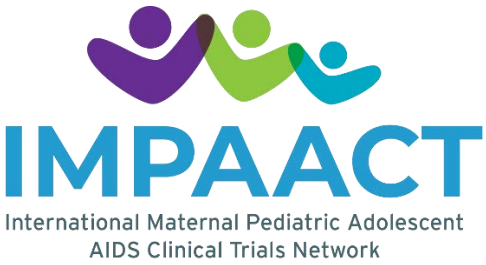

IMPAACT 2016

Evaluating a Group-Based Intervention to Improve Mental Health and ART Adherence Among Youth Living with HIV in Low Resource Settings

Manual of Procedures

Final Version 2.0
14 September 2023

IMPAACT 2016 Manual of Procedures Overview of Section Contents and Identification of Current Section Versions		
Section	**Current Version**	**Comments**
Section 1 Study Overview	Version 2.0 14 September 2023	No change from the prior version.
Section 2 Preparing for the Study	Version 2.0 14 September 2023	Updated to correspond with Protocol Version 2.0
Section 3 Study Resources	Version 2.0 14 September 2023	Updated to correspond with Protocol Version 2.0
Section 4 Participant Accrual	Version 2.0 14 September 2023	Updated to correspond with Protocol Version 2.0
Section 5 Study Procedures	Version 2.0 14 September 2023	Updated to correspond with Protocol Version 2.0
Section 6 Participant Monitoring, Management, and Safety-Related Reporting	Version 2.0 14 September 2023	Updated to correspond with Protocol Version 2.0
Section 7 Laboratory Considerations	Version 2.0 14 September 2023	Updated to correspond with Protocol Version 2.0
Section 8 Data Management Considerations	Version 2.0 14 September 2023	Updated to correspond with Protocol Version 2.0
Appendices	Version 2.0 14 September 2023	Updated Appendix I list of supplies Updated Appendix III website links

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1.0 Study Overview

IMPAACT 2016 is a **multi-site, two-arm, individually randomized controlled trial** to evaluate whether a trauma-informed cognitive behavioral therapy (TI-CBT) group intervention delivered by Indigenous Youth Leaders (IYL) is associated with improved mental health outcomes and antiretroviral therapy (ART) adherence in youth 15 - 19 years old living with HIV in sub-Saharan Africa.

The randomized trial is preceded by an adaptation process to ensure that the TI-CBT Youth Intervention Manual (used by IYL) and Caregiver Intervention Manual (used by adult study staff) to deliver the TI-CBT group intervention are relevant and acceptable per the local culture of each of the eight participating sites: Gaborone Prevention/Treatment Trials CRS 12701 (Botswana); Molepolole Prevention/Treatment Trials CRS 12702 (Botswana); University of North Carolina Lilongwe CRS 12001 (Malawi); College of Medicine JHU CRS 30301 (Malawi); St Mary's CRS 30303 (Zimbabwe); Seke North CRS 30306 (Zimbabwe); Harare Family Care CRS 31890 (Zimbabwe); and Soweto IMPAACT CRS 8052 (South Africa).

The adaptation process includes Focus Groups at select sites within a participating country and Pilot Testing of the intervention at each site. The TI-CBT Youth and Caregiver Intervention Manuals will be updated for each site to incorporate all-site and/or site-specific adaptations based on the Focus Groups and Pilot Testing, as needed. For guidance on the adaptation process, refer to the Guidance Document: Preparation and Adaptation of the Trauma-Informed Cognitive Behavioral Therapy (TI-CBT) Intervention.

Pilot Testing of the intervention will be conducted with up to 8 youth and up to 8 caregivers at each site. After successful completion of a Pilot test, the Randomized Trial will be initiated at each site. Collectively across all sites, approximately 192 - 256 youth participants will be enrolled and randomized to the TI-CBT Intervention or Discussion Control arm. Caregivers (as available and with youth permission) will be assigned to the same study arm as their youth. While on study, youth will meet as a group for six 2-hour group sessions (or an equivalent) led by IYL plus one booster session during follow-up, and caregivers will meet as a separate group for two 2-hour group sessions led by adult study staff plus one booster session during follow-up.

2.0 Preparing for the Study

Note: Refer to Section 11 of the IMPAACT Manual of Procedures (MOP) for comprehensive information on Study-Specific Pre-Implementation Activities. The IMPAACT MOP is available on the Resources page of the IMPAACT website:

https://www.impaactnetwork.org/resources/manual-procedures

In addition, study details, protocol team contact information, site details, and the study protocol and other study-related documents will be available on the study-specific webpage:

https://www.impaactnetwork.org/studies/impaact2016

2.1 Investigator Responsibilities

IMPAACT 2016 must be conducted in accordance with the United States (US) Code of Federal Regulations (CFR) and the International Conference on Harmonization (ICH) Consolidated Guidance for Good Clinical Practice (GCP). Sites must also comply with the Division of AIDS (DAIDS) policies

outlined in the DAIDS Site Clinical Operations and Research Essentials (SCORE) Manual, which are useful for interpreting and operationalizing the regulations and guidelines in accordance with DAIDS expectations. These policies are available at the following web site and must be followed throughout implementation of IMPAACT 2016:

https://www.niaid.nih.gov/research/daids-clinical-site-implementation-operations

IMPAACT 2016 also must be conducted in accordance with the IMPAACT Manual of Procedures and all site-specific policies, procedures, and guidelines applicable to human subjects research in general and/or the conduct of study procedures in particular. Copies of all applicable regulations, policies, procedures, and guidelines should be maintained in on-site essential document files.

Protocol Signature Page: The Investigator of Record (IoR) at each site must sign the IMPAACT 2016 Protocol Signature Page (PSP) to formally indicate their agreement to conduct the study in accordance with the protocol and all applicable regulations, policies, and guidelines. A copy of the PSP can be found in the IMPAACT 2016 protocol.

DAIDS Investigator of Record Form: The Investigator of Record (IoR) at each site must also sign a DAIDS Investigator of Record Form to formally indicate their agreement to conduct the study in accordance with the protocol and all applicable regulations, policies, and guidelines. The investigator responsibilities assumed by the IoR when signing this form are listed on the form, which is available at:

https://rsc.niaid.nih.gov/clinical-research-sites/protocol-registration-forms

Delegation of Duties: IoRs may delegate their obligations and responsibilities for conducting this study to other study staff; however, delegation does not relieve the IoR of their ultimate responsibility for all study procedures performed and all study data collected. Delegation of IoR responsibilities must be formally documented throughout the period of study implementation, consistent with the DAIDS SCORE Manual.

Ethical and Regulatory Approvals: Consistent with the regulations, policies, and guidelines cited above, the IoR at each site must obtain all applicable ethical and regulatory approvals to conduct IMPAACT 2016 prior to study initiation and maintain these approvals in good standing throughout the period of study implementation.

All sites are encouraged to request an acknowledgment of receipt for all documents submitted to their IRBs/ECs and to request that IRBs/ECs note the effective and expiry dates of all approvals. Because IMPAACT 2016 involves children (including adolescent) participants, IRBs/ECs must consider the potential benefits, risks, and discomforts of the study to children and assess the justification for their inclusion in the study. As part of this assessment, IRB/ECs must assess the level of risk to participants as described in protocol Section 12.2. Complete documentation of all correspondence to and from all responsible IRBs/ECs (e.g., complete copies of all submissions, responses, and approvals) must be maintained in on-site essential document files. All submission letters should list the date of the submission, the contents of the submission, and the version number and/or version date of each document submitted.

2.2 Protocol Registration

After obtaining all required IRB/EC approvals, each participating study site is responsible for submitting documentation of the approvals, and other required documentation, to the DAIDS Protocol Registration Office (PRO). Further information on the protocol registration process can be found in protocol Section 14.2 and in the DAIDS Protocol Registration Manual, which is available at:

https://rsc.niaid.nih.gov/clinical-research-sites/daids-protocol-registration-policy-and-procedures-manual

Upon confirming receipt of all required documentation, the PRO will issue an Initial Registration Notification that indicates successful completion of the process. Site staff are responsible for maintaining documentation of all submissions for the study, along with all associated approvals, notifications, and other correspondence from the DAIDS PRO. Registration Notification must be obtained for protocol Version 2.0, as a condition for Site-Specific Study Activation and conduct of the Pilot Test and Randomized Trial. The IMPAACT Operations Center is copied on notifications from the DAIDS PRO and will note completion of DAIDS PRO registration of protocol Version 2.0 when available.

2.3 Site-Specific Focus Group Implementation and Study Activation

Site-Specific Focus Group Implementation

Prior to Focus Group conduct, a site must be protocol registered, complete Focus Group-specific implementation requirements, and receive an Implementation Notice. To ensure readiness for the Focus Group, the Protocol Team has specified a set of Focus Group requirements that must be met in order to obtain the Implementation Notice. These requirements are listed on the IMPAACT 2016 Site-Specific Study Activation Checklist, which is available on request from the IMPAACT Operations Center Clinical Research Managers. For details on site-specific Focus Group implementation, refer to Section 3.3.2 in the Guidance Document: Preparation and Adaptation of the Trauma-Informed Cognitive Behavioral Therapy (TI-CBT) Intervention.

Site-Specific Study Activation

Prior to conducting any Pilot Test and Randomized Trial study procedures, each site must obtain all required approvals, complete the protocol registration process described above, and complete all study-specific activation requirements specified by the Protocol Team. To help ensure site readiness for study initiation, the Protocol Team has specified a set of study activation requirements that must be met in order to obtain approval to implement the Pilot Test followed by the Randomized Trial. These requirements are listed on the IMPAACT 2016 Site-Specific Study Activation Checklist, which is available on request from the IMPAACT Operations Center Clinical Research Managers.

Any questions related to the study activation process should be directed to the IMPAACT Operations Center Clinical Research Managers. On a site-by-site basis, when all activation requirements have been met, the Operations Center will issue a Site-Specific Study Activation Notice prior to initiating the Pilot Test. At each site, no Pilot Test and Randomized Trial study procedures may be performed prior to receipt of the activation notice.

Site-Specific Randomized Trial Implementation

On a site-by-site basis, upon completion of the Pilot Test, when all Pilot Test data is reviewed and adaptations are confirmed, the Operations Center will issue a Site-Specific Randomized Trial Implementation Notice. At each site, no Randomized Trial study procedures may be performed prior to receipt of the implementation notice.

2.4 Adaptation of TI-CBT Intervention

For guidance on how to adapt the TI-CBT Intervention using community stakeholder engagement, Focus Groups and Pilot Test, refer to the Guidance Document: Preparation and Adaptation of the Trauma-Informed Cognitive Behavioral Therapy (TI-CBT) Intervention, available on the IMPAACT 2016 website.

2.5 Study-Specific Personnel

A definition list for personnel is included in Figure 2-1 below.

Figure 2-1
Personnel Definitions

Personnel	Definition
Adult Study Staff	Study staff designated to facilitate or observe the caregiver TI-CBT group sessions OR the caregiver Discussion Control group sessions.
Indigenous Youth Leader (IYL)	21-30 year-old IYL from local HIV clinics designated to facilitate or observe the youth TI-CBT group sessions OR the youth Discussion Control group sessions.
Facilitator	An individual leading community engagement, a Focus Group, or TI-CBT or Discussion Group sessions (Pilot Test and Randomized Trial) as follows: • Facilitators leading community stakeholder engagement or a Focus Group may be an adult study staff (not designated to the Discussion Control Arm), local supervisor, site Investigator of Record (IoR), or other designee – excluding IYL. • Facilitators leading a youth group session or caregiver group session will be an IYL or adult study staff, respectively.
Observer	An individual observing a Focus Group, or an individual observing a youth group session or caregiver group session who will be an IYL or adult study staff, respectively. May take the place of a facilitator should a facilitator be unavailable to lead a youth or caregiver group session.
Local Supervisor	An individual (e.g., psychologist, nurse, IoR, other) with a working relationship with the site who is designated to supervise IYL or adult study staff.
On-site Study Clinician	An individual who is qualified and designated to address safety concerns and intervene as needed to maintain safety of youth and staff (refer to protocol Section 8.1). The local supervisor and/or IoR can also serve as the on-site study clinician.
Expert Trainer	An individual selected and provided by the Protocol Team to conduct on-site TI-CBT intervention training for the IYL, adult study staff and local supervisors and conduct supervision with site IoRs and local supervisors.

Indigenous Youth Leaders, Adult Study Staff and Local Study Supervisor

For guidance on recruiting, selecting, and training study-specific personnel including IYL, adult study staff, and local study supervisors, refer to the Guidance Document: Preparation and Adaptation of the Trauma-Informed Cognitive Behavioral Therapy (TI-CBT) Intervention.

For details on roles and responsibilities of IYL and adult study staff for the delivery of group sessions, refer to Section 5.7 of this MOP.

For details on roles and responsibilities of local study supervisors for regularly supervising IYL and adult study staff, refer to Section 5.8 of this MOP.

On-Site Study Clinician

The on-site study clinician may be the local study supervisor, IoR or other designee who serves to supervise the IYL and help monitor and evaluate youth participants' mental health risk and safety per protocol Section 8.1 and intervene as needed to address a safety concern or remove disruptive youth from the current group session per protocol Section 4.8.

For details on monitoring and evaluating youth mental health risk and safety, refer to Section 6.0 of this MOP.

Expert Trainer

The expert trainer will conduct on-site study-specific TI-CBT intervention training for the IYL and adult study staff designated to deliver or observe the youth and caregiver group sessions, respectively. Sites do not identify and select an expert trainer; the Protocol Team will identify and select the expert trainer for each site.

Once the IYL and adult study staff have been selected and designated to the TI-CBT Intervention or Discussion Control group, as outlined in the Guidance Document: Preparation and Adaptation of the Trauma-Informed Cognitive Behavioral Therapy (TI-CBT) Intervention, the Protocol Team, Operations Center, and expert trainer will work with sites to schedule the training.

For details on the roles and responsibilities of the expert trainer related to the training of IYL and adult study staff, refer to the Guidance Document: Preparation and Adaptation of the Trauma-Informed Cognitive Behavioral Therapy (TI-CBT) Intervention.

3.0 Study Resources

This section specifies the resources available to IMPAACT 2016 study site staff, including study-related communication and informational resources, the Data Management Center (DMC) Portal, eCRF completion and data entry, self-administered electronic questionnaire set up, and the file exchange utility.

3.1 Study-Related Information and Communications

All IMPAACT 2016 visits and procedures must be conducted in accordance with the study protocol. The purpose of this manual is to supplement the protocol, not to replace or substitute it. In the event this manual is inconsistent with the protocol, the specifications in the protocol take precedence. Please notify the IMPAACT Operations Center Clinical Research Managers of any such inconsistencies.

This manual will be reviewed with each protocol modification (clarification memorandum, letter of amendment, or full protocol amendment), and approximately annually, for any indicated updates. Operational guidance will be released as study-wide communications between these planned updates, as needed.

The IMPAACT 2016 protocol and related protocol documents, including the study-specific Laboratory Processing Chart (LPC) and Guidance Document: Preparation and Adaptation of Trauma-Informed Cognitive Behavioral Therapy (TI-CBT) Intervention, are available on the study-specific web page:

http://impaactnetwork.org/studies/IMPAACT2016.asp

The Protocol Team has developed study-specific contacts for various types of issues and questions, as shown in Figure 3-1. For issues and questions directed to the Protocol Team, a response from the appropriate team member can generally be expected within 24 hours. Always retain a copy of correspondence with the team in the relevant participant's study chart.

