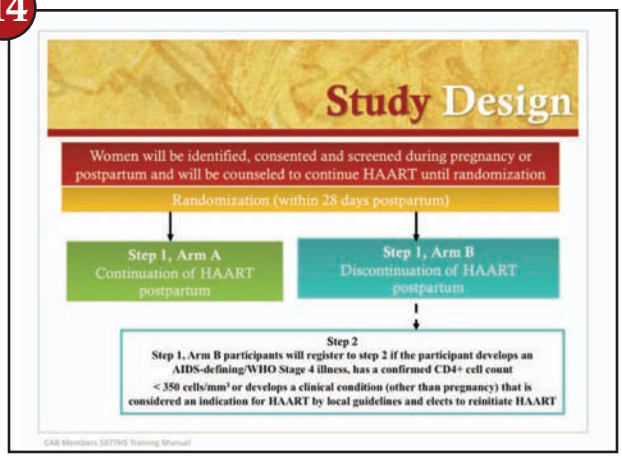
- This trial will recruit and screen pregnant or postpartum women who are on HAART solely for PMTCT with a CD4+ cell count ≥ 400 cells/mm^3 at HAART initiation and who are between 36 weeks gestation and 28 days postpartum.
- Women who are screened for the study will be counseled to continue their HAART until they are randomized.

13



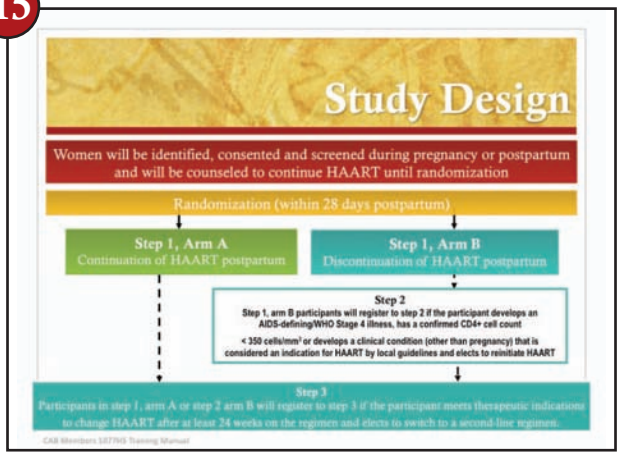
- Women will be randomly assigned "like flipping a coin: Heads = "Continue HAART" , Tails = "Stop HAART" arm of the study.
- Each arm has multiple steps.
- Step 1 in arm B is discontinuation of HAART postpartum while arm A is continuation of HAART.

14



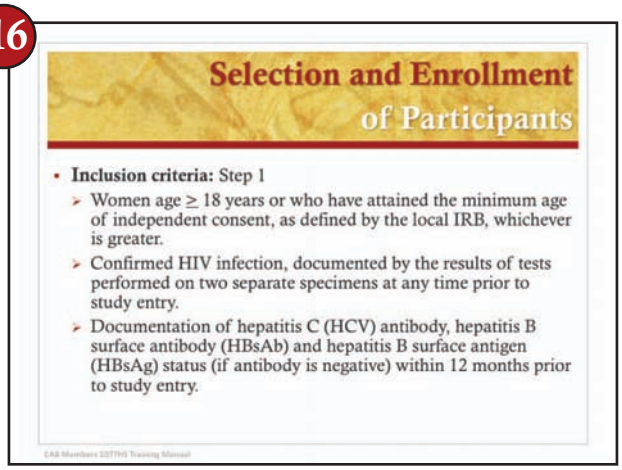
- To ensure patient safety arm B will move into step 2 if they develop AIDS defining/WHO stage 4 illness, has confirmed CD4+ cell count <350 cells/mm^3 or develops a clinical condition that is considered an indication for HAART.
- Moving into step 2 means that they are started on HAART.
- Arm A does not have step 2 as they are already on HAART from step 1.

