A Behavioral Science Agenda for HIV Therapeutics

Jane M. Simoni, Ph.D.
University of Washington

UCLA CHIPTS, May 16, 2023; Los Angeles, CA

Outline for Today

- Value of behavioral and social sciences (BSSR)
- Frameworks for incorporating BSSR in HIV therapeutic research
- Specific uses and methods of BSSR
- Barriers and strategies for success
- Long-acting ART: examples
- Conclusions/Discussion

Lessons Learned

When asked to reflect upon mistakes in his tenure as NIH Director, Dr. Francis Collins said:

"Maybe we underinvested in research on human behavior."
PBS Newshour 12/20/21

About 1 of 5 American adults have not received any Covid-19 vaccination
(CDC, 2022; Mayo Clinic, 2022)

FIRST OPINION

Ignoring behavioral and social sciences undermines the U.S. response to Covid-19

By Judith D. Auerbach and Andrew D. Forsyth March 9, 2022 Reprints

Lessons Learned -II

Former NIMH Director Dr. Thomas P. Insel oversaw $20 billion in federal funds and sharply shifted the focus of the NIMH away from behavioral research and toward neuroscience and genetics.

In his 2022 book Healing: Our Path From Mental Illness to Mental Health, he confessed: *"I should have been able to help us bend the curves for death and disability, but I didn't.*

For the most part [advances in neuroscience] haven't yet benefitted patients."

NY Times, 2/22/2022

Lessons Learned -III

Upon departing as chair of the White House Council of Economic Advisers, Dr. Cecilia Rouse repeatedly emphasized the need for humility in evaluating the Biden administration's policy choices in responding to the Covid epidemic and deeper economic problems, adding:

"Sometimes I, in this course of the last few years, I wished my Ph.D. was in psychology."

NY Times, 4/2/2023

Without attention to BSSR, the promises of even the greatest biomedical breakthroughs can fall short . . .

Oral PrEP could be a game-changer but for

-stubbornly low uptake (CDC, 2021)

- initial resistance from HIV care systems (Mayer, et al 2020)

-“PrEP whore” stigma in the community (Calabrese & Underhill, 2015; Rosengren, et al, 2021)

In the VOICE trials, we learned that we can not determine a product’s efficacy if people do not use it (Marazzo, et al., 2015)

False Dichotomy

- Treatment/cure/vaccine research vs. “prevention” efforts
- “Hard” vs. “soft” science (yet BSSR “hard” or difficult)
- BSSR often viewed as applicable only in the realm of prevention (e.g., for behavioral interventions, user-centered design, uptake enhancement)

"The behavioral and social sciences play a key role in HIV prevention research, because every strategy that can be utilized for preventing the acquisition or transmission of HIV has one or more associated behavioral components that can influence its efficacy. These components may affect the adoption and acceptance of a specific prevention approach or may be critical in determining the use, acceptability, and potential efficacy of these strategies.

NIAID. Behavioral and social science and HIV.

But therapeutics research also can benefit from BSSR; indeed, it is essential to making trial results valid and interpretable and, if products are successful, to making them acceptable to communities and widely adopted with no disparities in uptake or effectiveness.

Annals of Internal Medicine ORIGINAL RESEARCH

HIV Viral Suppression Trends Over Time Among HIV-Infected Patients Receiving Care in the United States, 1997 to 2015

A Cohort Study

Robin M. Nance, MS*; J.A. Chris Delaney, PhD*; Jane M. Simoni, PhD*; Ira B. Wilson, MD, MSc; Kenneth H. Mayer, MD; Bridget M. Whitney, MPH; Frances M. Aunon, MS; Steven A. Safren, PhD; Michael J. Mugavero, MD, MHSc; W. Christopher Mathews, MD, MSPH; Katerina A. Christopoulos, MD, MPH; Joseph J. Eron, MD; Sonia Napravnik, PhD; Richard D. Moore, MD, MHSc; Benigno Rodriguez, MD; Bryan Lau, PhD, ScM, MHS; Rob J. Fredericksen, PhD, MPH; Michael S. Saag, MD; Mari M. Kitahata, MD, MPH; and Heidi M. Crane, MD, MPH

