

Social-Behavioral Sciences (SBS) in IMPAACT

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26 January 2022

WHAT IS SBS?

- Behavioral and social sciences research at the NIH involves the systematic study of **behavioral**¹ and **social**² phenomena relevant to **health**³.
- ¹**“Behavioral phenomena”** refers to the observable actions of individuals or groups and to mental phenomena such as knowledge, attitudes, beliefs, motivations, perceptions, cognitions, and emotions.
- ²**“Social phenomena”** refers to the interactions between and among individuals, and to the characteristics, structures, and functions of social groups and institutions, such as families, communities, schools, and workplaces, as well as the physical, economic, cultural, and policy environments in which social and behavioral phenomena occur.
- ³**“Health”** refers to state of complete physical, mental, and social well-being and not merely the absence of disease or infirmity (as per [WHO](#)).
- SBS can involve a variety of quantitative and/or qualitative methods.

WHAT DO WE USE SBS FOR?

- SBS is a tool for answering key, policy-driving questions.
- Failing to answer these questions as part of efficacy/effectiveness evaluations risks
 - Delays in policy and practice translation
 - Producing effective interventions that no one can or wants to use, thus wasting huge investments of resources and time
- Including SBS in evaluation design (from conception) and nesting targeted SBS components in trials enables addressing the scientific and policy questions most efficiently, comprehensively and for the smallest additional investment.
- SBS components are tools to be used judiciously toward answering the key questions, we are *not* suggesting SBS as separate or additional.
- Applications of participant preferences and other patient reported outcomes can be part of licensing and FDA review.

POLICY/PRACTICE QUESTIONS THAT SBS CAN ANSWER:

Question	Construct
How will we implement this in local setting X?	Formative research
How will we measure and support intervention use?	Adherence
Will end users take up this intervention?	Acceptability
What are end-user priorities to inform intervention development?	Preferences
What is the likely impact in other settings or populations?	Modelling
How can it best be adapted for use in other settings or populations?	Transferability
How much will it cost?	Costing
How science can be explained to end-users?	Communication
Will this intervention be implemented by providers?	Feasibility/scalability
What difference will it make for the people locally?	Local social value

Using SBS to enhance lessons from clinical research

EXAMPLE 1: NESTED SBS INFORMING GUIDELINES

- The SHINE Trial evaluated the non-inferiority of a 4-month treatment regimen for children with non-severe TB at 5 sites in 4 countries.
- Two nested 'acceptability' evaluations:
 - A single-site qualitative evaluation during the lead-in study about the fixed dose combination study drug.
 - Standardized quantitative repeat measures case report forms (CRFs) for all study participants at all sites administered by clinical staff.
- Costs:
 - ~USD 15,000 for qualitative data collection/processing staff.
 - CRF development and training of clinical staff.
 - Engaging a social-behavioral scientist to lead the analysis.

EXAMPLE 1: NESTED SBS INFORMING GUIDELINES

- WHO Guideline Development Group (2021):
 - "The 4-month treatment regimen was non-inferior to the 6-month regimen for children treated for non-severe, smear-negative TB, presumed to be drug susceptible. Non-inferiority was consistent across all key analyses (including age groups, HIV status, type of TB and adherence)."
- But also, a shorter 4-month regimen:
 - Has local social value.
 - Is acceptable to end users.

Rapid communication on
updated guidance on the
management of tuberculosis in
children and adolescents