Figure 3-1
IMPAACT 2016 Study-Related Communications

Include the protocol number in the subject line of email messages

Topic	Contact
User Support	
Adding site staff to protocol email group (IMPAACT.prot2016@fstrf.org)	**User Support** user.support@fstrf.org *(include the protocol number in the subject line of your email message)*
Medidata Rave, DMC Portal or Medidata Patient Cloud App access	**User Support** user.support@fstrf.org *or by phone: +716-834-0900, ext. 7302*
General	
Protocol interpretation or study implementation, including administrative, ethical, regulatory, counseling, data, and laboratory operation	**IMPAACT 2016 Protocol Team** impaact.team2016@fstrf.org
Screening, Enrollment, and Data Management	
Participant eligibility, potential enrollment of an ineligible participant, and/or deviation from protocol requirements for eligibility determination and/or enrollment	**IMPAACT 2016 Protocol Team** impaact.team2016@fstrf.org
Co-enrollment and concurrent waves	**IMPAACT 2016 Clinical Management Committee** impaact.2016CMC@fstrf.org
Study Enrollment System	**DMC Randomization Support Office** rando.support@fstrf.org *or by phone: +716-834-0900, ext. 7301*
Adding designated site staff (limited to site IoR, study/nurse coordinator, and local supervisor) to electronic questionnaire alert email group for receiving mental health eligibility determination and safety alerts (email the staff name(s), title/role(s), and email(s))	**IMPAACT 2016 Protocol Data Managers** impaact.dm2016@fstrf.org

Topic	Contact
Electronic questionnaire, eCRF and other data management questions	
Participant Safety, Monitoring, and Study Management	
Expedited Adverse Event (EAE) Reporting	**DAIDS RSC Safety Office** **DAIDSRSCSafetyOffice@tech-res.com** *or by phone: 800-537-9979 or +301-897-1709* *or by fax: 800-275-7619 or +301-8977-1710* *Note: The 800 numbers above are toll free for calls made within the US and will not work when dialed internationally unless the call is initiated using a VPN or US-based internet calling service (e.g., Skype, Google Voice).*
DAIDS Adverse Experience Reporting System (DAERS)	**NIAID Clinical Research Management System** **CRMSsupport@niaid.nih.gov** *(questions also may be submitted from within the DAERS application)*
Concerns regarding mental health questionnaires including questions related to flagged high-risk response email notifications	**IMPAACT 2016 Clinical Management Committee** **impaact.2016CMC@fstrf.org**
Participant safety assessment, monitoring, psychiatric adverse events, reporting including social harms, and/or contamination concerns	
Any other aspect of participant management, protocol interpretation, or study implementation not listed above	**IMPAACT 2016 Protocol Team** **impaact.team2016@fstrf.org**

Active communication is expected between site staff, IYL, designated on-site study clinicians, and local study supervisors to monitor and manage youth mental health risk and safety (refer to protocol Section 7 and 8). The IMPAACT 2016 Clinical Management Committee (CMC) is composed of study team members who have been designated to provide as needed guidance to sites regarding all aspects of participant management, including but not limited to site questions pertaining to 1) clinical and mental health risk management questions and notifications, and 2) youth participant self-reported flagged high-risk responses sent via email notifications (refer to Sections 6.1 and 6.1.1 of this MOP; refer to protocol Section 7.1.2, 8 and 8.1.)

When submitting questions and notifications to the IMPAACT 2016 CMC, please address each of the points listed in Figure 3-2 and include in the email subject line the protocol, site, and PID numbers to help ensure that members have adequate information to respond in a timely manner. Always retain a copy of correspondence with the IMPAACT 2016 CMC in the relevant participant's study chart.

Figure 3-2
Communications with IMPAACT 2016 Clinical Management Committee

Questions and notifications for IMPAACT 2016 CMC: Copy and paste this listing into the body of your email message to IMPAACT.2016CMC@fstrf.org to ensure that all required information is included.

Include the protocol number, site number and PID in the subject line of your email.

1. Site name and number:
2. Name of person submitting query:
3. PID(s):
4. Study Component: Pilot Test *or* Randomized Trial
5. Study Arm: Youth TI-CBT Intervention, Youth Discussion Control, Caregiver TI-CBT Intervention *or* Caregiver Discussion Control
6. For consultation on (choose one):
   a. Eligibility or enrollment (describe in case description)
   b. Adverse event (specify severity grade in case description)
   c. Mental health risk and Safety Concern (e.g., social harm, group session disruption, mental health concern identified through flagged high-risk concern)
   d. Other (specify in case description)
7. Current week on study:
8. *For adverse events, mental health risk, or queries related to a specific group session, indicate the specific group session (e.g. Session 1, 2, 3, 4, 5, 6, or booster for youth, and Session A, B or booster for caregiver) and Group Identification Number (refer to Section 5.6 of this MOP for details on Group Identification naming convention):*
9. Case description and question or notification for CMC:

File a copy of the email exchange in the participant's study chart.

The IMPAACT 2016 protocol also details the circumstances in which IoRs, study coordinators, on-site clinician/supervisors, and/or designee must consult with the IMPAACT 2016 CMC. All protocol requirements must be followed. For ease of reference, a summary of issues requiring consultation with the IMPAACT 2016 CMC, is provided below in Figure 3-3. IoRs, study coordinators, local supervisors (or on-site study clinician), and/or designee receiving flagged safety alert emails are also encouraged to contact the IMPAACT 2016 CMC with any other issues, questions, or concerns related to questionnaire responses from study participants.

Figure 3-3
Required Consultation with the IMPAACT 2016 CMC

For details on participant safety and management, refer to the following sections in the protocol:

- **Section 4.8: Participant Withdrawal or Termination from the Study (Pilot Test/Randomized Trial)**
- **Section 7.1: Safety-Related Roles and Responsibilities**
- **Section 8: Participant Management**

Study Implementation

- Request approvals for co-enrollment in observational or other studies (refer to protocol Section 4.5).
- A participant fails to comply with study requirements and/or is disruptive so as to cause harm to self or others, seriously interfere with the validity of the study results, or otherwise acts in ways such that continuing in the group is not in the best interest of the participants and study site staff so that the site investigator or designee determines permanent discontinuation is warranted (refer to protocol Section 4.8)
- Site investigator or designee request for resumption of follow-up for a participant whose circumstances that led to their withdrawal or termination change, e.g., the participant return to the study site area after relocating (refer to protocol Section 4.8).

General Participant Management

- Consultation with the CMC by site investigators is required for the following as soon as possible and within three days of site awareness of event (refer to protocol Sections 7.1.1 and 8):
  - Psychiatric adverse events resulting in hospitalization
  - Adverse events involving suicide attempts
  - Any other occurrence that, in the opinion of the site investigator, could cause harm to a participant or others
  - Any unexpected concerns
- Consultation with the CMC regarding management of psychiatric adverse events resulting in hospitalization and/or involving suicide attempts that include premature discontinuation of the study intervention.
- Social harms

3.2 Data Management Center (DMC) Portal

The DMC Portal website provides information, documents, and tools to assist site staff with the data management aspect of conducting IMPAACT studies, including the 1) eCRF Completion Guide, which includes the electronic Case Report Forms (eCRFs) and forms instructions, 2) Data Collection eCRF/Questionnaire Schedules, 3) Forms Management Utility (FMU) for paper versions of participant-completed questionnaires, and 4) Study Enrollment System (SES). The DMC Portal can be accessed from the Frontier Science Foundation webpage at: **https://www.frontierscience.org/**

Site staff members apply for access to the Portal by submitting a registration form located at:

https://www.frontierscience.org/apps/cfmx/apps/common/register/index.cfm

All requests for DMC Portal access are subject to review and verification by User Support before processing. The site leader or site coordinator will be contacted by the DMC to ensure legitimate affiliation of the applicant.

Confirmation of registration will be sent via email from User Support. Click on the IMPAACT project link to enter the project website. A log-in screen appears. Enter your username (format: lastname.firstname) and the password that you set up when you registered for DMC Portal access.

To contact User Support, send an email message to user.support@fstrf.org or call +1 (716) 834-0900 x 7302.

3.3 Electronic Case Report Form (eCRF) Completion Guide and Data Entry

The IMPAACT 2016 eCRF Completion Guide and the IMPAACT 2016 Print Matrix are located on the DMC Portal under the Site Support category and the Medidata Rave Resources link. The eCRF Completion Guide and Print Matrix may be used as guides for source documentation purposes.

The eCRF Completion Guide contains the data collection eCRF/questionnaire schedules and all of the eCRFs with instructions and help text. These documents outline standards and guidelines which, when followed, will result in fewer queries, shorter delinquency lists, and most importantly, straightforward and timely analyses.

Printable versions of the participant-completed questionnaires in English and other needed languages are available in the FMU, located on the DMC Portal under the Case Report Form category.

Data entry into the eCRFs will be performed in Medidata Rave.

3.4 Self-administered Electronic Questionnaire Set Up

Self-administered electronic questionnaires will be completed by participants via the Medidata Patient Cloud application on an iPad, with iPadOS v12.0 or later, provided by the site. Fronter Science User Support will request that sites confirm who will require Patient Cloud site mode access.

In the event of staffing changes, sites are responsible for notifying User Support if new staff will require Patient Cloud access.

Prepare in Advance of Study Visits

IMPAACT 2016 Drink Image: Sites will need to download and print the IMPAACT 2016 Drink Image in the appropriate language(s) and make it available to youth participants when they are completing the QLW10109: IMPAACT 2016 AIDS Risk Behavior Assessment (Sexual Behavior and Alcohol/Drug Use) – Entry and the QLW10110: IMPAACT 2016 AIDS Risk Behavior Assessment (Sexual Behavior and Alcohol/Drug Use) – Post Entry using Patient Cloud. The IMPAACT 2016 Drink Image is located on the DMC Portal under the Site Support category and the Medidata Rave Resources link.

IMPAACT 2016 Introduction Paragraph: Sites will also need to download and print the IMPAACT 2016 Introduction Paragraph in the appropriate language(s) and read it to each participant at each visit before the participant begins completing the questionnaires. The IMPAACT 2016 Introduction Paragraph is located on the DMC Portal under the Site Support category and the Medidata Rave Resources link.

Sites should contact the IMPAACT 2016 Protocol Data Managers (PDMs) at impaact.dm2016@fstrf.org for initial assistance with the Patient Cloud application. Issues should be escalated to Medidata at patientcloudsupport@mdsol.com as appropriate. If the Patient Cloud application is not available, and initial troubleshooting efforts by the PDMs and Medidata are unsuccessful, the printable versions of the questionnaire(s) should be downloaded and printed from the FMU in the appropriate language(s) and completed by the participant on paper.

3.5 File Exchange Utility – Intervention Fidelity Evaluation Forms

Prepare in Advance of Each Group Session

Site staff will download and print the following IMPAACT 2016 Intervention Fidelity Evaluation forms from the FMU on the DMC Portal:

- Facilitator Intervention Fidelity Evaluation forms (FFE001 – FFE010)
- Observer Intervention Fidelity Evaluation forms (OFE001 – OFE010)

Each Intervention Fidelity Evaluation form is for a specific youth or caregiver session.

Prior to each group session, local supervisors or designees will complete the Header Information block on each page of each of the printed forms prior to distributing to IYL and Adult Study Staff facilitators and observers; refer to Section 5.6 for guidance on completing the Header Information block.

At Conclusion of Each Group Session

At the end of each group session, local supervisors will distribute appropriate forms to the facilitators and observers to complete prior to leaving.

After each group session, local supervisors will upload scanned copies of the completed paper fidelity forms to the File Exchange Utility. After selecting the appropriate File category from the dropdown list, local supervisors will enter the required identifying information for the file, and then click submit. The DMC will enter data from the completed paper forms directly into the central database.

4.0 Participant Accrual

Recruitment, screening, enrollment, randomization, informed consent, and retention procedures are described in the subsections below.

Accrual for the Pilot Test and Randomized Trial differ; an overview of each is provided below.

Pilot Test

Each site will enroll one group of 5 - 8 youth and one group of up to 5 - 8 caregivers of the enrolled youth to participate in the TI-CBT Intervention Group Sessions. Once a sufficient pool of eligible youth has been identified based on prior screening to fill one group (range of 5 - 8 youth), all youth will be enrolled on the same day. Participant accrual at a given site is expected to be completed within 60 days of the first screened eligible youth. The same timing of screening and enrollment applies to caregivers.

Randomized Trial

Collectively across all sites, approximately 192 - 256 youth participants (96 - 128 per arm), plus their caregivers (as available and with youth permission), will be enrolled into the Randomized Trial. Youth and their caregivers will be randomized to the same arm, either to the TI-CBT Intervention Arm or Discussion Control Arm. Each arm will have 12 - 16 groups collectively across all sites, with an average of eight youth (and their caregiver) participants per group (range 6 - 10). Each site is expected to conduct at a minimum one group per arm.

Once a sufficient pool of eligible youth (range of 12 - 20 youth) has been identified based on prior screening to fill two groups (one group per arm), all youth will be enrolled and randomized to an arm on the same day. Participant accrual for two groups at a given site is expected to be completed within 60 days of the first screened eligible youth. ***Mixed-gender groups must have a minimum of two participants of each gender.***

Single Wave*:* For the purpose of this manual, in the Randomized Trial, a set of two youth groups (one group per arm) and two caregiver groups (one group per arm) equals one wave. At each site, at least one wave will be accrued during the Randomized Trial.

Multiple Waves: Some sites may accrue two or more waves during the Randomized Trial, as determined by the IMPAACT 2016 CMC to meet the total Randomized Trial accrual of 192 - 256 youth participants. Sites must email the IMPAACT 2016 CMC (IMPAACT.2016CMC@fstrf.org) a request to accrue more than one wave.

Sites which receive approval to conduct multiple waves are expected to conduct the multiple waves sequentially (e.g., upon completion of a wave's group session 6, another wave's group sessions commence). However, if an additional wave is requested to be conducted concurrently with the another wave (e.g., group sessions of each wave overlap), sites must email the IMPAACT 2016 CMC a request to conduct concurrent waves. At a minimum, the request must include the following information to confirm site readiness and feasibility to conduct concurrent waves before proceeding with concurrent waves:

- The site's rationale for requesting concurrent wave (i.e., a pool of youth are available for enrollment)
- Supervisor confirmation of IYL and adult study staff readiness to facilitate concurrent waves
- Confirmation that IYLs, adult study staff and local supervisors have sufficient time, training, and resources
- Ability to schedule group sessions of different waves at different times to prevent cross-contamination
- Accrual pace

If your site is approved to conduct multiple concurrent waves, refer to Section 5.7.3 for guidance on scheduling and conducting group sessions of concurrent waves.

4.1 Site-Specific Accrual

For each site, accrual will begin after all required approvals are obtained and a site-specific study activation notice (prior to Pilot Test) or implementation notice (prior to Randomized Trial) is issued by the IMPAACT Operations Center. As a condition for site activation, each site will establish a study-specific SOP for participant accrual, which must be submitted to the protocol chairs and clinical research managers for review and approval. This SOP should minimally contain the following elements:

- Recruitment methods and materials (e.g., scheduling)
- Screening procedures
- Considerations for recruitment of youth and caregivers
- Methods for tracking recruitment
- Participant retention
- Ethical and human subjects considerations
- Staff responsibilities for all of the above (direct and supervisory)
- QC/QA procedures (if not specified elsewhere)

All sites are responsible for following their participant accrual SOP and updating the document if needed to meet site-specific accrual projections, throughout the study accrual period. Following the participant accrual SOP approval by protocol chairs and clinical research managers, if changes are made to the participant accrual SOP in connection with protocol requirements, it is not required to submit the SOP for an additional review after the site has been activated.

Once accrual is initiated, the DMC will report the number of participants enrolled to the Protocol Team at least monthly. Throughout the accrual period, the Protocol Team will review accrual and other performance data across sites to determine whether accrual targets should be adjusted across sites to achieve the study objectives most efficiently and to decide when to discontinue accrual at each site. Findings and recommendations from these reviews will be communicated to all sites, and all sites will adjust their accrual efforts accordingly. Similar adjustments may be made in response to IMPAACT Study Monitoring Committee (SMC) reviews of the study.

Selected operational considerations related to the recruitment, screening, and enrollment process are provided in the remainder of this section.

4.2 Participant Recruitment, Screening, and Enrollment Processes

Refer to protocol Section 4.6 for an overview of the participant recruitment, screening, and enrollment process for this study. Recruitment methods may vary across sites but are generally expected to rely on outreach to populations of 15 - 19 year-old youth living with HIV in care at participating study sites and local clinics, and their caregivers, as applicable.

Provided below is a reminder on the importance of rapid recruitment, screening, and enrollment.

Enrollment/randomization must occur within 60 days of each youth participant initiating the screening process.

From the day the first participant is screened the remaining pool of eligible youth (5 – 8) for the Pilot Test and (12 – 20) for the Randomized Trial must be rapidly identified, screened, complete Pre-Entry visit procedures and enrolled during the Entry visit within 60 days to prevent the need for re-screening.

Youth who are screened more than 60 days prior to enrollment must be re-screened for all inclusion and exclusion criteria prior to enrollment.

Contact the Protocol Team with any questions involving the recruitment, screening, and enrollment process.
While recruitment methods may vary across sites, screening and enrollment methods will be more standardized across sites, consistent with the requirements of protocol Sections 6.1.1-6.1.3, 6.2.1, 6.3.1-6.3.3.

A schematic overview of the recruitment, screening, and enrollment process is provided in Figure 4-1 for youth and Figure 4-2 for caregivers.