15



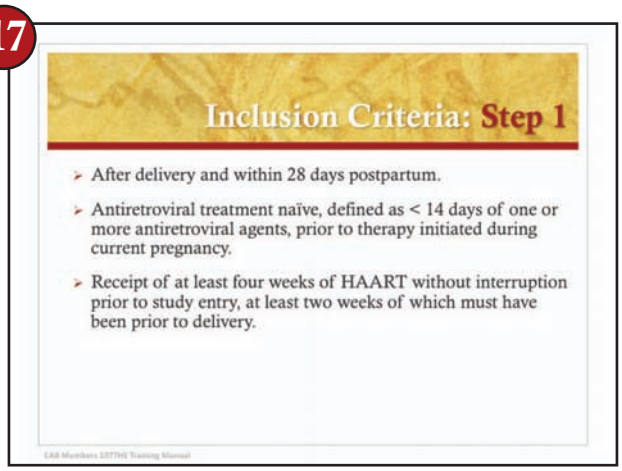
- Step 3 applies to both arms A and B.
- Participants will be considered to move to step 3 if they have met therapeutic indication to change HAART after at least 24 weeks on the regimen.

16



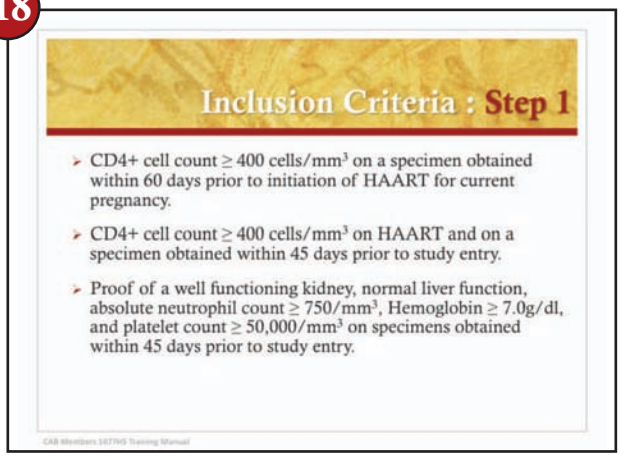
- A woman can not be a participant in this study if she is less than 18 years.
- The two documented HIV tests have to be from two separate specimens.

17



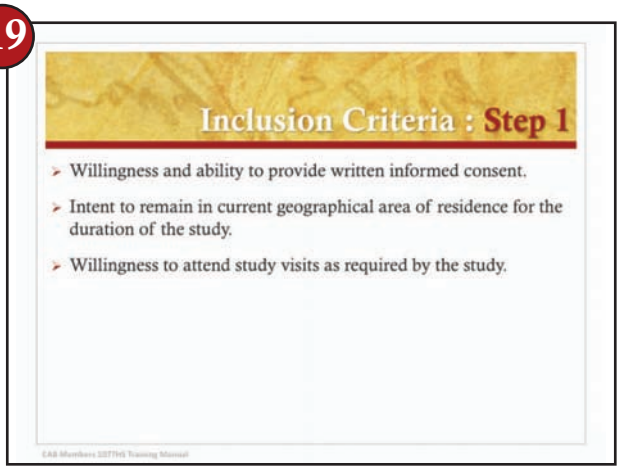
- History of receipt of ARV for PMTCT during prior pregnancies and immediately postpartum is permitted.
- Treatment interruption is defined as more than seven consecutive days of missed therapy.
- A woman can not be recruited after 28 days post delivery.

18



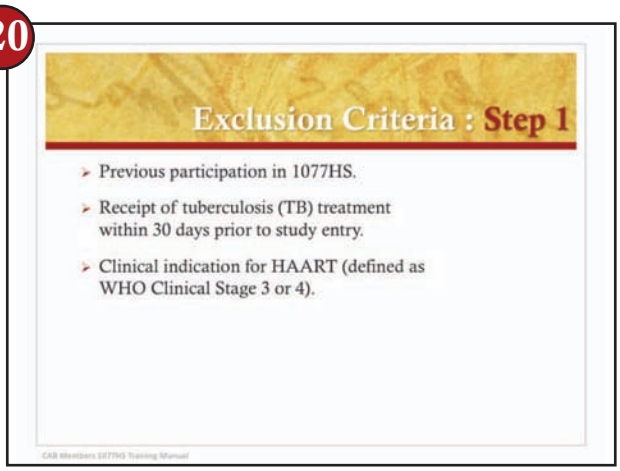
- Participants can be randomized to either continue HAART or stop HAART arm, for their safety CD4 levels should be above the cut off for initiating HAART.
- Creatinine is used to show renal function. Effect of antiretrovirals on the renal is one of the endpoint of the study. Good renal function is a requirement and is also used as a baseline to show effects of the medication on renal activities.
- Other blood tests ensures that the participant is in good health condition.