EXAMPLE 1: NESTED SBS INFORMING GUIDELINES

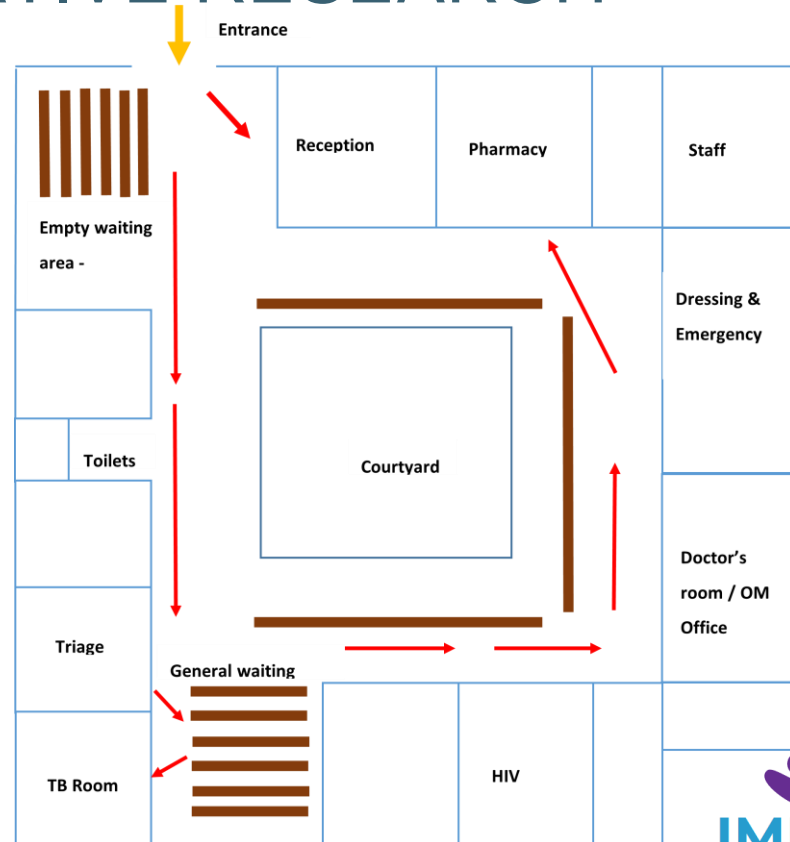
- Summary:
 - Appropriate choice of SBS tools.
 - Early engagement of socio-behavioral scientists.
 - Limited additional investment.
 - Able to address policy needs more directly.

EXAMPLE 2: FORMATIVE RESEARCH

- Formative research = a variety of methods / activities to inform project implementation.
- TB-CHAMP trial – Levofloxacin versus placebo for the prevention of TB disease in child contacts of MDR-TB: a phase III cluster randomised controlled trial (multiple sites in 1 country).
- TB-CHAMP formative research:
 - ~4 in-depth interviews + 2 days of semi-structured observations per facility to then write a summary report
 - Time required: ~1 week per facility
 - Costs: 1x graduate RA + ~10% of a senior SBS + minor 'other' = ~USD 500 / facility

EXAMPLE 2: FORMATIVE RESEARCH

- E.g., from report:



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- E.g., from report:

"Perceptions about placebos

Given the high TB burden at the clinic, staff are open to research that may improve outcomes for clients, even if this involves placebos in the short-term."

- Informed:
 - Facility selection (high yield, ease of implementation).
 - Implementation processes, e.g., case identification pathways.
 - Identified local (facility / community) level gatekeepers / supporters.
 - Built trust and cooperation with local health services.
- Broad Brush Surveys 'BBS': <https://doi.org/10.1177/1049732318809940>.



EXAMPLE 3: ACCEPTABILITY

- Acceptability = do 'end users' (children, caregivers, providers) like the intervention / innovation, and therefore, will future users take it up?
- Very easy to nest a short quantitative CRF for administration by clinical team.
- Examples:
 - TBTC Study 35 (3HP PK amongst children)
 - IMPAACT Study 2024 (1HP PK amongst children)
 - IMPAACT Study 2035 (TB Vaccine amongst adolescents)
 - IMPAACT Study 2020 (Shortened oral tx for MDR-TB)






2. In your assessment, how did the child appear to feel about the taste of the pills? (caregiver preferable or study personnel to answer)

1 Dislike very much 	2 Dislike 	3 Neutral 	4 Like 	5 Like very much 
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3. In your assessment, how did the child appear to feel about the number (amount) of pills in the dose? (caregiver preferable or study personnel to answer)

1 Way too many 	2 somewhat too many 	3 just a bit too many 	4 pretty much right amount 	5 Perfect amount 
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4. In your assessment, how did the child appear to feel about the size of the pills? (caregiver preferable or study personnel to answer)

1 Way too big 	2 somewhat too big 	3 just a bit too big 	4 pretty much right size 	5 Perfect size 
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5. Overall, how do you feel about the preparation of the doses? (caregiver to answer)

1 Very difficult 	2 Difficult 	3 Neutral 	4 Easy 	5 Very easy 
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6. Overall, how do you feel about the administration of the doses? (caregiver to answer)

1 Very difficult 	2 Difficult 	3 Neutral 	4 Easy 	5 Very easy 
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 - IMPAACT Study 2020 (Shortened oral tx for MDR-TB)
- Also, easy to do complementary qualitative data collection at a small number of purposively sampled sites (with capacity).