Figure 4-1
IMPAACT 2016 Recruitment, Screening, and Enrollment Process for Youth

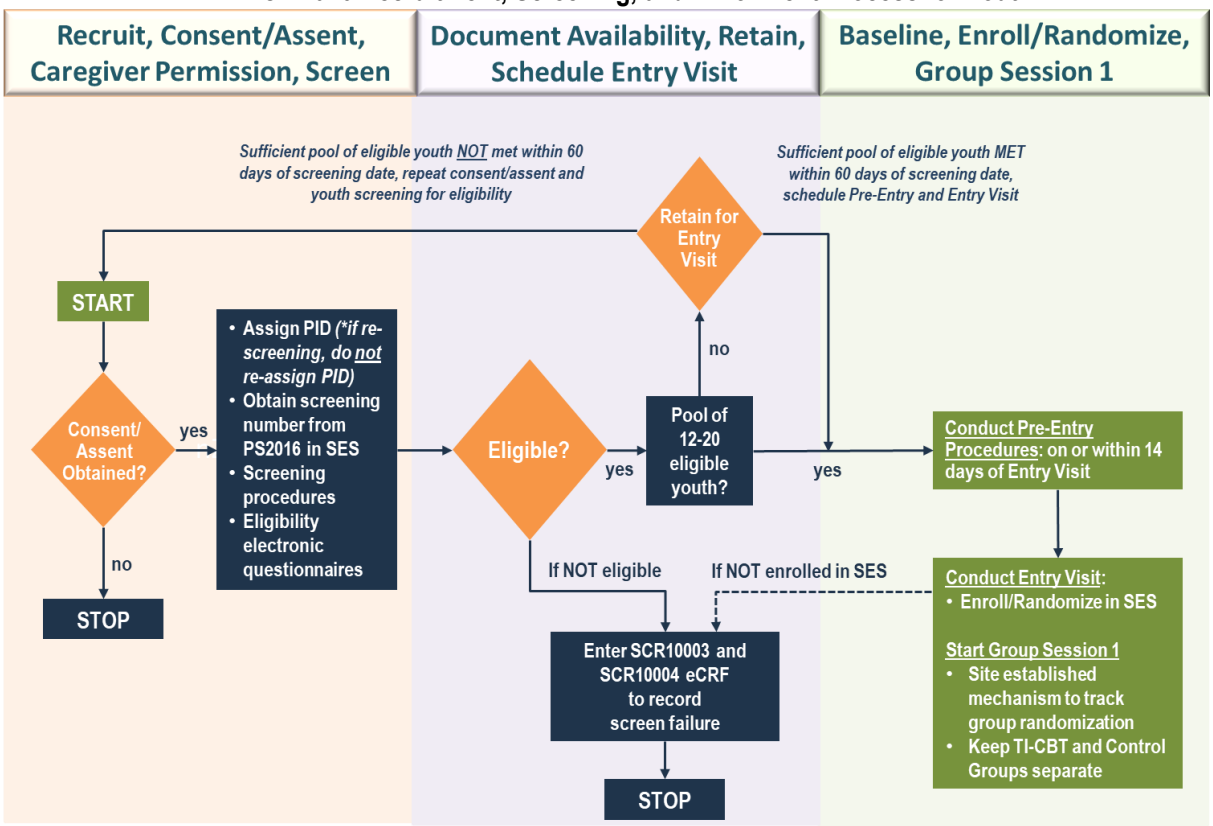
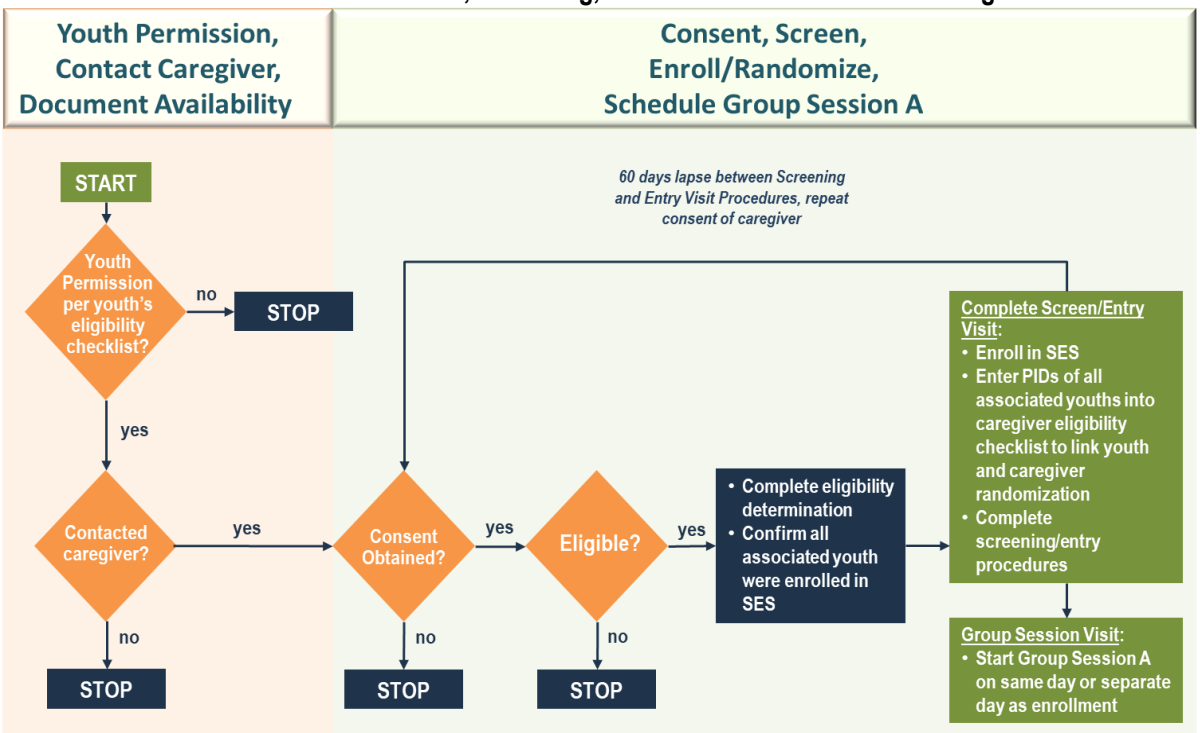


Figure 4-2
IMPAACT 2016 Recruitment, Screening, and Enrollment Process for Caregivers



4.3 Obtaining Informed Consent and Assent

This section contains operational guidance for obtaining informed consent and assent for IMPAACT 2016. This guidance complements, but does not duplicate, the comprehensive information on informed consent, assent, and other human subjects' considerations provided in Section 8 of the IMPAACT Network Manual of Procedures. Refer to the IMPAACT Network Manual of Procedures as needed. Also refer to protocol Section 12.3, Section 4.8 of the ICH Guideline for GCP, and the DAIDS SCORE Manual as needed.

Youth Participant

Inclusion criterion 4.1.2 specifies requirements for obtaining informed consent and assent from youth for this study, with two options depending on age of the potential youth participant listed below and additional details outlined in protocol Section 12.3.

- ***If of legal age and able to provide independent informed consent as determined by site SOPs and consistent with site IRB/EC policies and procedures:*** Willing and able to provide written informed consent for study participation. **Under this option, the potential participant must undergo the study informed consent process.**

- ***If not of legal age to provide independent informed consent:*** Parent or legal guardian, or other legally authorized representative is willing and able to provide written informed consent for study participation **and** potential participant is willing and able to provide written assent for study participation. **Under this option, the potential participant's parent, legal guardian, or other legally authorized representative must undergo the study informed consent process and the potential participant must undergo the study assent process. If the legal age of consent is reached any time following entry, the participant must undergo the study informed consent process at the next scheduled visit after the legal age is reached.**

For each potential youth participant, study site staff will be required to determine which of the two above-listed options apply, and to conduct informed consent and assent processes accordingly.

Each site must have on file a study-specific SOP or study-specific addendum to an existing SOP for obtaining informed consent and assent that addresses all aspects of the informed consent and assent processes for this study consistent with all applicable regulations (e.g., 45 CFR 46), DAIDS SCORE Manual, IRB/EC policies and procedures, and protocol specifications. Site staff involved in conducting informed consent and assent processes must follow these SOPs consistently. These staff must be designated on the study-specific delegation of duties log and must also be listed on the DAIDS Investigator of Record Form for the study.

Research regulations require that informed consent and assent be documented through the use of a written informed consent and assent form approved by the IRB/EC and signed and dated by the participant or the participant's legally authorized representative at the time of consent. Study sites must comply with all requirements and are encouraged to comply with all suggestions. To assist with compliance, site staff may use informed consent and assent coversheets or other similar materials. Each informed consent and assent process should also be documented in a signed and dated chart note. The note should document that informed consent or assent was obtained before conducting any study procedures. However, if an informed consent or assent coversheet is used, it is not necessary to transcribe or otherwise duplicate information recorded on the coversheet in the chart note.

Caregiver Participant

Inclusion criterion 4.3.2 specifies requirements for obtaining informed consent from caregivers for this study, with only one option: caregivers must be of legal age and able to provide informed consent to participate. Additional details are outlined in protocol Section 12.3.

Youth and Caregiver Participants

See Section 4.3.1 of this MOP for further guidance on adequate documentation of informed consent and assent to fulfill protocol inclusion criteria 4.1.2 and 4.3.2 for youth and caregivers, respectively. Figure 4-3 and Figure 4-4 provide instructions for entering informed consent and assent data into eCRFs.

Figure 4-3
Youth and Caregiver Participants Who Can Provide Independent Informed Consent

Informed consent for study participation (Youth and Caregiver)
• Enter the outcome of this informed consent process into the **LGW10006 : Informed Consent Status Log eCRF**. • Complete a log line entry for "protocol version" and select the protocol version number. • For the date of consent, enter the date when informed consent was provided.
Informed consent for non-protocol defined specimen storage and future use — research on HIV, the immune system, and other diseases (Youth only)
• Enter the outcome of this informed consent process into the **TRK10000: Specimen Consent for Non-Protocol Defined Testing eCRF**. • Enter "yes", "no" or "consent not specifically requested" in the first question under the Specimen Testing Other Than Genetic Testing section. • Enter the date when this informed consent decision was made in the second question under the Specimen Testing Other Than Genetic Testing section.
Informed consent for non-protocol defined specimen storage and future use — research involving genetic testing (Youth only)
• Enter the outcome of this informed consent process into the **TRK10000: Specimen Consent for Non-Protocol Defined Testing eCRF**. • Enter "yes", "no" or "consent not specifically requested" in the first question under the Human Genetic Testing section. • Enter the date when this informed consent decision was made in the second question under the Human Genetic Testing section.

Figure 4-4
Youth Participants Who Cannot Provide Independent Informed Consent

Informed consent and assent for study participation (Youth only)
• Enter the outcome of this informed consent process into the **LGW10006: Informed Consent Status Log eCRF**. Enter the outcome of this informed assent process into the **LGW10060: Informed Assent Status Log eCRF**. • Complete a log line entry for "protocol version" and select the protocol version number. • For the date of consent or assent, enter the date when informed consent or assent was provided.

Informed consent and assent for non-protocol defined specimen storage and future use — research on HIV, the immune system, and other diseases (Youth only)
• Enter the outcome of this informed consent process into the **TRK10000: Specimen Consent for Non-Protocol Defined Testing eCRF**. Enter the outcome of this informed assent process into the **TRK10078: Specimen Assent for Non-Protocol Defined Testing eCRF**. • Enter "yes", "no", or "consent/assent not specifically requested" in the first question under the Specimen Testing Other Than Genetic Testing section. • Enter the date when the informed consent or assent decision was made in the second question under the Specimen Testing Other Than Genetic Testing section.
Informed consent and assent for non-protocol defined specimen storage and future use — research involving genetic testing (Youth only)
• Enter the outcome of this informed consent process into the **TRK10000: Specimen Consent for Non-Protocol Defined Testing eCRF**. Enter the outcome of this informed assent process into the **TRK10078: Specimen Assent for Non-Protocol Defined Testing eCRF**. • Enter "yes", "no", or "consent/assent not specifically requested" in the first question under the Human Genetic Testing section. • Enter the date when the informed consent or assent decision was made in the second question under the Human Genetic Testing section.

Regulations require that persons providing informed consent or assent be given a signed copy of their informed consent or assent form. If the copy is declined, this should be documented, and the person should be offered an alternate form of study contact information (e.g., a contact card or appointment card) in lieu of the full informed consent or assent form.

4.3.1 Guidance on Adequate Documentation of Provision of Informed Consent and Assent (Inclusion Criteria 4.1.2 and 4.3.2)

Protocol inclusion criteria 4.1.2 (youth) and 4.3.2 (caregivers) specify requirements for obtaining informed consent and assent for this study, with two potential options depending on the age of the potential participant, as specified in Section 4.3 of this MOP. The protocol refers site staff to the study-specific MOP for guidance on adequate documentation of these criteria. **Adequate documentation should include the following:**

- Copies of (blank) study-specific informed consent (for potential youth and caregiver participants as applicable) and assent (for potential youth participants as applicable) forms approved by the site IRB/EC as well as the IRB/EC risk determination for the study, and any other directives provided by the IRB/EC pertaining to obtaining informed consent and assent for this study. It is generally expected that this documentation will be maintained in study-specific essential document files.

- Copies of IRB/EC policies and procedures pertaining to the legal age of consent for research, and expectations for obtaining assent from underage research participants. It is generally expected that this documentation will be maintained in study-specific essential document files.

- Copies of site SOPs for obtaining informed consent (for potential youth and caregiver participants as applicable) and assent (for potential youth participants as applicable) for IMPAACT 2016, including documentation of whether the youth or caregiver participant is of legal age to provide independent informed consent. It is generally expected that this documentation will be maintained in study-specific essential document files.

Note: Per protocol Section 4.6, the informed consent process "will include detailed review of the study informed consent and assent forms (as applicable), time to address any questions or concerns the potential participant, parent, or guardian may have, and an assessment of understanding before proceeding to informed consent and assent decisions." Site SOPs should describe how understanding will be assessed and documented.

- For each potential youth participant who is not able to provide independent informed consent, documentation of the name of the parent, guardian, or other legally authorized representative who took part in the study informed consent process and the relationship of this person to the potential participant. It is generally expected that this documentation will be maintained in individual participant research records.

- For each potential youth participant, documentation of the conduct of the informed consent and assent processes, as applicable, consistent with site SOPs and the DAIDS policy on *Requirements for Source Documentation in DAIDS Funded and/or Sponsored Studies.* See also Section 4.3 of this MOP.

- For each potential caregiver participant, documentation of the conduct of the informed processes, consistent with site SOPs and the DAIDS SCORE Manuals. See also Section 4.3 of this MOP.

- For each potential youth participant for whom informed consent and/or assent is provided, signed and dated informed consent and assent forms. It is generally expected that this documentation will be maintained in individual participant research records.

- For each potential caregiver participant for whom informed consent is provided, signed and dated informed consent forms. It is generally expected that this documentation will be maintained in individual participant research records.

4.3.2 Guidance on obtaining and documenting youth written permission for caregiver participation during consent/assent process per Inclusion Criterion 4.3.1

Per protocol Section 4.6, as part of the youth informed consent or assent process, youth will be asked whether they are willing to identify a caregiver and provide written permission for the caregiver to participate in the study. Written permission is source documented on the youth's informed consent or assent form by the youth writing an 'X' to indicate their decision as shown in Figure 4-5 below.

Figure 4-5
Written Permission Excerpt from the Sample Youth Informed Consent Forms

[Youth Participants Only]

For the optional caregiver participation, write a 'X' to indicate your decision.

_____ Yes, I agree to have my caregiver join the study

_____ No, I don't want to have my caregiver join the study

Site staff must enter the decision into the youth participant's eligibility checklist at the youth Entry Visit.

For all youth who write an 'X' to indicate yes or no: A youth's decision regarding caregiver participation will also be reported on the **EVW10053: IMPAACT 2016 Report of Caregiver Participation eCRF** shown in Figure 4-6.

For youth who write an 'X' to indicate "no, I don't want to have my caregiver join the study": site staff should ask the youth why they do not want their caregiver to join (e.g., doesn't have anyone they consider a caregiver, doesn't want caregiver involved, or specify other reason.), source document response, and enter response on the **EVW10053: IMPAACT 2016 Report of Caregiver Participation eCRF** shown in Figure 4-6.

- Site staff should explain to the youth that their caregiver will not be contacted on their behalf.
- However, if another youth who is under the care of the same caregiver agrees to invite the caregiver to join the study, the caregiver will be contacted ONLY on behalf of the youth who provided permission for caregiver participation.
- Further, explain to the youth that their caregiver will only engage in the study with any other youth who agreed to the caregiver's participation, and their caregiver will not be told that they (the youth) did not agree to the caregiver's participation.

For youth who write an 'X' to indicate "yes, I agree to have my caregiver join the study": site staff should ask the youth for their caregiver's name, phone number, and email to be able to contact the caregiver, and confirm if caregiver and youth share same household.