19



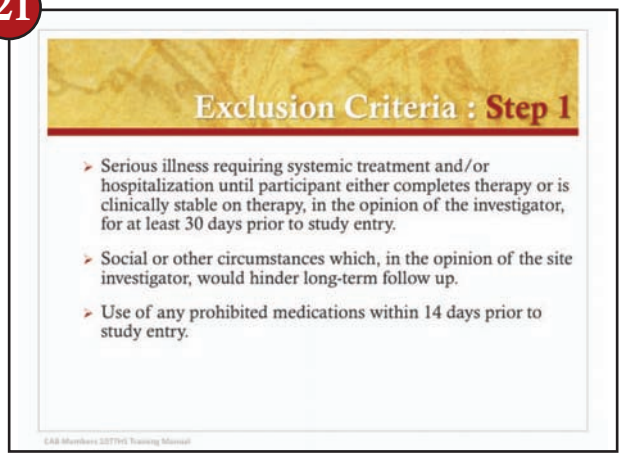
- An informed consent will ensure that participants are fully aware of the risks, benefits, and are participating willingly.
- The study involve follow up to assess clinical progress, record study parameters, and laboratory tests, it is paramount that the participant is willing and able to attend study visits.

20



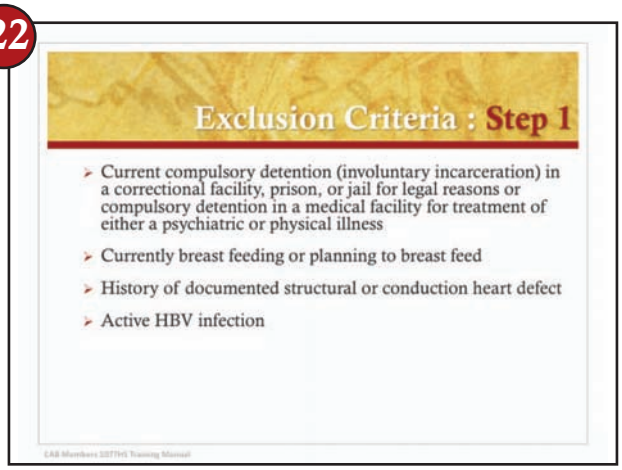
- Participants will be enrolled into PROMISE study only once.
- Participants are supposed to be randomized either into arm A continuation of HAART or arm B discontinuation of HAART, it is not ethical to withhold treatment from participants who qualifies for HAART. The study will not include participants who have clinical indication for HAART.

21



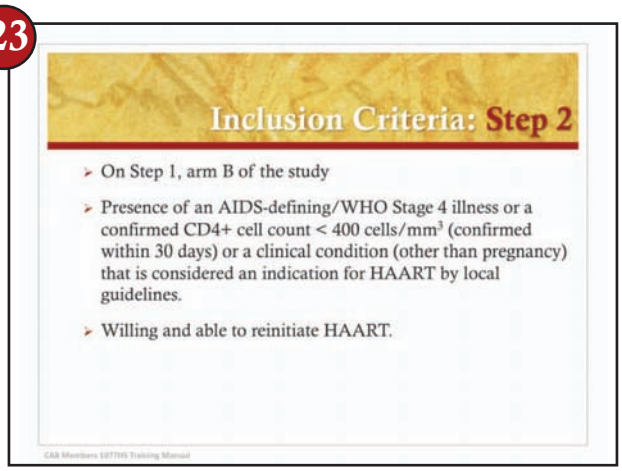
- Participants should be clinically stable during recruitment into the study. In case they had a serious illness then at least 30 days must pass prior to study entry.
- There are medications that have been identified to cause harm if taken concurrently with study drugs. Clinicians overseeing the study have MOP (Manual of Operations) that has a list of these prohibited medications.