EXAMPLE 4: 'PATIENT' ATTITUDES – Explanations for patterns in uptake / effect

- Patient attitudes = Questionnaires, especially repeat measures.
- CATALYST – The Pharmacokinetics, Safety and *Acceptability* of New Child-Friendly Formulations of Clofazimine and Moxifloxacin in Children Routinely Treated for Rifampicin-Resistant TB.
- CATALYST child and caregiver attitudes:
 - Completion of a Case Report Form at weeks 0, 2, 8, 16, and 24.
 - Administered by the clinical team.
 - Time required: ~15 minutes additional per assessment.
 - Costs: Training for clinical staff to administer, time of a senior SBS to design the CRF and conduct analyses.

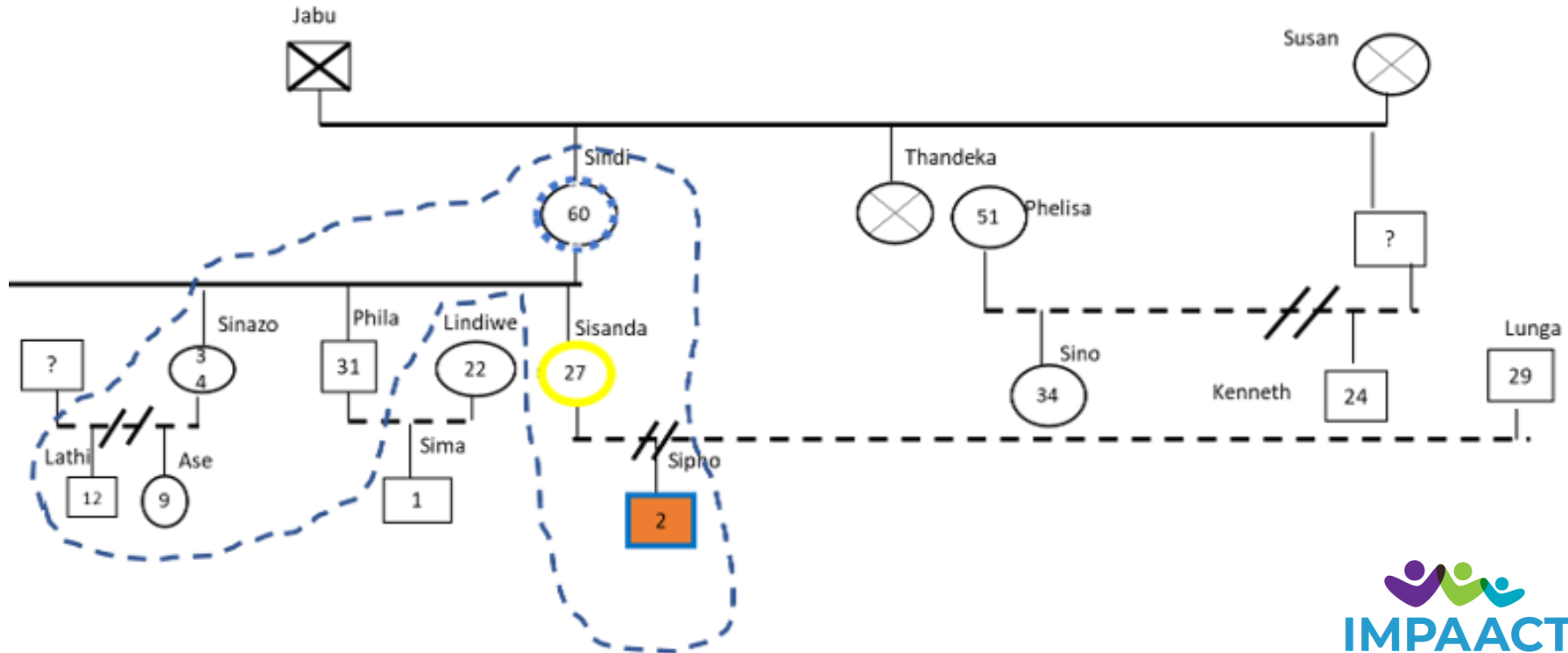
EXAMPLE 4: 'PATIENT' ATTITUDES – Explanations for patterns in uptake / effect

- Please indicate how strongly you agree/disagree with the following statements. For each statement, select either "Strongly agree", "Agree", "Neutral", "Disagree", or "Strongly Disagree":
 1. The size of the round brown tablet makes it easy for my child to swallow.
 2. My child likes the taste of the round brown tablet.
 3. I find it easy to administer the round brown tablet to my child.
 4. Administering the round brown tablet is easy.
 5. ...