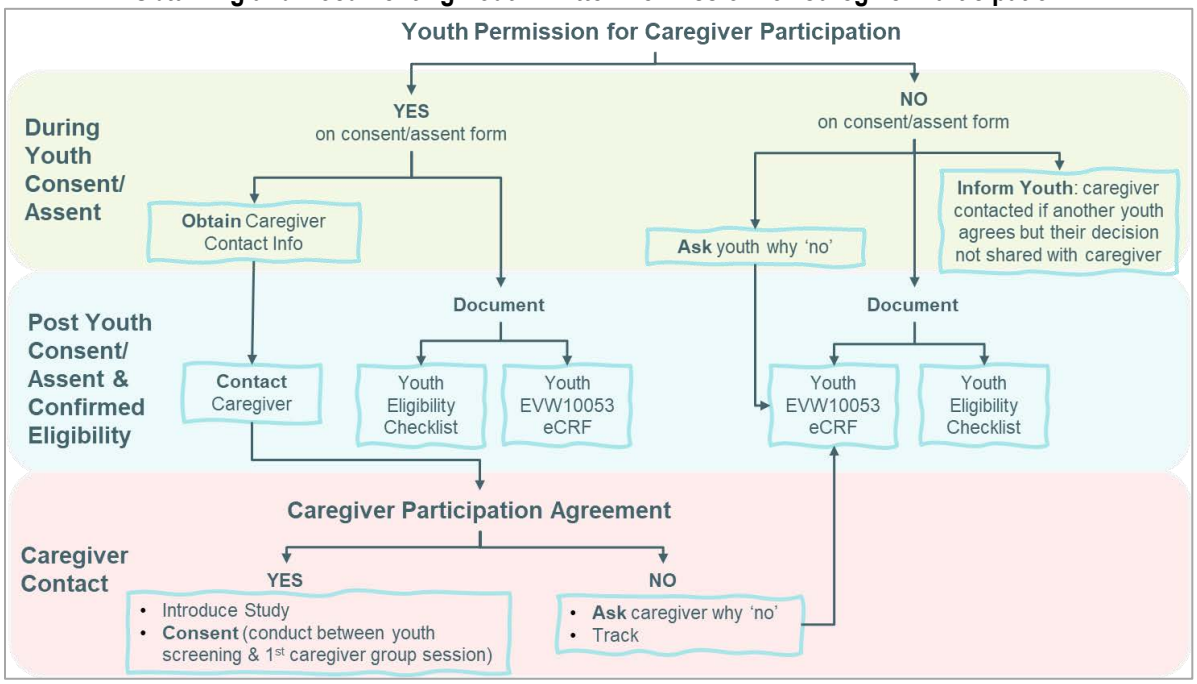
- If the identified caregiver agrees to participate, they will be introduced to the study and asked to provide informed consent for their own participation. Caregivers may be contacted, introduced to the study and provide consent at any point between youth screening and the first caregiver group session unless either the youth or caregiver is determined ineligible to participate in the study.
- If the identified caregiver does **not** agree to participate, they will not be asked to provide informed consent. Site staff should ask the caregiver why they do not want to participate (e.g., isn't interested, doesn't have time, couldn't be reached, disability/unable to travel to site, specify other reason), source document response, and enter response on the **EVW10053: IMPAACT 2016 Report of Caregiver Participation eCRF** shown in Figure 4-6. **Sites should establish a mechanism to track the number of caregivers identified who do not agree to participate; this data will be requested by the Protocol Team.**

Figure 4-6
EVW10053: IMPAACT 2016 Report of Caregiver Participation

Form: EVW10053: IMPAACT 2016 Report of Caregiver Participation	
Did the youth participant consent/assent to caregiver participation?	Yes ☐ No ☐
If No, why did the youth participant refuse consent/assent to caregiver participation?	Doesn't have anyone they consider a caregiver ☐ Doesn't want caregiver involved ☐ Other, specify ☐
If Other, specify [200]:	
Did the caregiver agree to participate?	Yes ☐ No ☐
If No, why did the caregiver refuse to participate?	Isn't interested ☐ Doesn't have time ☐ Couldn't be reached ☐ Disability/unable to travel to site ☐ Other, specify ☐
If Other, specify [200]:	
Do the youth participant and the caregiver live in the same household?	Yes ☐ No ☐

Figure 4-7 below outlines steps for obtaining and documenting youth written permission for caregiver participation.

Figure 4-7
Obtaining and Documenting Youth Written Permission for Caregiver Participation



4.4 Assigning Participant Identification Numbers

A participant identification (PID) number must be assigned to each potential participant for whom informed consent for study participation is obtained. The only exception to this requirement applies when a participant has previously been assigned a PID for another IMPAACT or ACTG study. In that case, the previously-assigned PID would be used for IMPAACT 2016. Study site staff should assign PIDs from lists provided by the DMC and should contact the DMC with any questions related to use of PID lists.

4.5 Screening for Eligibility

Participant eligibility criteria are provided in protocol Sections 4.1 and 4.2, and eligibility screening procedures are provided in protocol Section 6. Operational guidance related to selected eligibility criteria is provided in the remainder of this section. Sites are encouraged to perform procedures that are least burdensome and/or most likely to identify ineligibility first. Note that all screening procedures, must occur within 60 days prior to entry.

As described in protocol Section 4.6, a PID will be assigned to all potential participants for whom informed consent or assent for study participation is obtained. A study-specific screening number will also be obtained only for youth by completing the **PS2016 Screening Log** for IMPAACT 2016 in the DMC's Study Enrollment System (SES). Potential youth and caregiver participants found to meet all eligibility criteria will be enrolled in the study using the SES as described in Section 4.6 of this MOP.

For potential youth participants who are found to be ineligible, or who do not enroll in the study for any reason, the **SCR10003: Screening Failure eCRF** must be entered to record the screening outcome. If indicated on the SCR10003 that the reason for non-enrollment is due to the participant not meeting the inclusion/exclusion criteria, the **SCR10004: Screen Failure - Inclusion/Exclusion Log eCRF** must be entered to record the criteria not met.

It is the responsibility of the IoR and other designated study site staff to ensure that all required screening procedures are performed and adequately documented, and that only participants who meet the study eligibility criteria are enrolled. Each study site must have on file a study-specific SOP for eligibility determination that describes how study site staff will fulfill this responsibility; all sites must follow their SOPs when assessing eligibility for all potential participants.

In the event that study site staff identify that an ineligible participant has been enrolled, the Protocol Team must be consulted as soon as possible and ideally within 24 hours of site awareness per the communication procedures described in Section 3.0 of this MOP.

Re-Screening for Eligibility

The term "screening attempt" is used to describe each time a participant screens for the study, ending at the time the screening window for that participant closes. A total of two screening attempts for the Pilot Test and two screening attempts for the Randomized Trial are allowed for a given participant (e.g., participants may re-screen once per Pilot Test or Randomized Trial).

If all screening and enrollment procedures are not completed within 60 days of obtaining written informed consent and assent (as applicable) for screening, the participant must repeat the entire screening process except:

- A new PID should not be assigned (Note: For youth only, obtain a new screening number from SES for second screening attempt)

- For youth only, if HIV infection is documented, a repeat test is not required
- For youth only, previously-documented medical and medications history information should be reviewed and updated through the date of re-screening (it is not necessary to re-record history information that was previously documented)

Informed consent and assent (as applicable) are required for each screening attempt, and previously-provided consent or assent does not "roll over" to a subsequent screening attempt/window.

4.5.1 Screening Medical History and Chart Reviews

For youth, the listing of Eligibility Screening Procedures in protocol Sections 6.1.1 and 6.3.1 requires site staff to "review medical records to assess study requirements related to HIV infection per inclusion criterion 4.1.3 and ARV history per inclusion criterion 4.1.5."

Medical History: Some of the study eligibility criteria require consideration of medical history information to be obtained from potential youth participants, as well as detailed review of youth participants' medical records. Study sites are encouraged to develop operational tools to guide and document this process. These may include a structured medical history source document, with medical history questions to be asked and fields to record participant responses and/or a medical record review tool to record medical record review findings.

Source Documentation: Adequate source documentation must be available in each potential participant's study record to substantiate their eligibility for the study in relation to the protocol-specified eligibility criteria. Monitors and auditors may request original source documents or certified copies to verify eligibility in relation to each inclusion and exclusion criterion. Further guidance related to these documentation requirements can be found in the following sections of the DAIDS policy on *Requirements for Source Documentation in DAIDS Funded and/or Sponsored Clinical Trials:* Certified Copies, Entry Criteria, Medical History, Medical Records, Screening.

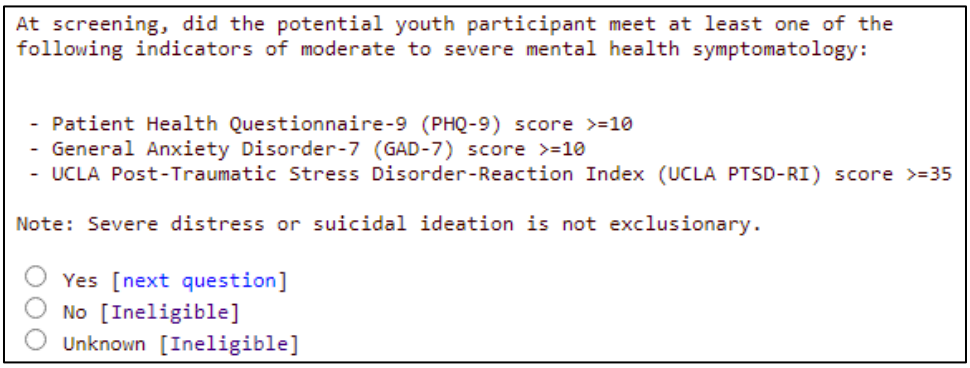
4.5.2 Guidance on Indicators of Moderate to Severe Mental Health Symptomology per Inclusion Criterion 4.1.6

Per inclusion criterion 4.1.6, potential youth participants must demonstrate mental health symptomology to participate in the study. As part of the study eligibility determination and confirmation process, the three participant self-reported mental health questionnaires must be administered to youth to assess for symptoms related to depression (Patient Health Questionnaire-9 or PHQ-9), anxiety (General Anxiety Disorder or GAD-7) and trauma (UCLA PTSD Reaction Index). The questionnaires will be self-administered as electronic questionnaires using the Medidata Patient Cloud application on a site-provided iPad, in the participant's chosen language that would optimize the participant's performance. Refer to Section 5.4 of this MOP for details on self-administered electronic questionnaires.

Eligibility Email Alerts: For a youth to meet inclusion criterion 4.1.6, a minimum score must be obtained on at least one of the three mental health questionnaires. An email alert indicating whether or not a given participant obtained a minimum score on each of the three required questionnaires will be sent in real-time to a site email group that includes designated site staff (limited to the site IoR, study and/or nurse coordinator, and local supervisor, who may also be serving as the on-site study clinician and/or IoR). The scores will not be provided in these emails. **If a participant completes a paper questionnaire, site staff will need to expeditiously key the data into the applicable paper version of the questionnaire eCRF in Medidata Rave to receive the email alert.**

As outlined in Figure 3-1, sites should email the Protocol Data Managers the name(s), email(s), and title(s) (e.g., IoR and local supervisor) of designated site staff to receive the email alerts. Recipients of the alerts should forward the eligibility alerts as needed to site staff designated to complete participant eligibility checklists. Such site staff must enter 'yes' or 'no' into the designated question (refer to Figure 4-8) on the participant's eligibility checklist to confirm the participant's eligibility per inclusion criterion 4.1.6.

Figure 4-8
Item in the IMPAACT 2016 Eligibility Checklist



4.5.3 Guidance on Obtaining and Documenting Youth Shared Households and Shared Caregivers

Prior to Youth Entry Visit: Upon receipt of youth permission of caregiver participation and confirming youth eligibility, and before the youth entry visit, site staff should collect information on which youth share the same households or share the same caregivers. During the Youth Entry Visit, site staff will document this information on the **EVW10053: IMPAACT 2016 Report of Caregiver Participation eCRF** (refer to Figure 4-6).

Tracking Shared Households and/or Shared Caregivers

Track: Sites should establish a mechanism to track which youth share the same household and/or share the same caregivers.

At the time of enrollment, this information on which youth share the same households or share caregivers should be used to determine which youth should be enrolled first (note: youth who share households and/or caregivers should be enrolled first, refer to Section 4.6 for guidance on enrollment).

4.6 Enrolling Eligible Participants

Contact the Protocol Team with any questions about eligibility, and adequate documentation thereof, prior to enrollment.

Youth Participants

Youth participants will be considered enrolled in this study upon successful entry of eligibility checklist data into the SES, which will result in the generation of a Study ID Number (SID). After youth eligibility is confirmed, enroll youth participants by completing the 2016 Version 2 eligibility checklist within the SES.

Caregiver Participants

While the caregiver may be contacted and provide informed consent for their own participation at any point between the youth screening and the first caregiver group session, the caregiver should only be enrolled after ALL youth who consented for the caregiver's participation are enrolled.

After caregiver eligibility is confirmed, enroll caregiver participants by completing 2016 Version 2 eligibility checklist within the SES. Questions within the eligibility checklist will capture the youth PID numbers to link the youth and caregiver participants.

Order of Enrollment

Pilot Test and Randomized Trial: Enroll all youth who live in the same household or share a caregiver first. *(For the randomized trial, this will ensure that slots available to the same arm.)*

Randomized Trial: Record the randomized assignment in the participant chart and make a note on the screening/enrollment log or any other relevant document. This information should be easily accessible to confirm attendance for their group session.

4.7 Screening and Enrollment Logs

Per the DAIDS SCORE Manual, study sites are required to document screening (including screening failures) and enrollment activity on screening and enrollment logs. These logs may be maintained electronically but must be 21 CFR Part 11 compliant if the log is considered a source document. Screening and enrollment logs may be maintained separately or combined into one log. Screening and enrollment logs should be updated in real time and completed after a participant provides informed consent for screening.

4.8 Participant Retention

Per protocol Section 4.7, each site must establish and implement SOPs that target retention rates that are sufficient to reliably estimate the primary study outcomes. Such SOPs may be included in the required participant accrual SOP listed on the site-specific study activation checklist (refer to Section 4.1 of this MOP). The following guidance provides suggested retention procedures sites may incorporate into the participant accrual SOP and implement when feasible and acceptable per local regulations. Sites are not limited to only the following suggested retention procedures and are encouraged to incorporate best practices per local regulations.

During Screening and Pre-Entry Visit: youths' birthdate, email, phone numbers, and home address should be obtained to help us locate participants in the future. If the youth has a social media account they would like to communicate with, such as Instagram, SnapChat, WhatsApp, or Facebook, obtain the name and/or number of the account. Collect the same contact information for caregivers. In addition to the youth and caregiver information, collect the name and contact information for at least two other individuals who "will always know where the youth/caregiver is in the event that their contact information has changed." Youth and caregivers should indicate how they would like the site staff to refer to themselves should they contact the "other" individuals.

Contact information for the youth, caregiver, and "others" should be updated as needed at each study visit, and youth and caregivers should be telephoned/emailed/texted monthly to update information during

the follow-up study period. The contact information should be used to enable scheduling, address scheduling issues and barriers, and remind participants of when their study visits and group sessions will be conducted.

Before Each Group Session: Youth (and caregivers where relevant) should be contacted the day before group sessions and study visits to confirm attendance.

Following Each Group Session: Phone calls, text messages, emails, or other methods intended as retention techniques may be provided following each study visit to demonstrate the team's appreciation of participation. The same methods could be used prior to the next session as a reminder and incentive to return. Other methods may be implemented at the discretion of the site IoR or designee such as acknowledging a participant's birthday by phone call, text message or email.

Confirm with the IRB any materials and/or methods that may be provided to participants per site standards, including but not limited to social media accounts, phone calls, text messages, emails, or other methods.

5.0 Study Procedures

5.1 Procedures (Pilot Test only)

Youth participants will perform procedures per protocol Sections 6.1.2 and 6.2.1. Mock procedures include hair and blood collection. All youth and caregiver participants will complete the self-administered electronic questionnaires. The purpose of the mock procedures and administration of the electronic questionnaires is for each site to assess the logistical feasibility and duration to complete all youth procedures on the same day or up to 14 days prior to the Group Session 1, and all caregiver procedures on the same day or up to 60 days prior to the Group Session A.

As part of the procedures, site staff should conduct the following:

- Complete each step of the blood collection procedure outlined in Section 7.1 and LPC, excluding the actual needle stick of drawing blood with each youth participant.
- Complete each step of the hair collection procedure outlined in Section 7.2, excluding Step 3 (cutting of hair) and Step 8 (complete/entering into LDMS) with each youth participant.
- Have each youth and caregiver participant complete all self-administered electronic questionnaires designated for their Pre-Entry Visit (youth) or Screening/Entry Visit (caregiver).

5.2 Targeted Medical and Medication History (Study Visits)

Targeted medical and medication history information, focused on psychiatric history and medication, will be collected per the schedule of evaluations as described in protocol Section 6.5.

Site staff will review available medical records in advance of a youth's scheduled visit during which targeted medical and medication history is to be collected per the schedule of evaluations (Pre-Entry and Follow-up Study Visits) to identify new information. During the youth's scheduled visit, site staff will query youth and/or their caregivers on an individual basis in a private setting separate from other participants. Adequate source documentation of information collected must be maintained in the participant's study record and entered into eCRFs as listed in Figure 5-1.