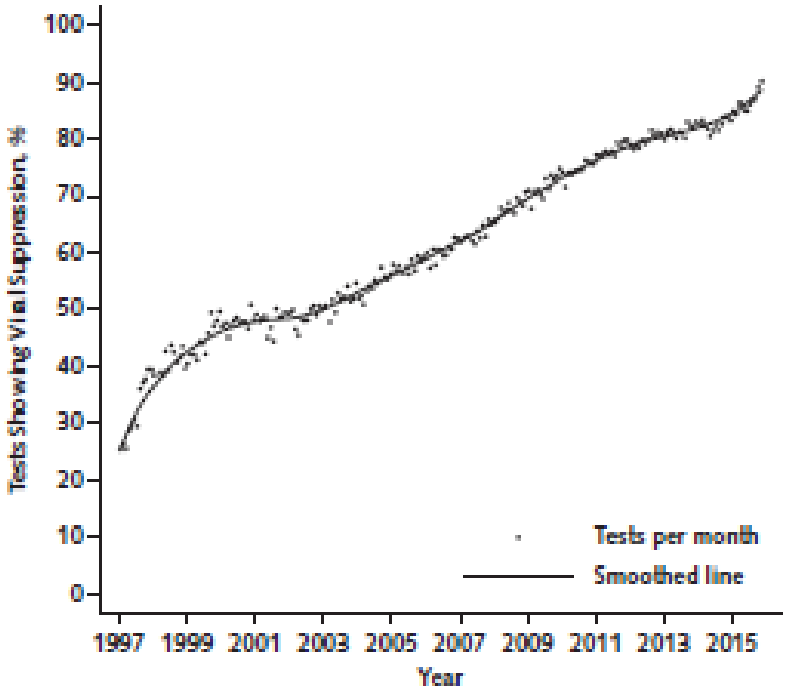
CNICS Study
31,931 PLWH

2010-2015:

No concomitant increase in ADH (82% with >90% ADH) or decrease in illicit substance use (18%/yr)

Integrase strand inhibitors associated with greater viral suppression

Figure 1. Percentage of tests showing viral suppression over time among all patients.



<u>Disparities</u>:
Younger age
Black race

BSSR can be Impactful

When we do conduct rigorous BSSR, we see results, even on biomedical outcomes such as viral suppression and even with a range of different interventions …

AIDS and Behavior (2022) 26:1853–1862
https://doi.org/10.1007/s10461-021-03534-z

SUBSTANTIVE REVIEW

Psychosocial Interventions to Promote Undetectable HIV Viral Loads: A Systematic Review of Randomized Clinical Trials

Forrest Toegel[1,2] · Andrew M. Rodewald[1] · Matthew D. Novak[1] · Sarah Pollock[1] · Meghan Arellano[1] · Jeannie-Marie Leoutsakos[1] · August F. Holtyn[1] · Kenneth Silverman[1,3]

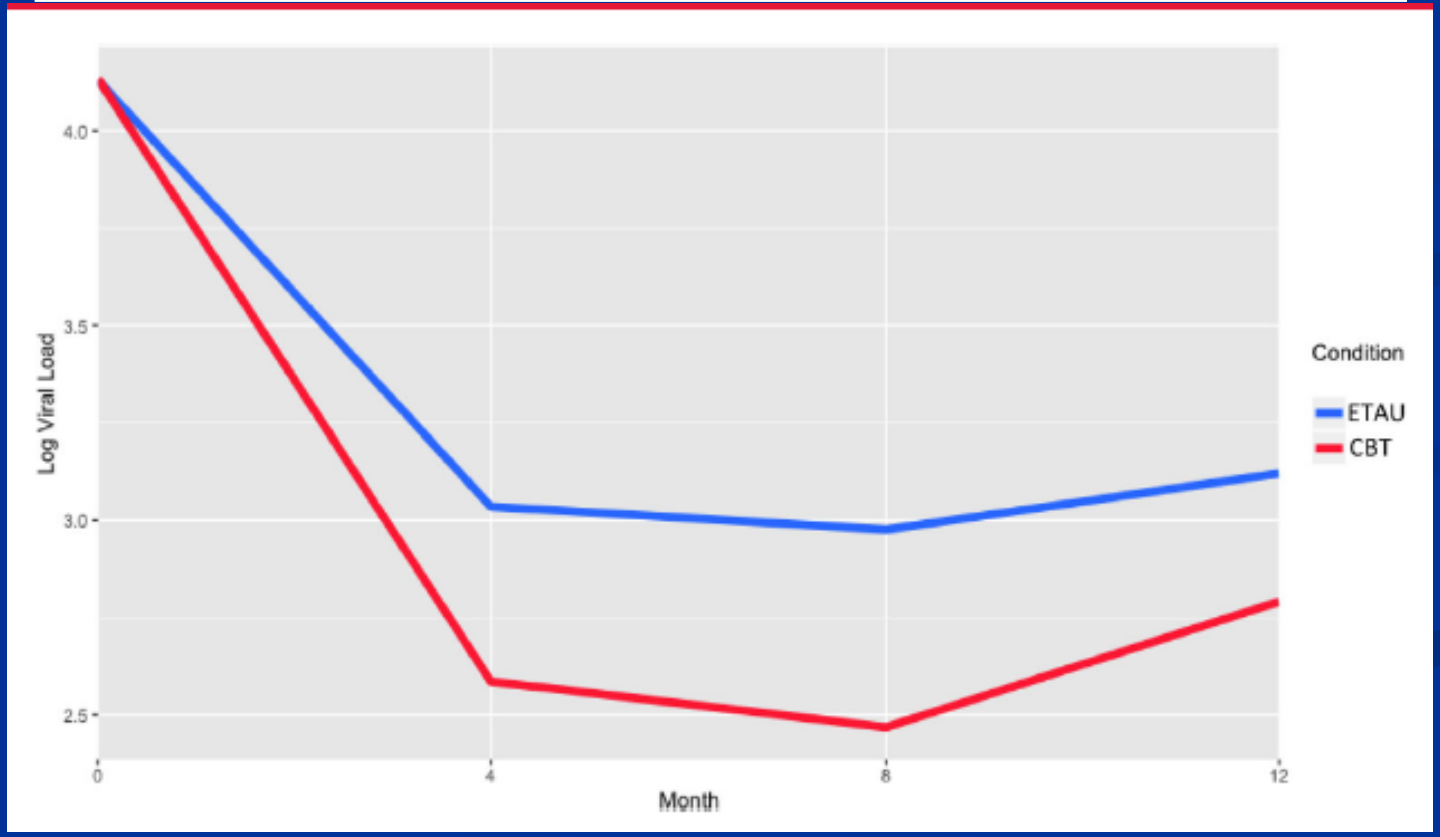
Safren SA et al. *Journal of the International AIDS Society* 2021, **24**:e25823
http://onlinelibrary.wiley.com/doi/10.1002/jia2.25823/full | https://doi.org/10.1002/jia2.25823