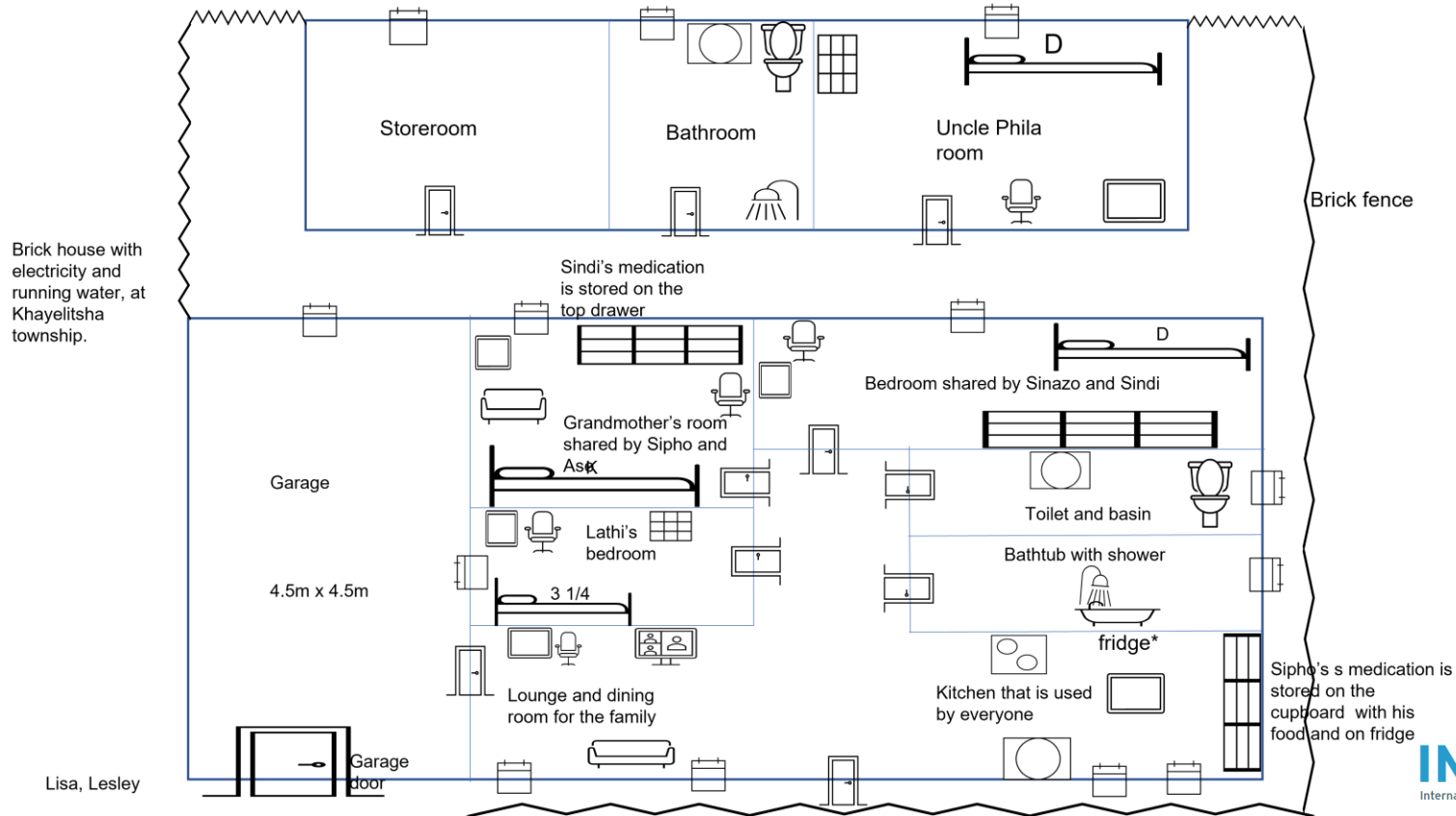
EXAMPLE 5: 'PATIENT' EXPERIENCES – Transferability, Local Social Value, Acceptability ...