Figure 5-1
IMPAACT 2016 Targeted Medical and Medication History Documentation

Assess for and Source Document	Enter into eCRF
Gender identity (Pre-Entry Visit Only – should not be performed at sites that have formally opted out of collection of gender identity).	• DMW10004: Gender Identity Interview
Been diagnosed with a mental illness (if yes, diagnosis and dates of diagnosis)	• MHW10000: Medical History Log
Attempted suicide (if yes, number of times; dates of all attempts)	• MHW10000: Medical History Log (if prior to enrollment) • ADE10006: Adverse Events Log (if new events on or after day of enrollment)
Received non-study mental health services (if yes, what kind of services – record any diagnosis resulting from the service; dates provided)	• MHW10000: Medical History Log (resulting diagnoses, if prior to enrollment) • ADE10000: Adverse Events Log (resulting diagnoses, if on or after day of enrollment)
Received referral from study site staff to non-study mental health services (if yes, date and outcome of referral)	• EVW10049: IMPAACT 2016 Youth Referrals (only for IPL, 6- and 12-month Follow-up Visits in Randomized Trial)
Received psychiatric medications (if yes, medications received and dates of use)	• CMW10013: Concomitant Medications Log
Occurrences of insomnia, psychiatric disorders, and suicidal ideation meeting adverse event criteria specified in protocol Section 7.2	• ADE10006: Adverse Events Log (only for new events at visits following enrollment)

In addition to information collected and entered into eCRFs, youth will also self-report information using the electronic questionnaires; refer to Section 5.4 for details on self-administered electronic questionnaire administration.

Safety Email Alerts: Any response(s) suggesting a safety concern or risk will generate a safety email alert to the site's patient cloud alert email group composed of designated study site staff (refer to Section 6.0 for details on designating staff and managing safety alerts); study site staff should review relevant information with the on-site study clinician, or IoR and/or designee in advance of a participant's scheduled visit and enter relevant information into eCRFs per Figure 5-1.

5.3 Ascertaining Gender Identity (Study Visits)

Gender identity will be ascertained from the youth at the Pre-Entry Visit. The initial questions on the form ask if the interview was administered to the youth participant, and if not, why. Note that the interview should be administered to the youth participant only, without the parent or guardian present; the informed consent form for IMPAACT 2016 indicates that these questions are being asked without the parent or guardian present. This procedure should not be performed at sites that have formally opted out of collection of gender identity data, in accordance with policies specified in the IMPAACT Network MOP.

5.4 Self-Administered Electronic Questionnaire Data Collection (Study Visits)

All questionnaires for youth and caregiver participants will be conducted via self-administered electronic questionnaires using the Medidata Patient Cloud application to enable assessments for eligibility and/or study outcomes for analyses. Refer to protocol Sections 5.5 and Schedule of Evaluations in protocol Appendices I-A, I-B, II-A and II-B for details on when questionnaires are administered to youth and caregivers.

All questionnaires should be completed by the participants in a quiet, private space using the Medidata Patient Cloud application on a site-provided iPad. If the Medidata Patient Cloud application is inaccessible for an unforeseen cause, participants will complete paper versions of the questionnaires, which will be printed from the FMU on the DMC Portal, provided to participants, and then keyed into Medidata Rave by study site staff.

Designated study site staff will log into the Medidata Patient Cloud application and complete the following steps:

1) **Clinician View Mode**: In Clinician View mode, study site staff will select the study, site and appropriate participant and visit. While youth participants are in screening, they will be listed under their Screening Number. After youth participants enroll, they will be listed under their PID number.
2) **Country/Language**: The study site staff will be asked to confirm the participant's country and language. All questionnaires are available in English and local languages. The study site staff will then read the IMPAACT 2016 Introduction Paragraph (available on the DMC Portal under the Site Support category and the Medidata Rave Resources link) to the participant in the participant's preferred language.
3) **Patient View Mode**: The study site staff will then select Begin Patient Onboarding to enter Patient View mode and give the iPad to the participant to complete the registration (only required once at first log in) and then the questionnaires for the applicable visit.
4) **Review/Modify/Submit**: After completing each questionnaire, the participant will be presented with an opportunity to review and/or modify their responses. The participant will then submit the data, after which they will no longer be able to review or edit their responses.

Participants should be instructed to carefully read and follow the directions provided at the beginning of each questionnaire as directions for each questionnaire may differ. Study site staff should remain in the room while the participant completes the electronic questionnaires at a distance that maintains privacy, to answer the participant's questions as needed.

Completion of the questionnaires involves a significant time commitment for the participants. Before beginning questionnaire administration, the designated study site staff should assess whether the participant is rested, alert, and how they feel. Snacks and water should be available in case the participant has not eaten prior to the visit. Short breaks are acceptable although they should be brief and only as needed to increase response validity.

Refer to Section 6.1 of this MOP for guidance on monitoring and addressing mental health risks and safety concerns identified in a youth's responses to one or more questions suggesting a risk of suicide, suicidal ideation, or other safety concerns.

Multiple youth under the care of the same caregiver

Should there be more than one youth participating in the study under the care of the same caregiver, the caregiver will be instructed by the site to only complete questionnaires for one youth as follows:

- If more than one enrolled youth are under the care of the same caregiver, and **more than one youth** agreed to the same caregiver participation: the caregiver will be randomly***** assigned to complete questionnaires for **only one** of the enrolled youth throughout the duration of the study.

  *******Each site will be responsible for establishing a mechanism to randomly assign each enrolled caregiver to the PID number of the appropriate enrolled youth. Each assignment will remain effective for the duration of the study so that a given caregiver completes all questionnaires for the same youth PID throughout the entire study. Documentation of the assignments should be securely stored on-site.*

- If more than one enrolled youth are under the care of the same caregiver, but **only one youth** agreed to the caregiver participation: the caregiver will complete questionnaires for the enrolled youth who agreed to their participation. However, the site will not disclose to the caregiver which youth agreed or did not agree to the caregiver participation to maintain confidentiality of a youth's choice.

5.5 Logistical Attendance Data and Fun Had, Knowledge Learned Collection (Group Sessions)

During the Pilot Test and Randomized Trial, study site staff will enter participant group session attendance and data collected from participants of their perception of fun had and knowledge learned from attending each group session into the **EVW10048: IMPAACT 2016 Group Session Feedback eCRF**.

Logistical Attendance Data

During Group Sessions: Per protocol Section 5.5.5, during each group session, the IYL and adult study staff should be the designated study site staff to collect logistical data on study participant attendance and punctuality. The IYL and adult study staff will confirm the answers to the following questions for each participant at each group session:

- Did the study participant attend the scheduled group session?
- Did the study participant stay for at least half of the group session?

Post Group Sessions: Immediately following the end of the group session, IYL and adult study staff observers should provide designated study site staff with participant logistical data to enter into the **EVW10048: IMPAACT 2016 Group Session Feedback eCRF** in Medidata Rave in Figure 5-3 below.

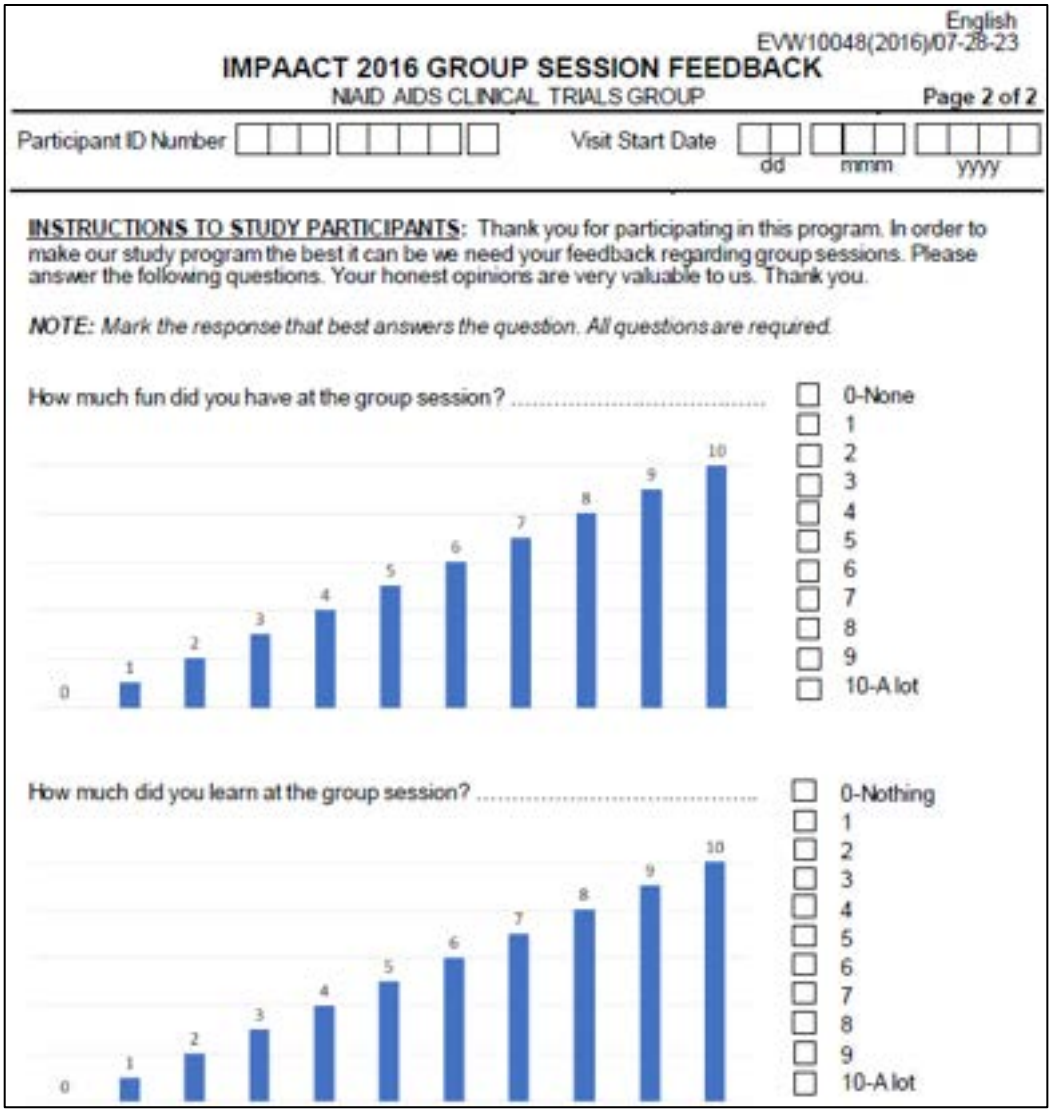
Participant Reported Fun Had and Knowledge Learned Data

Following Group Session: Per protocol Sections 3.1 and 5.5.5, following each group session and before participants leave the session, each youth and caregiver will report on a paper form their perception of 1) how much fun they had at the given group session, and 2) how much they learned at the given session, both on a scale from 0-10, with 0 representing 'no fun'/'learned nothing' and 10 representing 'a lot of fun'/'learned a lot.'

Sites are responsible for printing the paper version of the EVW10048: IMPAACT Group Session Feedback Form to serve as a place for the youth and caregivers to report their responses; example of the paper version of EVW10048 shown below in

Figure 5-2. English and translated versions of the paper EVW10048 form are accessible on the DMC Portal within the FMU.

Figure 5-2
English Paper Version of EVW10048: IMPAACT 2016 Group Session Feedback eCRF in FMU for Participants



English
EVW10048(2016)07-28-23

IMPAACT 2016 GROUP SESSION FEEDBACK

NIAID AIDS CLINICAL TRIALS GROUP

Page 2 of 2

Participant ID Number ☐☐☐☐☐☐☐ Visit Start Date ☐☐ dd ☐☐☐ mmm ☐☐☐☐ yyyy

INSTRUCTIONS TO STUDY PARTICIPANTS: Thank you for participating in this program. In order to make our study program the best it can be we need your feedback regarding group sessions. Please answer the following questions. Your honest opinions are very valuable to us. Thank you.

NOTE: *Mark the response that best answers the question. All questions are required.*

How much fun did you have at the group session? .....

☐ 0-None
☐ 1
☐ 2
☐ 3
☐ 4
☐ 5
☐ 6
☐ 7
☐ 8
☐ 9
☐ 10-A lot

How much did you learn at the group session? .....

☐ 0-Nothing
☐ 1
☐ 2
☐ 3
☐ 4
☐ 5
☐ 6
☐ 7
☐ 8
☐ 9
☐ 10-A lot

Study site staff **who are not the group leaders** should distribute the forms to participants and reassure them that their individual answers will not be shared with the IYL and adult study staff group leaders.

Study site staff will read the following questions aloud to youth and caregiver participants while showing a response cue card (0 = 'no fun'/'nothing learned' to 10 = 'a lot of fun'/'a lot learned') at the end of each group session:

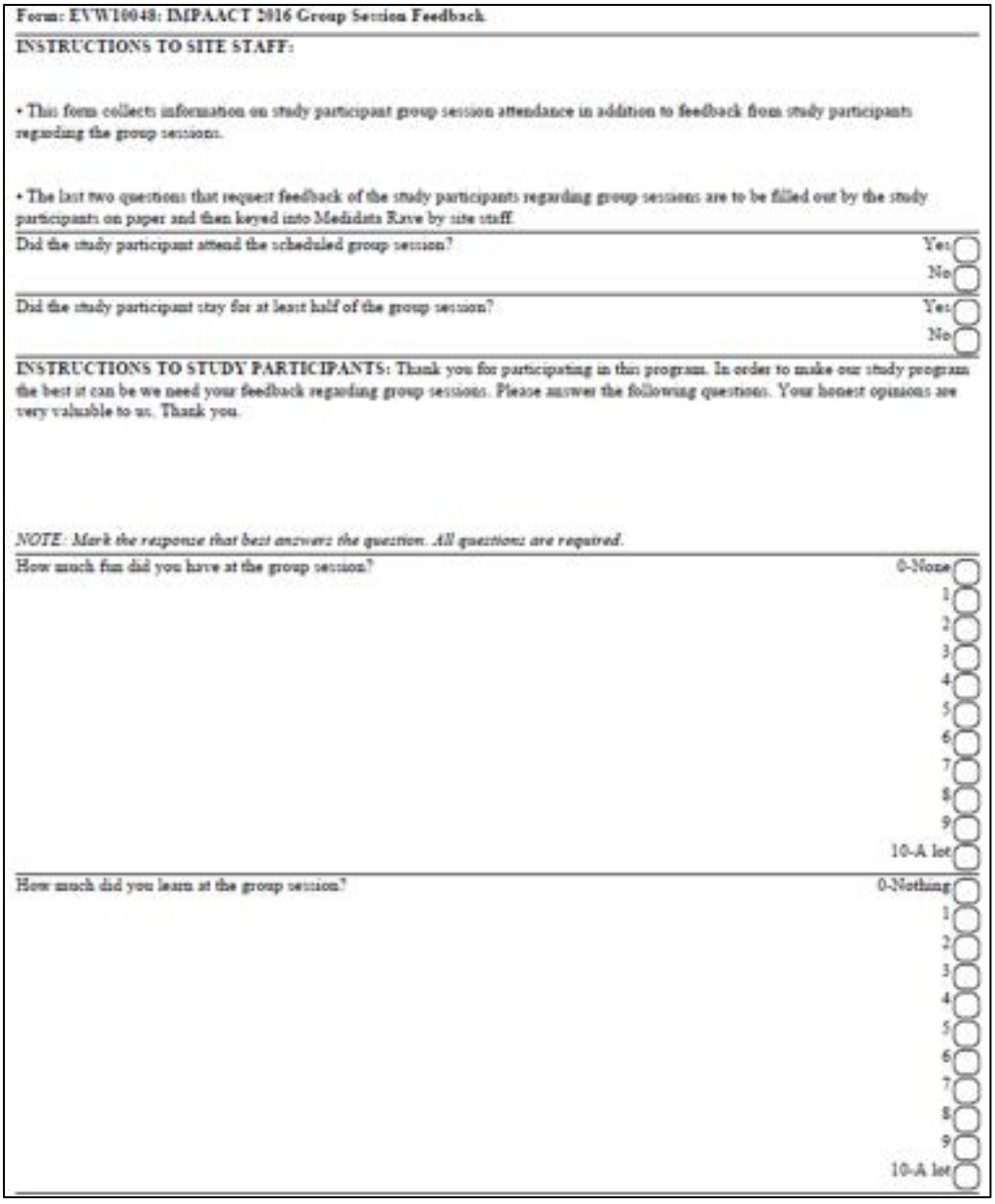
- How much fun did you have at the group session? Youth and caregivers will then mark their response from 0 – 10.

- How much did you learn at the group session? Youth and caregivers will then mark their response from 0 – 10.

Study site staff will ask participants to complete the paper form and will collect the completed forms from all participants at the end of the session. Study site staff will not share participant responses with IYL and adult study staff, and IYL and adult study staff group leaders should not review youth and/or caregiver reports to preserve confidentiality and avoid youth and caregivers responding in a way to please the group leaders.

Post Group Session: Immediately following the end of the session, site staff will enter the responses into the **EVW10048: IMPAACT 2016 Group Session Feedback eCRF** in Medidata Rave; example of the EVW10048 eCRF shown below in Figure 5-3.