22



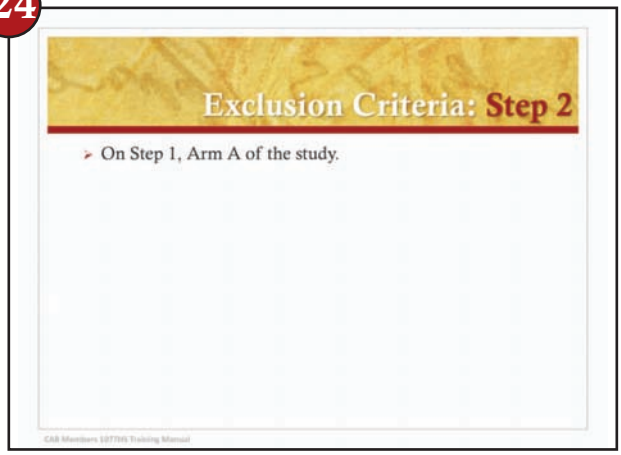
- The study will not include participants in institutions either medical or correctional.
- Although the study will not include participants with documented structural or conduction heart defect specialized assessment to rule out those conditions is not a pre-requirement. Abnormal heart sounds alone are not an exclusion criteria.
- Active HBV can be shown by evidence of HBV DNA levels>2000 IU/mL in the presence of elevated ALT but testing for HBV is not required for study screening or enrollment.

23



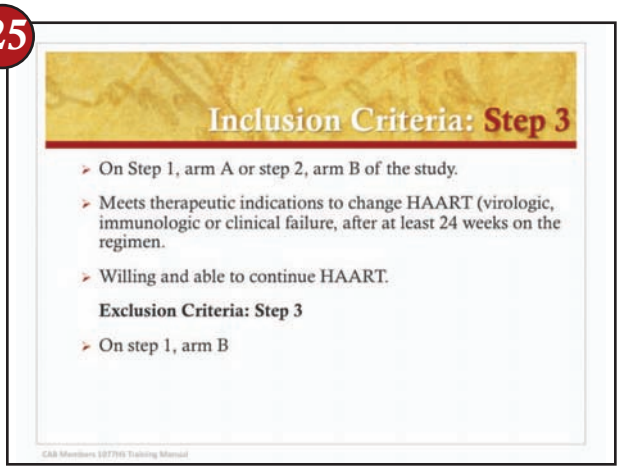
- Participants will move from step 1 to step 2 in arm B.
- Developing an AIDS defining symptom or CD4+ cells count falling below the cut-off point are indicators to start HAART and as a result the participant will move to step 2.
- Taking HAART as prescribed requires determination from the participant, confirmation of willingness from the participant is crucial before enrollment into step 2.

24

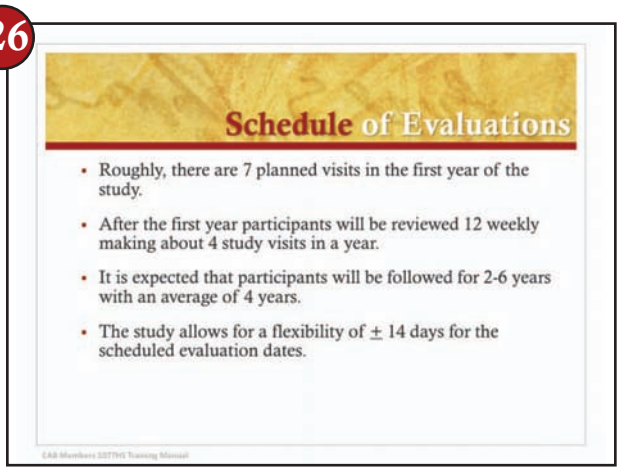


- Step 1, arm A are already on HAART postpartum, they will change to another form of HAART when the regimen has shown failure
- Change of HAART is moving into step 3. It is important to note that arm A does not have step 2
- Can reinforce the message by referring the study diagram on slide no 15

25

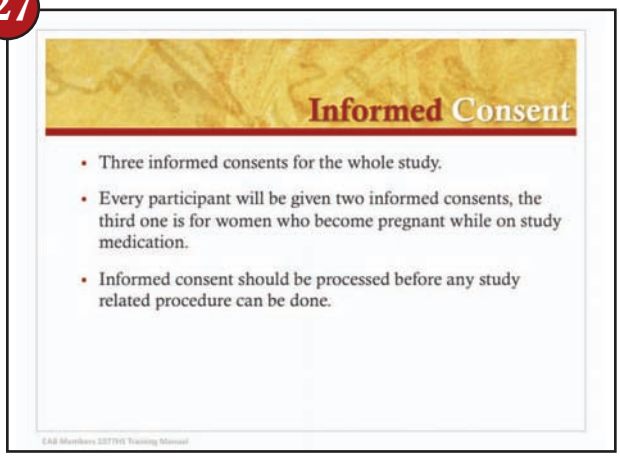


26



- The first visit is for screening, followed with a recruitment visit and then evaluation after 4 weeks.
- Participants who join early will be in the study for much longer than those who join late.
- Every participant will be followed until 84 weeks after the last participant is randomized into the trial.