- Patient = In-depth qualitative data, over time, participatory tools.
- CATALYST – The Pharmacokinetics, Safety and *Acceptability* of New Child-Friendly Formulations of Clofazimine and Moxifloxacin in Children Routinely Treated for Rifampicin-Resistant TB.
- CATALYST Child and Caregiver Experiences:
 - ~4 in-depth interviews per participant of ~90 minutes per participant.
 - Includes a variety of tools such as 'body mapping' to facilitate responses.
 - Must be conducted by a skilled SBS graduate.
 - Costs: 1x graduate RA + ~10% of a senior SBS + minor 'other'.

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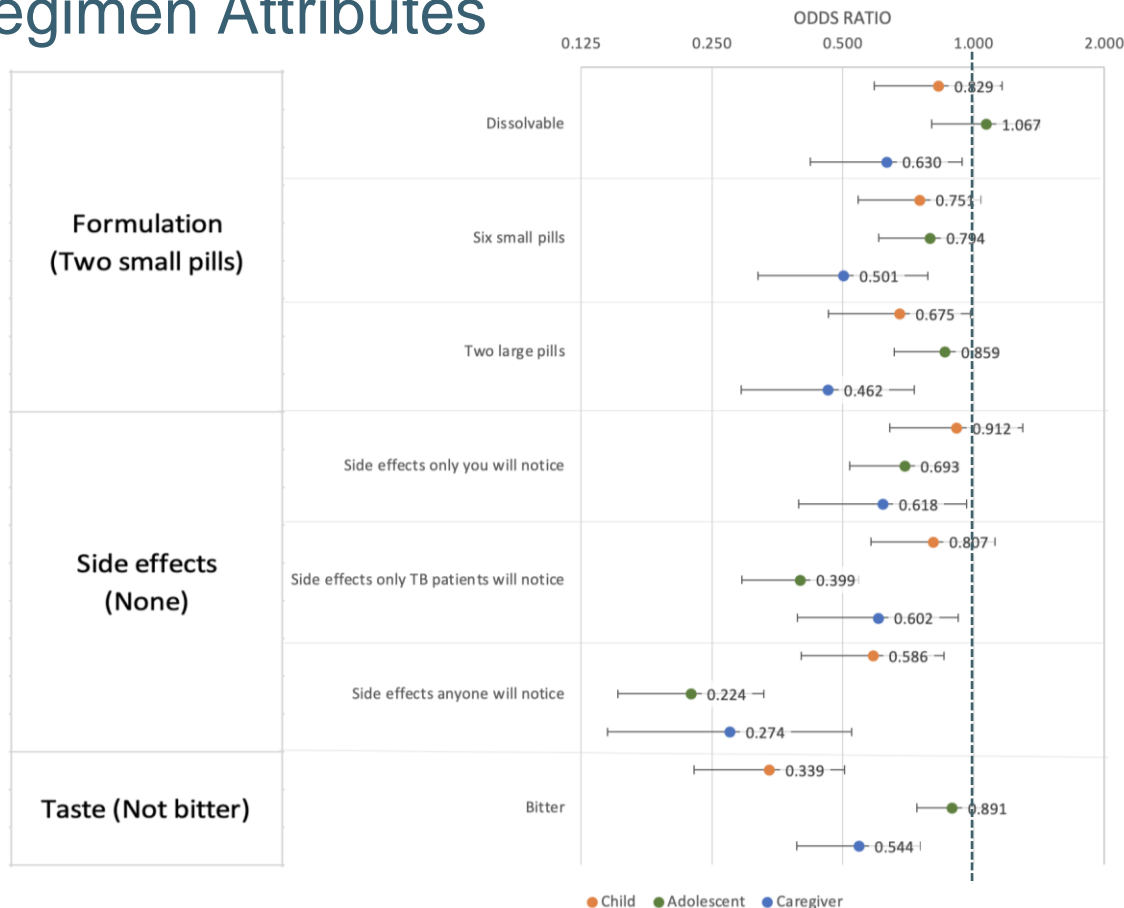