Figure 5-3
EVW 10048: IMPAACT 2016 Group Session Feedback eCRF in Medidata Rave for Site staff



Form: EVW10048: IMPAACT 2016 Group Session Feedback

INSTRUCTIONS TO SITE STAFF:

• This form collects information on study participant group session attendance in addition to feedback from study participants regarding the group sessions.

• The last two questions that request feedback of the study participants regarding group sessions are to be filled out by the study participants on paper and then keyed into Medidata Rave by site staff.

Did the study participant attend the scheduled group session? Yes ☐ No ☐

Did the study participant stay for at least half of the group session? Yes ☐ No ☐

INSTRUCTIONS TO STUDY PARTICIPANTS: Thank you for participating in this program. In order to make our study program the best it can be we need your feedback regarding group sessions. Please answer the following questions. Your honest opinions are very valuable to us. Thank you.

NOTE: Mark the response that best answers the question. All questions are required.

How much fun did you have at the group session? 0-None ☐ 1 ☐ 2 ☐ 3 ☐ 4 ☐ 5 ☐ 6 ☐ 7 ☐ 8 ☐ 9 ☐ 10-A lot ☐

How much did you learn at the group session? 0-Nothing ☐ 1 ☐ 2 ☐ 3 ☐ 4 ☐ 5 ☐ 6 ☐ 7 ☐ 8 ☐ 9 ☐ 10-A lot ☐

5.6 Intervention Fidelity Evaluation Forms (IYL and Adult Study Staff / Group Sessions)

Refer to protocol Section 5.4 for details on the assessment of the TI-CBT intervention fidelity.

In the TI-CBT arm only, IYL and adult study staff facilitators will self-report, and IYL and adult study staff observers will provide observer ratings on the fidelity of intervention delivery using paper versions of the IMPAACT 2016 Facilitator Intervention Fidelity Evaluation forms (FFE001 – FFE010) or IMPAACT 2016 Observer Intervention Fidelity Evaluation forms (OFE001 – OFE010), respectively.

Accessing Intervention Fidelity Evaluation Forms

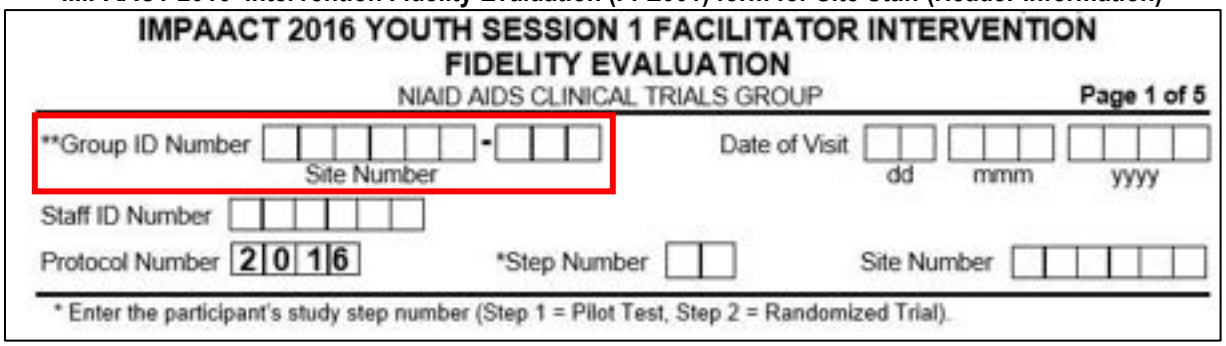
Intervention fidelity evaluation forms are available to download from the FMU on the DMC Portal, and paper forms are completed at the end of each youth and caregiver group session (Pilot Test and Randomized Trial); see Section 3.5 for steps to access the forms.

Completing Intervention Fidelity Evaluation Forms

Prior to each group session, local supervisors or designees will complete the Header information block on each page of the printed intervention fidelity evaluation form prior to distributing them to IYL and Adult Study Staff facilitators and observers.

Group Identification (ID) Number: To identify which group session an individual intervention fidelity evaluation form submission is associated with, IYL and adult study staff must enter a Group Identification (ID) Number on each page of the form; example is shown below in Figure 5-4.

Figure 5-4
IMPAACT 2016 Intervention Fidelity Evaluation (FFE001) form for Site Staff (Header Information)



The **Group Identification Number** naming convention is Site #-[Y or C][T or D][Pilot, 1, 2 or 3…], where:

Y = Youth group	P = Pilot Test
C = Caregiver group	1 = 1st wave in Randomized Trial
T = TI-CBT Intervention	2 = 2nd wave in Randomized Trial
D = Discussion Control	3 = 3rd wave in Randomized Trial

Examples include (refer to Section 4.0 of this MOP for definition of a wave):

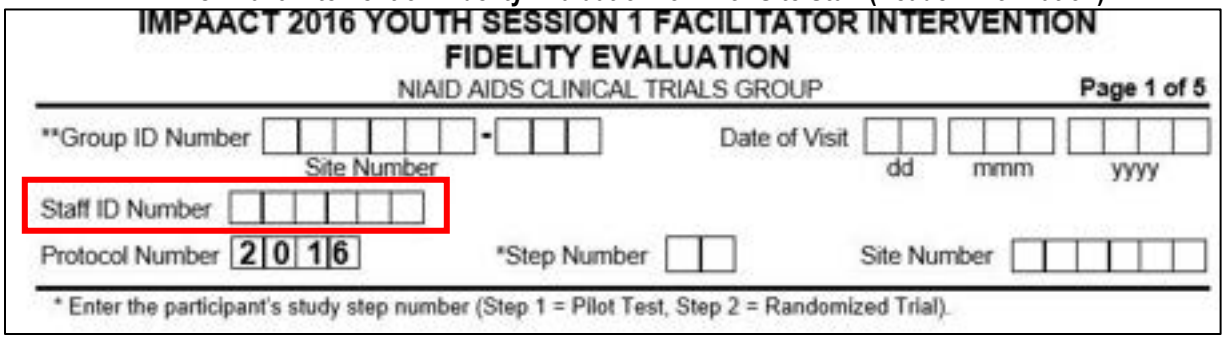
111111-YT1 = At site 111111, a **Y**outh group in **T**I-CBT of the **1**st wave in the Randomized Trial
222222-YD2 = At site 222222, a **Y**outh group in **D**iscussion Control of the **2**nd wave in the Randomized Trial

333333-YTP = At site 333333, a **Y**outh group in **T**I-CBT of the **P**ilot Test
444444-CTP = At site 444444, a **C**aregiver group in **T**I-CBT of the **P**ilot Test
555555-CD1 = At site 555555, a **C**aregiver group in **D**iscussion Control of the **1**st wave in the Randomized Trial

Facilitator and Observer Staff Identification (ID) Number: To identify which IYL or Adult Study Staff facilitator or observer completed the intervention fidelity evaluation form for a given group session, a unique Staff Identification (ID) Number for each IYL and Adult Study Staff must be entered on each page of the form; example shown below in Figure 5-5.

Staff Identification (ID) Numbers will be assigned by site supervisors or designees to each IYL and Adult Study Staff using a listing of identification numbers generated by the Data Management Center. Each IYL and Adult Study Staff will retain their unique staff identification number for the duration of the study.

Figure 5-5
IMPAACT 2016 Intervention Fidelity Evaluation form for Site Staff (Header Information)



Submitting Intervention Fidelity Evaluation Forms to Data Management Center

All completed paper intervention fidelity evaluation forms are to be immediately provided to the local supervisor(s) who will review and upload scanned copies of the completed paper forms to the File Exchange Utility on the DMC Portal; refer to Section 3.5.

Site Use of Intervention Fidelity Evaluation Forms during Supervision Meetings

The local supervisor(s) will use the intervention fidelity evaluation forms to guide discussions during the supervision meetings with IYL and adult study staff; refer to Section 5.8 of this MOP. Completed intervention fidelity evaluation forms should be securely stored on site.

5.7 Group Sessions

5.7.1 Preparation

Practice for the TI-CBT Intervention Group Sessions

After IYL and adult study staff are fully trained to competence as determined by the expert trainer, IYL and adult study staff will continue to practice delivering the group sessions during their supervision as described in Section 5.8 of this MOP. IYL and adult study staff will specifically practice the next upcoming session during the week prior to that session. The practice will occur with the local supervisor and other IYL or adult study staff who will provide feedback to ensure fidelity to the intervention manual and comfort delivering the content.

Notes from the practice sessions may be kept for training purposes and further reviewed during the debrief supervision meeting that occurs between the local supervisor and the IYLs or adult study staff within one week after each intervention session and/or reviewed during the weekly meeting between the local supervisor and expert trainer (refer to protocol Section 5.3.1). IYL and adult study staff trained on the TI-CBT intervention should ONLY practice with other facilitators and observers assigned to the TI-CBT intervention and NOT with those assigned to the discussion control group.

Scheduling Group Sessions

Site staff are responsible for confirming participant availability for group sessions and subsequently arranging the scheduling of each session.

At the end of each group session, site staff should work with IYL and adult study staff to remind participants of the date and time of their next group session while confirming their attendance for the next group session.

Real-Time Documentation of Group Assignment and First Group Session for Randomized Trial

For the first youth group session, site staff must establish a real-time documentation process to record the youth participant's randomization arm and retain the source documentation.

Upon receipt of the assignment arm, site staff must ensure each participant is directed to the correct location where their group (TI-CBT or Discussion Control) will meet for the first group session.

Supplies for the TI-CBT Intervention Group Sessions

Sites are advised to have all necessary supplies available for the practice as well as prior to administering the TI-CBT intervention group sessions to participants. The existence of these materials should be re-checked prior to each session to ensure none have been lost. This will ensure all materials are available before the intervention begins and prevent duplicate orders of supplies that may be re-used in subsequent sessions. Practice sessions should be conducted in the actual study intervention space to ensure it provides adequate space and privacy.

Flip chart paper, markers, pens, and handouts should be ready before each intervention session. Refer to **Appendix** I of this MOP and the first page of the TI-CBT Youth and Caregiver Intervention Manuals for each group session to find what materials are needed for that session.

Logistical Considerations (Room Set-Up, Refreshments, Transportation)

For both the TI-CBT intervention and discussion control groups, the rooms should be reserved in advance with adequate chairs, tables, and working space. On the day of the group session, the materials should be set up in advance of participant arrival so IYL and adult study staff can interact with participants as they arrive and help them feel at ease. Participants should be given a reminder the day prior to the session, in order to maintain session attendance.

Drinks and snacks should be ordered in advance and provided at the end of the group session. As applicable, staff should be prepared to provide transportation compensation and inform participants of their next visit .

It is recommended that sites have an SOP with designated responsibilities for IYL, adult study staff, local supervisor(s), and on-site study clinicians (who may also be the local supervisor) to ensure study sessions and discussion control groups occur smoothly and safely.

5.7.2 Conducting Group Sessions

Attendance

The local supervisor and on-site study clinician (the same individual may serve as both the local supervisor and on-site study clinician) should be on site in a separate room from the participants during all youth and caregiver sessions (TI-CBT Intervention and Discussion Control) to address safety concerns or other emergency situations (refer to Section 6.1 of this MOP for guidance on managing safety or emergency concerns). All group sessions will be delivered by two trained and designated IYL (youth sessions) or adult study staff (caregiver sessions) facilitators and observed by a third trained IYL (youth sessions) or adult study staff (caregiver sessions).

If one of the two group facilitators is unable to attend the session, the observer will take their place. If this occurs, the local supervisor will become the designated observer, and will complete the fidelity ratings and note taking during the session.

Arrival and Set-Up

IYL and adult study staff group leaders and observers should arrive 30 minutes prior to the start of the group session to set up the space with chairs in a half circle for participants; additional chairs for group leaders will be at the front, and chairs for observers will be to the side or back of the room.

For the TI-CBT group sessions only, in advance of a scheduled session (e.g., a few days prior to a session), IYL and adult study staff designated to the TI-CBT Intervention group should re-check to ensure that all materials are present as described in Section 5.7.1 of this MOP. If any materials are missing, IYL and adult study staff should immediately inform the local supervisor or designated site staff so they can replace the missing materials. IYL and adult study staff should set up TI-CBT intervention materials in advance of participant arrival, including the flip chart, handouts, and writing utensils.

Greet Participants and Track Attendance

Once the room is prepared for the group session, IYL and adult study staff should warmly greet participants as they arrive and help participants feel comfortable and at ease. IYL and adult study staff should encourage participants to sit where they like and continue to engage with participants in a friendly and open manner as the group waits for everyone to arrive.

As is often the case, participants may arrive late to the session. IYL and adult study staff, in consultation with the local supervisor, should use discretion regarding how long to wait for all participants to arrive. As a general rule, once there are at least five participants present, the group session should begin, although not before the stated start time. The group session can begin early if all participants are present. The local supervisor should be aware when all participants are present and the group session begins.

In the event a participant has not arrived but is expected to attend (e.g., the participant confirmed attendance the day before the group session), the local supervisor and/or IYL/adult study staff should attempt to reach the participant following the group session to encourage attendance at future group sessions. Participants should be invited to arrive late rather than miss the full group session. Similarly, if a

participant needs to leave early, they should be encouraged to attend as much of the group session as possible.

Late arrivals (>15 minutes after the session begins) and early departures (> 30 minutes before the session ends) should be noted on the participants' study files for the local supervisor and/or IYL/adult study staff to reference if reaching out to participants to encourage full attendance. Refer to Section 5.5 and Figure 5-3 for guidance on documenting attendance in an eCRF.

Delivering the TI-CBT Intervention

For the TI-CBT Intervention group sessions only, IYL and adult study staff should follow the structure and script provided in the TI-CBT Youth and Caregiver Intervention Manuals, respectively, but avoid reading it word-for-word. This will be emphasized in the training of IYL and adult study staff. IYL and adult study staff should be comfortable with the content and materials to be able to deliver the activities smoothly.

The IYL and adult study staff observers should monitor the timing of each activity, take notes throughout the group session for later use during weekly supervision to enhance delivery, and address concerns that arise. The observers do not take part in the group unless indicated in the TI-CBT Youth and Caregiver Intervention Manuals, or if a primary facilitator is absent.

The IYL and adult study staff observers should also complete the IMPAACT 2016 Treatment Fidelity Evaluation form for each specific activity, and at the end of the group session complete the more general questions (refer to Section 5.6 of this MOP for guidance on completing and processing the form).

Ending Each Group Session

At the end of the group session, the IYL and adult study staff should distribute the snacks. During the snack, IYL and adult study staff should leave the room so designated site staff, such as the local supervisor, can implement the procedures described in Section 5.5 of this MOP. Site staff will collect the completed forms and not share individual responses with IYL and adult study staff.

At the conclusion of the group session, IYL and adult study staff should put away all materials and notify the local supervisor or designated study site staff if any materials need replacement in preparation for the next group session.

5.7.3 Concurrent Waves of Group Sessions

Refer to Section 4.0 of this MOP for additional guidance on obtaining approval for conducting waves.

If multiple waves are initiated and are concurrent (each wave's group sessions overlap), group sessions of different waves should be scheduled at different times to avoid contamination. Timing should be discussed with the IMPAACT 2016 CMC to ensure smooth processing. The same preparation (refer to Section 5.7.1 of this MOP) and conduct (refer to Section 5.7.2 of this MOP) will be required. Supervision will proceed as usual per Section 5.8 of this MOP.

5.8 Supervision of Indigenous Youth Leaders and Adult Study Staff

Per protocol Section 5.3, the expert trainer will conduct supervision of the local supervisors in the form of weekly remote meetings per country or site, as agreed upon by the local supervisors and expert trainer.

The local site IoR and/or local supervisors, as designated, will then provide direct supervision to the IYL and adult study staff.

5.8.1 TI-CBT Intervention Arm

Prior to the Pilot Test, the local supervisor who took part in the training for IYL and adult study staff for delivering the TI-CBT intervention will continue to oversee IYL and adult study staff practice of the TI-CBT Intervention delivery. Practice will continue until IYL and adult study staff are deemed competent by the expert trainer and local supervisor, express confidence and familiarity with the material, and demonstrate the ability to deliver the intervention smoothly to participants, as described in Section 3.5 of the Guidance Document: Preparation and Adaptation of the Trauma-Informed Cognitive Behavioral Therapy (TI-CBT) Intervention. It is expected that IYL and adult study staff will require practice in delivering of all sessions a minimum of three times before competency is obtained.

Ongoing Supervision of IYL and Adult Study Staff during Pilot Test and Randomized Trial

After each group session, the local supervisor will review the completed IMPAACT 2016 Treatment Fidelity Evaluation forms (refer to Section 5.6 of this MOP for guidance on completing and processing the form) and observer notes to identify any challenges and/or concerns with intervention delivery. These forms and notes will be used in supervision with IYL and adult study staff to facilitate improvement and/or remediate concerns as needed. If additional training is determined to be needed, the local supervisor will provide additional training to the IYL and/or adult study staff.