27

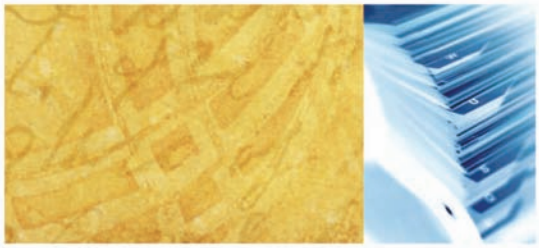


- The first informed consent is for screening and enrollment, no participant can be screened or enrolled before providing this consent. No protocol procedures of any kind including screening procedures may be done prior to completing the informed consent process.
- The second informed consent is for specimen storage and future use: A participant can decline this consent and still participate in the study but her samples will not be stored for future use. The samples will be stored for the duration of the study so that they can be used for testing that is specified in the protocol. After the study is done, any remaining specimens from participants who do not consent will be destroyed.
- The third is informed consent for women who become pregnant while on study medication. The aim is to provide more information about effect of medication on the developing baby.
- Lower Age limit for this study is 18 years or age specified by the local IRB which ever is greater.

1

Case Studies

1077HS



2

Cases for discussion

Case 1	Case 2	Case 3
• Can someone who has made her mind to continue taking HAART after delivery be enrolled to 1077HS? Why?	• If a woman had pregnancy related high blood pressure and then developed convulsions (eclampsia) that necessitated admission to the hospital for 29 days post delivery, does she qualify to be enrolled to 1077HS?	• Why is the selection and enrollment part of the protocol important? What will happen if everybody is recruited?

3

Cases for discussion

Case 4	Case 5	Case 6
• What is the minimum number of consent forms a participant will be given during the study?	• The local IRB has set the minimum age for a participant to give consent for clinical studies as 16 years. Can a 17 year-old pregnant woman meeting all other criteria give consent for the study?	• If a participant in Arm B step 1 becomes pregnant, will she require a new informed consent process?

Role-play or drama

Inquisitive Husband

Gregory and Anne are expecting their first born child in less than 3 weeks. Anne was diagnosed with HIV infection during antenatal screening at her first antenatal visit (at 16 weeks). She is on HAART for PMTCT and has responded very well; she now has an undetectable viral load and a CD4 count of 750 (up from 500).

A healthcare worker at Anne's clinic has identified Anne as a potential participant in 1077HS. Gregory is worried about Anne entering a clinical trial and doesn't understand the purpose of the study and why Anne should join. Since Gregory knows you from your church, and knows that you are a CAB member for the research team implementing 1077HS, he approached you for help in understanding why research is continuing now that we have effective medicines for people living with HIV and for PMTCT. What will you tell him?

CAB Member:

The research that Anne has been invited to participate in will determine if women like Anne, who do not need HAART for their own health, but receive HAART for preventing-mother-to-child transmission, should continue or stop taking HAART after delivery. The current standard of care is to stop HAART after delivery, but there is no research-based evidence supporting the approach. We could help doctors improve on the medical care given to women like Anne if we can gather the evidence needed to answer this question.

Explain to Gregory about the importance of clinical research. Although we have various medicines for treating the disease we still need medicines that are effective, have less side-effects and have simple, easy to follow regimens. We need research to get a cure for HIV, and also vaccines that will prevent transmission of the virus. In the case of the PROMISE study, the study is designed to find answers to questions of how best to treat women like Anne. By taking part in the study Anne, can help contribute to finding answers that might help other women like her.

Husband:

Behave as a real husband would in this situation. Ask questions that you think he would ask to understand more about this clinical trial and about clinical research in general.

Observers:

Watch the role play and comment on the advice given. Was it accurate and understandable? Did the CAB member address the main concerns of the father? Did the CAB member remain neutral (explain the purpose of the study without trying to recruit the couple)? Did the CAB member's discussion fit the role of the CAB? Discuss the difficulties faced by both the husband and the CAB member.