EXAMPLE 6: USER PREFERENCES

- User preferences = What are end-user priorities to inform intervention development?
- TPT preferences amongst children, adolescents and their caregivers – stand-alone study commissioned by the South African TB Think Tank.
- A Discrete Choice Experiment (DCE):
 - Quantitative behavioral economics method used to understand:
 - Relative importance of preferences of health services characteristics.
 - Trade-offs people make.
 - Total benefit and satisfaction derived from different combinations.
 - Participants make choices in a series of hypothetical scenarios.
 - Useful for formulating patient-centered policies, designing programs that maximize uptake, and predicting demand for healthcare services.

EXAMPLE 6: USER PREFERENCES

Drug Regimen Attributes



EXAMPLE 7:

A5300B/I2003B PHOENIx



- A5300B/I2003B: Phase III trial of delamanid vs isoniazid for prevention of MDR-TB among household contacts
 - 25 sites in 10 countries currently
 - 825 household contacts from 508 index cases
- Formative work
- Objective adherence monitoring
 - evriMED1000 device in all sites (except Wisepill device in Thailand)
 - Reminder alarms/SMS



(a)



(b)



(c)

ADHERENCE MONITORING IN PHOENIX

- Objective estimates of adherence
 - Drug use (day-to-day and persistence)
 - Assessment by individual and study site
- Impact on the trial
 - Enable better understanding of biological efficacy
 - Ability to identify sites and individuals with challenges and make improvements in near real-time
 - Approach accounts for 1) use of prevention medication and 2) household nature of the study
 - Facilitates tailored adherence support (e.g., study engagement vs individual or household challenges)
 - Relatively small budget and infrastructure

Phoenix Feasibility- Willingness to take MDR-TB preventive therapy
A semi-structured KAP questionnaire was adapted for MDR-TB from the WHO guide for tuberculosis KAP survey development

Key findings

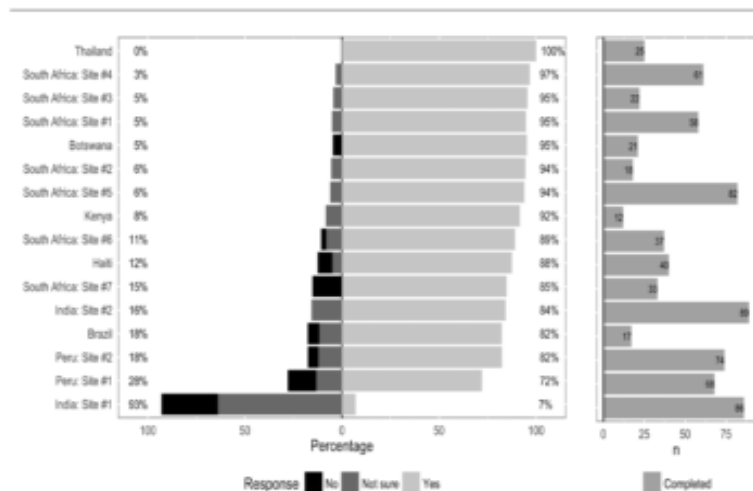


Figure 2. Willingness of multidrug-resistant tuberculosis (MDR-TB)/rifampicin-resistant tuberculosis (RR-TB) household contacts to take newly developed MDR-TB preventive therapy, stratified by clinical research site (left panel). Number of enrolled MDR-TB/RR-TB household contacts at each clinical research site (right panel).

- **Appropriate MDR-TB knowledge was demonstrated by 66% of enrolled HHCs,**
- **HHC willingness to take hypothetical, newly developed MDR TPT was high overall (79%).**
- The study also found that **appropriate TB-related knowledge, being comfortable speaking with family and friends about taking MDR TPT, and, most notably, confidence in properly taking TPT** were all associated with increased willingness to start treatment.
- Concerns about **Side effects of MDR-TPT** was found to be associated with **decreased willingness**
- **The study provides important evidence for the potential uptake of effective TPT when implemented.**

HOW CAN WE INTEGRATE SBS INTO CLINICAL TRIALS?