IYL and adult study staff will meet with local supervisors twice before each group session during the Pilot Test and the Randomized Trial*:

- In the first meeting, as applicable, IYL and adult study staff will review the prior session, facilitator fidelity forms, and observer fidelity forms.
- In the second meeting, IYL and adult study staff will practice the upcoming group session.

*Note: prior to the first group session (e.g., Group Session 1 for youth and Group Session A for caregivers), IYL and adult study staff will meet with local supervisors to practice the first group session.

The local supervisor should take notes regarding IYL and adult study staff performance to review with IYL and adult study staff during the supervision session and with the expert trainer during weekly remote meetings.

Local supervisors should not disclose which IYL and/or adult study staff the information within the fidelity form is about, however general themes can be shared with facilitators to help improve the administration of the intervention.

Local Supervisor and Expert Trainer Meetings

The expert trainer will conduct supervision of the local supervisors in the form of weekly remote meetings, per country or per site, as agreed upon by the local supervisors and expert trainer. During these meetings, local supervisors will discuss the observers' notes, the facilitator and observer fidelity forms, and other issues that arise during supervision with IYL. Ideally, the expert trainer supervision meetings will occur with all local supervisors across all participating sites within one country simultaneously to build capacity of sites to work together. These meetings should be scheduled at a time that works for all parties involved.

5.8.2 Discussion Control Arm

Ongoing Supervision of IYL and Adult Study Staff during Randomized Trial

The local supervisor or other designee who is not exposed to the TI-CBT group sessions or training will meet with IYL and adult study staff leading the Discussion Control Groups before each group session during the Randomized Trial.

Meetings will be unstructured, and IYL and adult study staff should be encouraged to discuss and troubleshoot any concerns or issues that arise during the groups. It is ideal that a designee who is not exposed to TI-CBT meet with the IYL and adult study staff if site resources allow for it to prevent contamination; sites may consult with the CMC if the same person (e.g., local supervisor) will supervise both arms.

Care should be taken NOT to bring in content from the TI-CBT intervention during these meetings.

6.0 Participant Monitoring, Management, and Safety-Related Reporting

6.1 Youth Participant Safety Monitoring and Management

Refer to protocol Sections 6.6, 6.7, 7, and 8.1 for details on procedures addressing potential psychiatric concerns, social harms and suicidal ideation among youth participants, information on safety monitoring and reporting, and monitoring safety concerns among youth participants.

During the consent process, potential youth and caregiver study participants are informed that their participation in the study and responses to assessments will be kept private and confidential except in the cases of child abuse or risk of self-harm or harm to others. Occasionally, site staff must balance their concerns about the well-being of the participants with the promise to keep their responses and comments confidential. In some cases, such disclosures are required by law to be reported in order to maintain individual safety. In these cases, participants should be informed if the report is disclosed to the Protocol Team and/or local supervisor for further review.

Any participant information **should only be discussed in a clinical or research setting** unless referrals are made per site standard of care. Where a youth participant discloses any safety concerns or risks, the on-site study clinician may need to involve the caregiver to plan for youth safety. In these cases, the on-site study clinician should inform the youth that the on-site study clinician will be speaking with the caregiver to plan for safety. Additional training will be provided to on-site study clinicians, should they need/request it.

It is the site staff's responsibility to share their awareness of safety concerns with the site IoR, local supervisor, and on-site study clinician so that together the study site staff can make the best decisions on how to assist the youth participant responsibly, attempting to ensure participant's current safety. Study site staff, including but not limited to IYL and adult study staff, will be trained to identify and respond appropriately to youth participants who report safety concerns and will be encouraged to communicate with the IoR, local supervisor, and/or on-site study clinician for guidance as needed. Refer to Sections 6.1.1, 6.1.2, and 6.1.3 of this MOP for guidance on managing participant self-administered electronic questionnaire safety email alerts, social harms and suicidal ideations/attempts, respectively.

Participants (or their parent/guardian/caregiver) may discuss sign(s) or symptom(s) experienced by the youth participant(s) suggesting a safety concern to study site staff, including but not limited to:

- Youth expresses safety concern for self or others, or caregiver expresses safety concern for youth, during group sessions or follow-up visits.
- Youth expresses safety concern for self or others, or caregiver expresses safety concern for youth, by phone.
- Youth response to a pre-specified electronic questionnaire item is flagged for safety concern and a safety email alert is sent to designated site staff.

If a participant reports or exhibits a safety concern, the following steps will occur to ensure participant safety:

1. Upon site staff awareness of a safety concern, the site staff will immediately contact the on-site study clinician and share any safety concern(s) received.
2. The on-site study clinician will further evaluate the participant before the participant leaves the clinic/site to provide appropriate care, treatment, and support that is consistent with their study-specific roles and responsibilities, and according to standard of care. Refer to Appendix II of this MOP for example questions to ask youth participants during an evaluation to help determine imminent risk.
3. The on-site study clinician will notify the site IoR or designee of information collected and will follow local policies for management of such situations including engaging immediate/first responders as applicable.
4. The on-site study clinician and IoR or designee will also follow local reporting policies and legal statutes, including reporting to child protection or other appropriate agencies, as well as arranging referrals to appropriate support, counseling or treatment resources.

After the safety of the participant is ensured according to the steps above, the IoR or designee will notify the IMPAACT 2016 CMC per Figure 3-2 and source document the event, as applicable per protocol Sections 7 and 8. All reported safety concerns/social harms will be source documented and will be managed consistent with the guidance provided in protocol Section 8. Follow-up contacts will also be conducted as needed to document resolution of reported signs and symptoms.

To facilitate rapid communications, the on-site study clinician and local supervisor should be on-site during study visit evaluations and group sessions as well as provide up-to-date contact information to the protocol site staff.

6.1.1 Self-Administered Electronic Questionnaires: Safety Concerns

The electronic questionnaires include questions surrounding feelings, behaviors, or situations that could be upsetting to youth. Some questions are about feelings of sadness and/or depression, symptoms of anxiety, and traumatic experiences and violence. Some questions are about risky behaviors, such as drinking too much alcohol, using drugs, and sexual activities. As described in the protocol, the purpose of the questionnaires is to evaluate how TI-CBT may decrease mental health symptoms. **There is a wealth of research that shows that asking youth these types of questions does not increase the likelihood or risk of self-harm or harm to others**. However, sometimes youth reveal concerning symptoms or signs of distress during psychosocial or mental health evaluations when directly asked.

Safety concerns could arise from a participant's response to one or more question(s) in the questionnaires, if the participant's answer(s) suggest a risk for suicide, recent suicidal ideation, any past suicide attempt, or other safety concerns (e.g., youth reports risk of harming themselves or others, or physical and/or sexual abuse). It is important that the on-site study clinician is available for immediate consultation and referral/intervention if recent suicidal ideation is considered or an

attempt is reported by participants, refer to Section 6.1.2 of this MOP for additional guidance on social harms.

Any response suggesting a safety concern or risk will generate a safety email alert, which will be sent in real-time to a site email group with designated study site staff (limited to the site IoR, study and/or nurse coordinator, and local supervisor who may also be serving as the on-site study clinician and/or IoR). If a participant completes a paper questionnaire, site staff will need to expeditiously key the data into the applicable paper version of the questionnaire eCRF in Medidata Rave to receive the email alert. **Study site staff (if not the on-site study clinician) in receipt of safety email alerts must notify the on-site study clinician(s) of every safety alert immediately upon receipt.** As outlined in Figure 3-1, sites should email the Protocol Data Managers the name(s), email(s), and title(s) (e.g., IoR and local supervisor) of designated site staff to receive the email alerts.

The on-site study clinician and/or counselor will follow the guidelines in Section 6.1 of this MOP, starting with further evaluating the participant before the participant leaves the clinic/site to ensure immediate safety and to provide appropriate care, treatment, and support consistent with their study-specific roles and responsibilities, and according to standard of care.

As a condition for site activation, each site is required to create a study-specific SOP or addendum for Safety Monitoring and Adverse Event Reporting requirements. This document should include, as described in protocol Section 8.1, the following elements:

- Emergency response guidance,
- Describe procedures to evaluate imminent risk and next steps,
- Specific referral information and lines of communication (e.g., inpatient hospital contact detail, other standard of care resources), and
- Roles, and responsibilities for site staff to respond to participants in crisis.

6.1.2 Social Harms

Refer to protocol Section 6.6 and guidelines in Section 6.1 of this MOP for details on procedures and steps for responding to potential youth social harms.

Upon site awareness of a social harm(s), defined as a non-medical adverse consequence(s) of their study participation (e.g., unintentional or unwanted disclosure of HIV-status to others, verbal bullying, physical bullying, and/or other social harm), designated study site staff and IYL should source document the social harm(s). Each social harm occurrence should be entered into the **LGW10018: IMPAACT 2016 Youth Social Harms Log eCRF.**

Per protocol Section 6.6 and in accordance with local standard of care and site SOPs, designated study site staff will make every effort to provide follow-up support and counseling to the participant as necessary, and/or refer participants to non-study resources.
In addition, the following steps should be taken:

1. Designated study site staff should provide appropriate follow-up with the participant as soon as possible to determine if there are changes in the social harm occurrence and impact on the participant; changes in the social harm occurrence should be source documented and a new social harm(s) should be entered into the **LGW10018 eCRF**.

2. Per protocol Section 6.6, while maintaining participant confidentiality, study sites may engage their CAB members in exploring the social context surrounding instances of social harms, to minimize occurrence and identify appropriate follow-up actions to be taken.
3. It is suggested that sites develop SOPs to minimize and prevent a social harm from re-occurring.

Sites may consult with the IMPAACT 2016 CMC as needed.

6.1.3 Suicidal Ideation/Attempts

Grade 2 or higher suicidal ideation should be entered into the **ADE10006: Adverse Events Log eCRF**; refer to protocol Section 6.7 and guidelines in Section 6.1 of this MOP for details on responding to and documenting new suicidal ideation events expressed in youth participants at visits following enrollment.

Immediate on-site evaluation

In the event that a participant (youth or caregiver) reports a youth's recent or current suicidal ideation or any prior suicide attempts, the on-site study clinician should evaluate the youth immediately following the group session and/or study visit procedures, depending on when the disclosure occurs, as outlined in step 2 in Section 6.1 of this MOP. The group session and/or study visit procedures should be completed prior to further evaluation. If the disclosure is made during a group session, group leaders will be trained to respond to such disclosures. For example, group leaders will let the participant know they are concerned about the disclosure and will follow up with the participant at the end of the session.

Each site should have a standard procedure to evaluate if a participant is at imminent risk, per protocol Section 6.7.

One approach is provided in Appendix II of this MOP in which the on-site study clinician determines the recency of the ideation/attempt, if there is a plan to carry it out, and whether the participant has the means to carry out the plan. Special training will be provided to on-site study clinicians to conduct these evaluations. If a participant is determined to be at imminent risk, the on-site study clinician should follow the standard of care at the site. This may include hospitalization and/or contacting authorities.

6.2 Expedited Adverse Event Reporting

Per protocol Section 7.3.2, **serious adverse events assessed as related to study participation** must be reported as expedited adverse events (EAEs) for this study. Consistent with the DAIDS EAE Manual, a serious adverse event is an untoward medical occurrence that result in psychiatric adverse events (e.g., insomnia, psychiatric disorders [including anxiety, depression, mania, and psychosis] and suicidal ideation or attempt) occurring among youth participants.

Serious adverse events are not expected to occur commonly in this study; nonetheless, each adverse event that does occur must be assessed by the IoR or designee for seriousness (per the definition shown above) as well as relationship to study participation (per the definitions provided in protocol Section 8), with the outcome of these assessments documented in the participant's study chart. The severity of each event should also be similarly assessed (per the DAIDS AE Grading Table) and documented. Site IoRs are encouraged to contact the Protocol Team with any questions or concerns related to assessing seriousness and/or reporting events as EAEs.

For each participant, the EAE reporting period begins at enrollment and ends 30 days after the last study procedure is performed.

Events meeting EAE reporting criteria should be reported using the DAIDS Adverse Experience Reporting System (DAERS) following procedures specified in Version 2.0 of the DAIDS EAE Manual and other associated instructional and operational resources, which are available at:

http://rsc.tech-res.com/clinical-research-sites/safety-reporting/manual

DAERS incorporates a report printing function that should be used to print all EAE reports—including modifications and updates—for filling in participant study records. Automated email messages confirming submission of EAE reports also should be printed and filed with the print-out of the associated EAE report.

Note: Per protocol Section 7.2, safety-related data collection for this study will be limited to psychiatric adverse events and/or social harms, and any such conditions meeting the definition of an adverse event will be entered into the **ADE10006: Adverse Events Log eCRF**. Any event reported as an EAE through DAERS must also be entered into an Adverse Event Log eCRF.

7.0 Laboratory Considerations

Protocol Section 6, the Schedule of Evaluations (SoE) and Laboratory Processing Chart (LPC) are the primary sources of information on specimen collection, processing, testing, storage, and shipping for this study; both clinic and laboratory staff should routinely refer to these documents for further operational guidance as needed.

The remainder of this section provides detailed operational instructions for youth blood and hair collection. FAQs and other operational guidance will be added to this section as needs for such guidance are identified.

7.1 Blood Collection

Refer to the listing of On-Study Procedures in protocol Section 6 and additional guidance for blood collection in protocol Section 6.8.1.

Refer to the LPC for detailed blood collection, processing, testing, storage, and shipping instructions.

7.2 Hair Collection

Approximately 50-60 strands of hair will be collected from enrolled study youth participants. Hair should be collected from the head (scalp) only, and not from other anatomical locations; hair collection is not required from youth participants who are bald. A sample of 50-60 strands is about the same diameter as a standard pencil eraser or drinking straw.

Hair samples should be collected consistent with the “hair collection protocol” shown in this section. Following collection, hair samples should be logged into the LDMS, and the zipper bags should be labeled with LDMS-generated labels. Hair samples should be kept at room temperature and in a dark place at each site until a request is received to ship the samples for testing.

Hair Collection Protocol

Materials Required

- Piece of aluminum/tin foil
- Desiccant packets
- Scissors/Razors/Hair clips
- Zipper bags
- Alcohol swabs/pads
- 2 – Patient labels
- Hair Sample Collection Report Form for relevant study (IMPAACT 2016 Pharmacokinetics Specimen Collection-Single [PKW10063])

Suggest making these "hair kits" ahead of time.

Step 1

Before each sample is taken, clean the blades of a pair of scissors with an alcohol pad and allow blades to completely dry.

Clean off the blades of scissors between patients.

Step 2

Lift up the top layer of hair from the occipital region of the scalp. Isolate a small thatch of hair (~50-60 fibers of hair) from underneath this top layer.

If helpful, a hair clip can be used to keep the top layer of hair away.

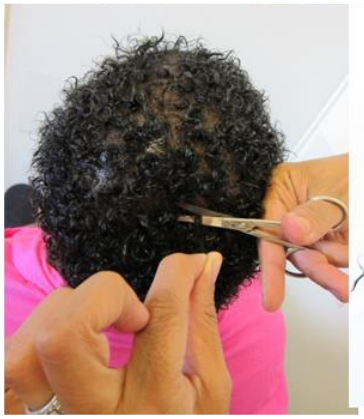
Step 3

Cut the small hair sample as close to the scalp as possible.

STRAIGHT HAIR

CURLY HAIR

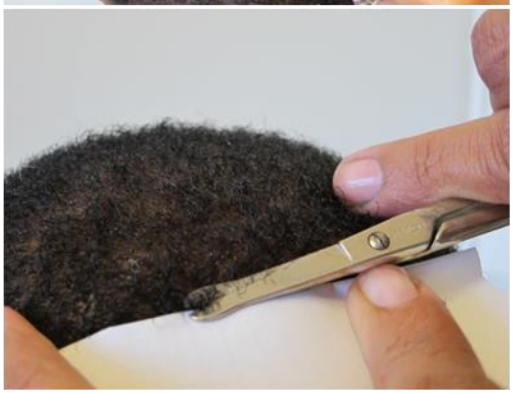




SHORT HAIR

Can let hair fall directly into piece of tin foil when very short/cropped (no need to label end since it is very short)



BRAIDED HAIR

Cut hair thatch from in-between braids or dread locks

Step 4

Keep your fingers on the part of the hair that is FURTHEST away from the scalp and put the hair sample down on an unfolded piece of tin foil.

Cut hair thatch from in-between braids or dread locks

Step 5

Put a thin label over the end of the hair sample that was FURTHEST away from the scalp.

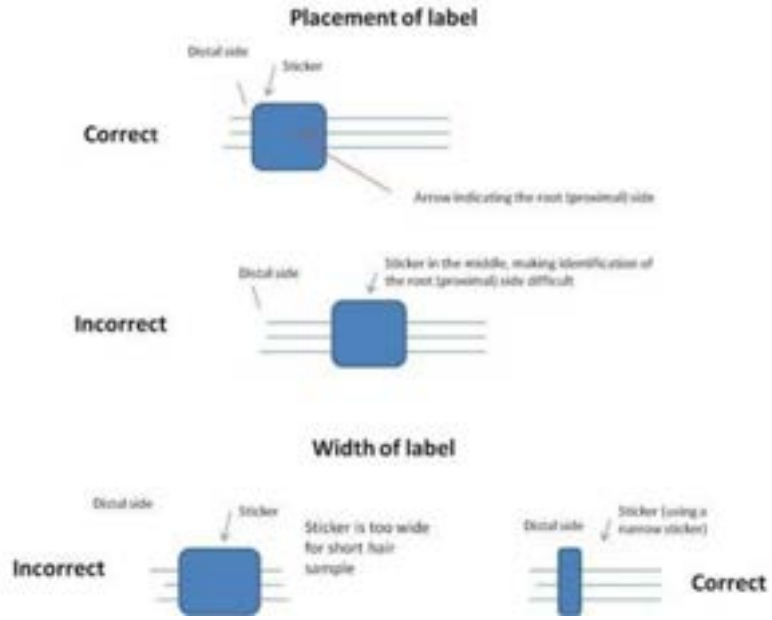
If hair is very short just let it fall into the piece of tin foil and no need to label the distal end.

Step 6
Refold the foil over to completely enclose the hair and place a study ID label on the folded piece of foil. 
Step 7
Place the folded piece of foil inside the plastic zipper bag with the desiccant packet inside and seal the bag. 
Step 8
Complete/enter IMPAACT 2016 Pharmacokinetics Specimen Collection (PKW10063)
Storage of Hair
Hair samples should be logged into the LDMS and the zipper bags should be labeled with LDMS-generated labels. Hair samples should be kept at room temperature and in a dark place at each site until a request is received to ship the samples for testing.

Correct methods for hair labeling

The collector should ensure that the label is not placed centrally on the piece of hair, but distally to allow the laboratory to distinguish between the root (proximal, closest to the scalp, where the hair is cut) and distal (farthest from the scalp) end. The sticker should be narrow enough when placed on a short section of hair to be able to distinguish the two ends.

Drawing an arrow to the root end via marker on the piece of tin foil can help distinguish the two sides if there is any confusion.



Good collection: Distal end (side farthest from scalp) labeled

Bad collection: Distal end should have been labeled (long enough) but not

Okay not to label because too short

8.0 Data Management Considerations

Refer to protocol Section 10. Further information on data collection expectations is available in the eCRF completion guide developed by the DMC for this study, which is available on the DMC portal. eLearning modules and other operational guidance on use of Medidata Rave are also available on the DMC portal.

Appendix I: Session-specific supplies for TI-CBT Intervention Group Sessions

(Notes: All sites are to acquire the supplies in the tables below for use in both the Pilot Test and Randomized Trial. Some supplies can be reused in subsequent group sessions. Focus Group host sites which previously acquired specific supplies for the identified session(s) delivered in the Focus Groups do not need to re-acquire such supplies unless there are insufficient quantities.)

Youth Group Sessions ***(IYL should bring their Youth Intervention Manual to all youth group sessions)***			
Session Part	**Supply Item** ***(handouts, worksheets, diagrams, certificate template located in the Youth Intervention Handout file)***	**Quantity**	**Check box if on site for session**
Session 1 Supplies (review Session 1 Supplies Checklist in Youth Intervention Manual)			
A – Ice breaker	Beach or soccer ball with written questions on the ball	1	
B – Group Rules (pre-written by IYL)	Write Group Rules on flip chart (confidentiality, attention, respect, acceptance, attendance, silence cell phones) and Display on wall or flip chart	1	
D – Introduce Stress	Flip chart, markers	Minimum 1 of each item	
D – HIV Knowledge	HIV Knowledge Handout (print copies)	1 per youth, 1 poster size	
D – Introduce Stress	Stress Reaction Cycle Handout (print copies) and Display poster size on wall or flip chart	1 per youth, 1 poster size	
F – Body Awareness	Body size paper (large enough to draw an outline of each youth's body)	1 per youth	
G –Mark Sensations and Feelings	Box of assorted colored markers for youth to share	Multiple boxes at site discretion	
Session 2 Supplies (review Session 2 Supplies Checklist in Youth Intervention Manual)			
A – Group Rules	Display pre-written Group Rules on wall or flip chart	1 from previous session	
C – Review Stress	Stress Reaction Cycle Handout (print copies) and Display poster size on wall or flip chart	1 per youth, 1 poster size from previous session	
D – Small groups for Stressors and Responses	Group Worksheet: Stress Response (print copies)	2 (1 per small group)	
E – Stressors and Responses, H – Health Response	Flip chart, markers	Minimum 1 of each item	
I – Assignment	Assignment: Stress and Happiness Worksheet (print copies)	1 per youth	

Session 3 Supplies (review Session 3 Supplies Checklist in Youth Intervention Manual)			
A – Group Rules	Display pre-written Group Rules on wall or flip chart	1 from previous session	
B – Review Session 2 assignment, D – Stressful/ Pleasant Events	Flipchart, markers	Minimum 1 of each item	
C – Thoughts-Feelings-Behaviors (T-F-B)	Thoughts-Feelings-Behaviors Cognitive Triangle Handout (print copies)	1 per youth, 1 poster size	
E – Small groups for T-F-B	Plain white piece of paper and markers	1 set per youth	
I – Assignment	Assignment: Thoughts-Feelings-Behaviors (T-F-B) Blank Cognitive Triangle Worksheet (print copies)	1 per youth	
Session 4 Supplies (review Session 4 Supplies Checklist in Youth Intervention Manual)			
A – Group Rules	Display pre-written Group Rules on wall or flip chart	1 from previous session	
C and D – Small groups for Gender Roles/Expectations	Flip chart paper and markers	2 sets per small group	
F – Family and Community Roles	Basket	1	
F – Family and Community Roles	Small pieces of paper (write each of the following roles on a piece of paper - parent, aunt, uncle grandparent, teacher, church leader, community authority, male friend, female friend, neighbor, female elder, male elder, doctor, nurse, counselor)	15 (At site discretion if more roles)	
G – Large Group Discussion	Local statistics on Gender-Based Violence (identify and prepare current local Gender-Based Violence statistics to share during the session)	Verbalize or print handout	
G – Large Group Discussion	Flip chart with markers	1	
H – Assignment	Assignment: Gender-based Messages Worksheet (print copies)	1 per youth	
Session 5 Supplies (review Session 5 Supplies Checklist in Youth Intervention Manual)			
A – Group Rules	Display pre-written Group Rules on wall or flip chart	1 from previous session	
C – Interpersonal Interactions	Plain white piece of paper and pens or markers	2 sets	
D – Role Play for Interactions	T-F-B Cognitive Triangle Diagram Handout (use copy from Session 3)	1	
D – Role Play for Interactions	Flipchart with markers	1	
E – Small Group Safe Sex Demonstration	External (male) and Internal (female) Condoms	1 per youth	
E – Small Group Safe Sex Demonstration	Plain white piece of paper and pens or markers	1 set per small group	
H – Assignment	Assignment: Thoughts-Feelings-Behaviors T-F-B Unhealthy Interactions Worksheet (print copies)	3 per youth	

Session 6 Supplies (review Session 6 Supplies Checklist in Youth Intervention Manual)			
A – Group Rules	Display pre-written Group Rules on wall or flip chart	1 from previous session	
B – Review Homework, C/G – Small Groups, H – T-F-B	Flip chart sheet with markers	1 set per small group	
B – Review Assignment	T-F-B Unhealthy Interactions Worksheet (print copies)	1 per youth	
C – Small Groups for lessons learned	Flip chart paper and pens or markers	1 set per small group	
F – Body Drawings	Box of assorted colored markers for youth to share	Multiple boxes at site discretion	
F – Body Drawings	Body maps from Session 1	1 per youth	
G – Small Groups for Reflecting on Sessions	T-F-B Cognitive Triangle Diagram Poster (use copy from Session 3)	1	
Celebration	Certificates (print personalized copy with youth name)	1 per youth	
Celebration	Supplies per site discretion		
Booster Session Supplies (review Booster Session Supplies Checklist in Youth Intervention Manual)			
A – Welcome	Display pre-written Group Rules on wall or flip chart	1 from previous session	
B – Deep Breathing, E – Capacitor	Music	2	
C – TFB, D – Gender-Violence	Flipchart (with markers)	1	
C – TFB	Vignette #1: Claude's vignette (print copies)	1 per youth	
C – TFB	Vignette #2: Claudette's vignette (print copies)	1 per youth	
D – Gender-Violence	Definition of Sex and Gender Handout (print copy)	1	
D – Gender-Violence	T-F-B that Promotes Gender Equality Worksheet (print copies)	1 per youth	
D – Gender-Violence	T-F-B Cognitive Triangle Diagram Handout (use copy from Session 3)	1	

Caregiver Group Sessions ***(Adult study staff should bring their Caregiver Intervention Manual to all caregiver group sessions.)***			
Session Part	**Supply Item** ***(handouts, worksheets, diagrams, certificate template located in the Caregiver Intervention Handout file)***	**Quantity**	**Check box if on site for session**
Session 1 Supplies (review Session 1 Supplies Checklist in Caregiver Intervention Manual)			
B – Group Rules	Write Group Rules on flip chart (confidentiality, attention, respect, attendance, silence cell phones) and Display on wall or flip chart	1	
B – Group Rules, C – HIV Knowledge, D – Stigma, E – Adherence Obstacles	Flip chart, markers, tape, and scissors	Minimum 1 of each item	
C – HIV Knowledge	HIV Knowledge Handout (print copies)	1 per caregiver, 1 poster size	
C – HIV Knowledge, D – Stigma, E – Adherence Obstacles	Plain white piece of paper (or notepad) and pens or markers	1 set per small group	
E – Adherence Obstacles	Adherence Care and Treatment Meaning Handout (print copies) and Display poster size on wall or flip chart	1 per caregiver, 1 poster size	
G – Assignment	Assignment: Adherence Support Worksheet (print copies)	1 per caregiver	
Session B Supplies (review Session 2 Supplies Checklist in Caregiver Intervention Manual)			
A – Group Rules	Display pre-written Group Rules on wall or flip chart	1 from previous session	
D – Adherence Importance	Adherence Care and Treatment Meaning Handout (print copies), and Display poster size on wall or flip chart	1 per caregiver, 1 poster size	
D – Adherence Importance	Flipchart, markers	Minimum 1 of each item	
E – Role Plays	Adherence Plan Handout (print copies), and Display poster size on wall or flip chart	1 per caregiver, 1 poster size	
F – Celebration	Certificates (print personalized copy with caregiver name)	1 per caregiver	
F – Celebration	Supplies per site discretion		
Booster Session Supplies (review Booster Session Supplies Checklist in Caregiver Intervention Manual)			
B – HIV Knowledge	Display pre-written Group Rules on wall or flip chart	1 from previous session	
C – HIV Knowledge, E – Adherence Obstacles, F – Stigma	Flipchart, markers	Minimum 1 of each item	
D – Adherence Importance	Adherence Meaning Handout (print copies), and Display poster size	1 per caregiver, 1 poster size	
G – Adherence Plan	Adherence Plan Handout (print copies), and Display poster size	1 per caregiver, 1 poster size	

Appendix II: Evaluating participants for imminent risk of suicide and abuse

A. Example questions for evaluating youth participants for imminent risk of suicide

The following questions may be used by the on-site study clinician when evaluating a youth participant who discloses suicidal ideation or attempt: plan to hurt or kill self, attempt to hurt or kill self, or cutting.

On-site study clinician should remind the youth of the following: "At the beginning of this study you signed a consent (or assent) form indicating that your responses to questionnaires and study participation will be kept confidential except in cases where you may be at risk of harm. The questionnaire you took today (or during the group session/follow-up visit, you/your caregiver/your peer) suggested you have had thoughts of ending your life or hurting yourself. I am worried about your safety, and I would like to ask you some questions about it. If you remember, I am required to report any situations in which you may be in danger. I know that this might be difficult for you. I would appreciate your honesty in helping me understand what you are feeling or thinking or what has happened to you."

1. I know this might be uncomfortable for you, but can you tell me a little more about these thoughts?

2. Are you currently having thoughts of hurting yourself? (**If yes → Imminent risk**)
   On-site study clinician: currently means having thoughts right now

3. Do you have a plan for hurting yourself? (**If yes → Imminent risk**)

IF YES TO #3, GO TO QUESTION 4. If NO TO #3, GO TO QUESTION 5.

4. Can you tell me more about what you were thinking of doing to hurt yourself?

   a. Do you have these things (insert: gun, knife, pills, etc.) you would need to do it? (e.g., If participant says they would use a gun, does she have access to a gun, etc.) (**If yes → Imminent risk**)

5. Have you tried to hurt yourself before?

   a. If yes, would you feel comfortable sharing what happened with me?
   On-site study clinician: note the incident if youth is comfortable sharing with you

6. Does anyone know that you've been having these thoughts? If so, who?

7. Do you currently have a therapist? If yes, does your therapist know?

8. Have you ever been hospitalized for trying to hurt yourself?

9. How upset are you now that we've talked about this?

10. Do you feel like you can stay safe tonight? (**If no → Imminent risk**)

Following the evaluation, the on-site study clinician will notify the site IoR or designee of information collected, per Step 2 in Section 6.1 of this MOP, and complete the remaining steps. As described in Section 6.1.3 of this MOP, if a participant is determined to be at imminent risk, the on-site study clinician should follow the standard of care at the site.

B. Example questions for evaluating youth participants for imminent risk of abuse

The following questions may be used by the on-site study clinician when evaluating a youth participant who discloses abuse: sexual or physical.

<u>On-site clinician should remind the youth of the following</u>: "At the beginning of this study you signed a consent (or assent) form indicating that your responses to questionnaires and study participation will be kept confidential except in cases where you may be at harm. The questionnaire you took today (or during the group session/follow-up visit, you/your caregiver/your peer) suggested we should discuss some of your experiences further to better understand. I am worried about your safety, and I would like to ask you some questions about it. If you remember, I am required to report any situations in which you may be in danger.

I know that this might be difficult for you. I would appreciate your honesty in helping me understand what you are feeling or thinking or what has happened to you. I'm not sure which items were true for you, but these might be things like: (a) Someone tried to make you do sexual things, (b) Someone tried to touch you, (c) You felt forced to have sex, (d) An older person had sex with you, or (e) Someone tried to physically hurt you such as hit you."

1. I know this might be uncomfortable for you, but can you tell me more about what happened?
2. When did this happen?
3. Where did this happen?
4. How old were you when it happened?
5. What is/was this person's relationship to you?
   (On-site study clinician: If the perpetrator is in a position of authority or guardianship, immediate action should be taken per local standard of care.)
6. How old is (was) he/she?)
7. Do you live with this person or do you see them on a regular basis? (**If yes → Imminent risk**)
8. When was the last time you saw this person?
9. How much time does this person spend around you now?
10. Is it still going on right now? (**If yes → Imminent risk**)
11. Does anyone know about this? If so, who?
12. Do you currently have a therapist? If yes, does your therapist know?
13. Are Department of Child and Family Services (DCFS) or the police currently involved?
14. Is there another incident that you experienced? **If no, skip to question 15. If yes, repeat questions above.**

May ask these questions for ALL SITUATIONS even if no abuse occurred

15. Do you feel safe? **(If no → Imminent risk)**
    (On-site study clinician: If no, PROBE further: "Why don't you feel safe?" "Do you think you can stay safe tonight?" etc.)

16. Do you think this person might hurt you again now or in the future? **(If yes → Imminent risk)**

17. How upset are you now that we have talked about this?

18. **[If very upset]** Do you think you might hurt yourself? **(If yes → Imminent risk**)

    a. [If yes] Do you have a plan?

    b. [If yes] Have you tried to hurt yourself in the past?

Following the evaluation, the on-site study clinician will notify the site IoR or designee of information collected per Step 2 in Section 6.1 of this MOP, and complete the remaining steps.

Appendix III: Standard of Care Resources

The African Network for the Care of Children Affected by AIDS (ANECCA)

The African Network for the Care of Children Affected by AIDS (ANECCA) with support from AIDS Free developed and published the *Handbook on Counselling and Psychosocial Care for Children and Adolescents Living with and Affected by HIV in Africa* and a *Pocket Guide*, a condensed version of handbook designed for on-the-job use. Sites are encouraged to use this handbook and pocket guide for standard of care information on HIV clinical care; growth and development; mental health; child protection; counseling and communication; disclosure; loss, grief, and bereavement; adherence; sexual and reproductive health; transition of care; support systems; and monitoring and evaluation of psychosocial services.

A PDF of the Handbook is available at:

https://anecca.org/wp-content/uploads/2019/02/ANECCA-Handbook-on-PSS.pdf

A PDF of the Pocket Guide is available at:

https://anecca.org/wp-content/uploads/2018/11/Anecca-Pocket-Guide-2018.pdf