- When developing trials, consider what targeted questions (beyond effectiveness) could or should be answered by the trial and could be included as nested components.
 - E.g., Integrate objective adherence monitoring to optimize interpretation of efficacy findings and/or identify necessary supports.
- When developing interventions, consider how to get an early sense of relevant socio-behavioral factors that could impact later development and/or implementation.
 - E.g., Assess preferences, acceptability, and formative SBS during early phases of drug development.
- When developing protocols, consider how to communicate with participants.
 - E.g., Assess hesitancy to optimize enrollment and retention to increase trial efficiency.
 - E.g., Choose best approaches to guide decision making.

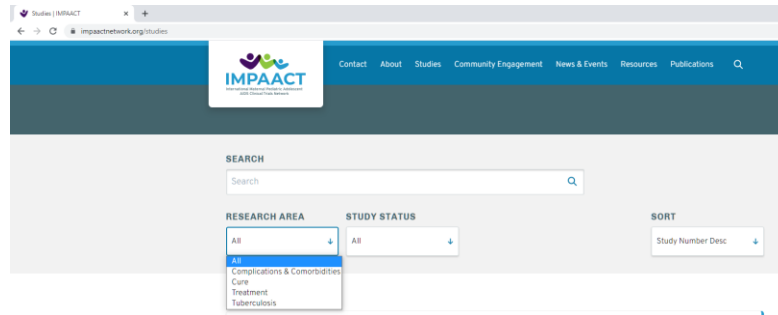
IMPAACT Resources

KNOWING YOUR IMPAACT RESOURCES

- What data is available?
 - Ancillary studies: DACS, DR, NWCS
 - IMPAACT Website -> Studies -> Submit a Research Proposal -> Scroll to: https://www.impaactnetwork.org/sites/default/files/inline-files/NWCS_DACS_DR_7June2021_Final.pdf
- Can think retrospectively (ancillary studies) or proactively (putting common measures across all new studies) or thinking about common SBS gaps.

KNOWING YOUR IMPAACT RESOURCES CONTINUED

- What studies is IMPAACT conducting?
 - IMPAACT studies can be found by going to the website: Studies -> IMPAACT Study Snapshots (<https://www.impaactnetwork.org/studies/impaact-study-snapshots>)



IMPAACT Protocols Snapshot: In Development through Closed to Follow Up

Protocol #	Title	Sites	Study Status	Research Area	Protocol to Sites (Projected)	Open to Accrual (Projected)	1st Participant Enrolled (Projected)	Closed to Accrual (Projected)	Closed to Follow Up (Projected)	Target Accrual	Actual Accrual as of report date
IMPAACT 2035/ HIVIN 604	A Phase III Clinical Trial to Evaluate the Safety and Immunogenicity of VPM1002 and BCG Re-Vaccination in HIV-Infected and HIV-Uninfected Pre-Adolescents	TBD	In Development	Tuberculosis	780	780	780	780	780	780	NA
IMPAACT 2034	An Open-Label, Single-Arm Study to Assess the Pharmacokinetics, Safety and Acceptability of Phosphamidon in Children with Multidrug-Resistant or Extensively Drug-Resistant Tuberculosis (MDR-TB or XDR-TB)	TBD	In Development	Tuberculosis	780	780	780	780	780	780	NA
IMPAACT 2029	Phase III Study of Switching to Fixed-Dose Combination Dolutegravir/Rilpivirine among Virologically Suppressed Children and Adolescents Living with HIV	US/INTL	In Development	Treatment	15-Apr-21	15-May-21	14-Jul-21	14-Jul-22	31-Dec-23	40	NA
IMPAACT 2025	Daily Versus Three Months of Weekly Isoniazid and Rifampin in HIV-Infected Pregnant and Postpartum Women	TBD	In Development	Tuberculosis	780	780	780	780	780	780	NA
IMPAACT 2024	Phase III Dose Finding and Safety Study of Daily Rifampin Combined with Isoniazid (RIF) for Tuberculosis Prevention in Infants, Children and Adolescents	TBD	In Development	Tuberculosis	780	780	780	780	780	780	NA
IMPAACT 2023	A Phase I Trial to Evaluate the Safety and Pharmacokinetics of Dolutegravir in Neonates Exposed to HIV-1 Infection	TBD	In Development	Treatment	31-Mar-21	14-Jul-21	13-Aug-21	13-Aug-23	14-Dec-23	72	NA
IMPAACT 2022	Phase II Study of the Efficacy and Feasibility of Long-Acting Injectable Antiretroviral Medications in Non-Adherent Youth with HIV	TBD	In Development	Treatment	780	780	780	780	780	70	NA
IMPAACT 2020	A Phase II Study of Shortened One Treatment for Multidrug-Resistant Tuberculosis in Children (SMART Kids)	INTL	In Development	Tuberculosis	780	780	780	780	780	168 children and 168 caregivers	NA
IMPAACT 2028	Long-Term Clinical, Immunologic, and Virologic Profiles of Children who Received Early Treatment for HIV Infection	US/INTL	Pending	Cure	31-Dec-20	31-Mar-21	31-Mar-21	30-Nov-26	30-Nov-27	250	NA
IMPAACT 2032	Pharmacokinetics and Safety of Remdesivir for Treatment of COVID-19 in Pregnant and Non-Pregnant Women in the United States	US	Pending	COVID-19	05-Aug-20	12-Feb-21	07-Mar-21	01-Sep-21	01-Sep-22	40	NA
IMPAACT 2026	Pharmacokinetic Properties of Antiretroviral and Anti-Tuberculosis Drugs during Pregnancy and Postpartum	US/INTL	Pending	Treatment	04-Feb-20	17-Mar-21	15-Mar-21	11-Mar-26	11-Mar-26	325	NA
IMPAACT 2016	Evaluating a Group-Based Intervention to Improve Mental Health and ART Adherence Among Youth Living with HIV in Low Resource Settings	INTL	Open to Accrual	Complications	08-Nov-18	27-Nov-19	780	780	780	256	0
IMPAACT 2019	Phase III Study of the Pharmacokinetics, Safety, and Tolerability of Abacavir/Dolutegravir/Lamivudine Dispersible and Immediate Release Tablets in HIV-1-Infected Children Less Than 12 Years of Age	US/INTL	Enrolling	Treatment	08-Oct-18	20-Jul-20	09-Sep-20	09-Sep-21	09-Sep-24	75	41

TBD = information is to be added once timeline is clearer

Grey text boxes indicates a projected (rather than actual) date

Based on data available through 26 January 2021

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January 2021 Study Snapshot

RESOURCES TO CONSIDER

- Create or use resources:
 - Common forms across protocols (with potential for modification as needed).
 - Create a tool to facilitate SBS within IMPAACT studies.
 - Approaches for specific populations (e.g., children by age, pregnant women).
- Engage specific sites with existing or desired SBS capacity (e.g., qualitative interviewing or costing analysis)

SBS ADVISORS

- Socio-behavioral scientists are available to IMPAACT studies to answer questions and guide study development
- Jessica Haberer and Nicole Montañez are representatives from the IMPAACT SBS Core
- Collaborative group on TB SC who have worked in IMPAACT studies interested in building SBS in IMPAACT

SUMMARY FOR INTEGRATION

Items to consider in development

- What do researchers want to understand about infants, children, adolescents, pregnant, postpartum people, and TB?
 - Where and what are the gaps in knowledge?
 - What is helpful to know to gain understanding of clinical research challenges and how to tackle them? E.g., adherence
- Increase participant knowledge in a bidirectional way.
- Keep conversations going and collaborative (pharma, colleagues, Core, other investigators, participants, community).

RECAP - FUTURE ENGAGEMENT & RECOMMENDATIONS

- SBS is a tool to answer questions.
- Make SBS part of what you do – this will strengthen the committee's scientific agenda.
- Think about operational components of increased integration:
 - Incorporating items early in development
 - Ask sites questions about their capabilities and needs
 - Increase additional site training and capacity building
 - Utilize community to ask appropriate questions and help identify gaps
- Reach out to your network:
 - Social Scientists in your network
 - Reach out to the Social Behavioral Sciences Core
 - SBSC Members are now on each committee
 - Plan for additional learning and networking events soon!

Acknowledgments

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SBSC members: Rivet Amico, Jessica Haberer, Renee Heffron, Rachel Kidman, Kenneth Ngure, Jennifer Libous, Nicole Montañez, Ellen Townley, Tafadzwa (Fadzi) Kasambira impaact.sbscore@fstrf.org



THANK YOU!