JIAS
JOURNAL OF THE INTERNATIONAL AIDS SOCIETY

RESEARCH ARTICLE

Treating depression and improving adherence in HIV care with task-shared cognitive behavioural therapy in Khayelitsha, South Africa: a randomized controlled trial

Steven A. Safren[1,§], Conall O'Cleirigh[2,3], Lena S. Andersen[4], Jessica F. Magidson[5], Jasper S. Lee[1], Sierra A. Bainter[1], Nicholas Musinguzi[6], Jane Simoni[7], Ashraf Kagee[8] and John A. Joska[4]



An EMR-Based Alert with Brief Provider-Led ART Adherence Counseling: Promising Results of the *InfoPlus Adherence* Pilot Study Among Haitian Adults with HIV Initiating ART

Nancy Puttkammer[1] · Jane M. Simoni[2] · Tracy Sandifer[1] · Jean Marcxime Chéry[3] · Witson Dervis[3] · Jean Gabriel Balan[3] · Jean Geto Dubé[4] · Guirlaine Calixte[5] · Ermane Robin[6] · Kesner François[6] · Cameron Casey[2] · Ira Wilson[7] · Jean Guy Honoré[3]

A Randomized Controlled Trial of the *Shikamana* Intervention to Promote Antiretroviral Therapy Adherence Among Gay, Bisexual, and Other Men Who Have Sex with Men in Kenya: Feasibility, Acceptability, Safety and Initial Effect Size

Susan M. Graham[1,2] · Murugi Micheni[2] · Oscar Chirro[2] · Joseph Nzioka[2] · Andrew M. Secor[3] · Peter M. Mugo[2] · Bernadette Kombo[4] · Elise M. van der Elst[2] · Don Operario[5] · K. Rivet Amico[6] · Eduard J. Sanders[2,7] · Jane M. Simoni[8]

A Behavioral Adherence Intervention Improves Rates of Viral Suppression Among Adherence-Challenged People Living with HIV in South India

Maria L. Ekstrand[1,2] · Elsa Heylen[1] · Matilda Pereira[2] · Jacob D'Souza[2] · Shoba Nair[3] · Amanda Mazur[1] · Ranjani Shamsundar[3] · B. N. Ravi Kumar[4] · Sara Chandy[3]

Community-based antiretroviral therapy versus standard clinic-based services for HIV in South Africa and Uganda (DO ART): a randomised trial

*Ruanne V Barnabas, Adam A Szpiro, Heidi van Rooyen, Stephen Asiimwe, Deenan Pillay, Norma C Ware, Torin T Schaafsma, Meighan L Krows, Alastair van Heerden, Philip Joseph, Maryam Shahmanesh, Monique A Wyatt, Kombi Sausi, Bosco Turyamureeba, Nsika Sithole, Susan Morrison, Adrienne E Shapiro, D Allen Roberts, Katherine K Thomas, Olivier Koole, Anna Bershteyn, Peter Ehrenkranz, Jared M Baeten, Connie Celum, for the Delivery Optimization of Antiretroviral Therapy (DO ART) Study Team**

The long-term effects of a family based economic empowerment intervention (Suubi +Adherence) on suppression of HIV viral loads among adolescents living with HIV in southern Uganda: Findings from 5-year cluster randomized trial

Fred M. Ssewamala[1,2,3]*, Darejan Dvalishvili[2], Claude A. Mellins[4], Elvin H. Geng[5], Fredderick Makumbi[6], Torsten B. Neilands[7], Mary McKay[2,3], Christopher Damulira[8], Proscovia Nabunya[2], Ozge Sensoy Bahar[2,3], Gertrude Nakigozi[9], Godfrey Kigozi[9], William Byansi[2], Miriam Mukasa[8], Flavia Namuwonge[8]

Point-of-care HIV viral load testing combined with task shifting to improve treatment outcomes (STREAM): findings from an open-label, non-inferiority, randomised controlled trial

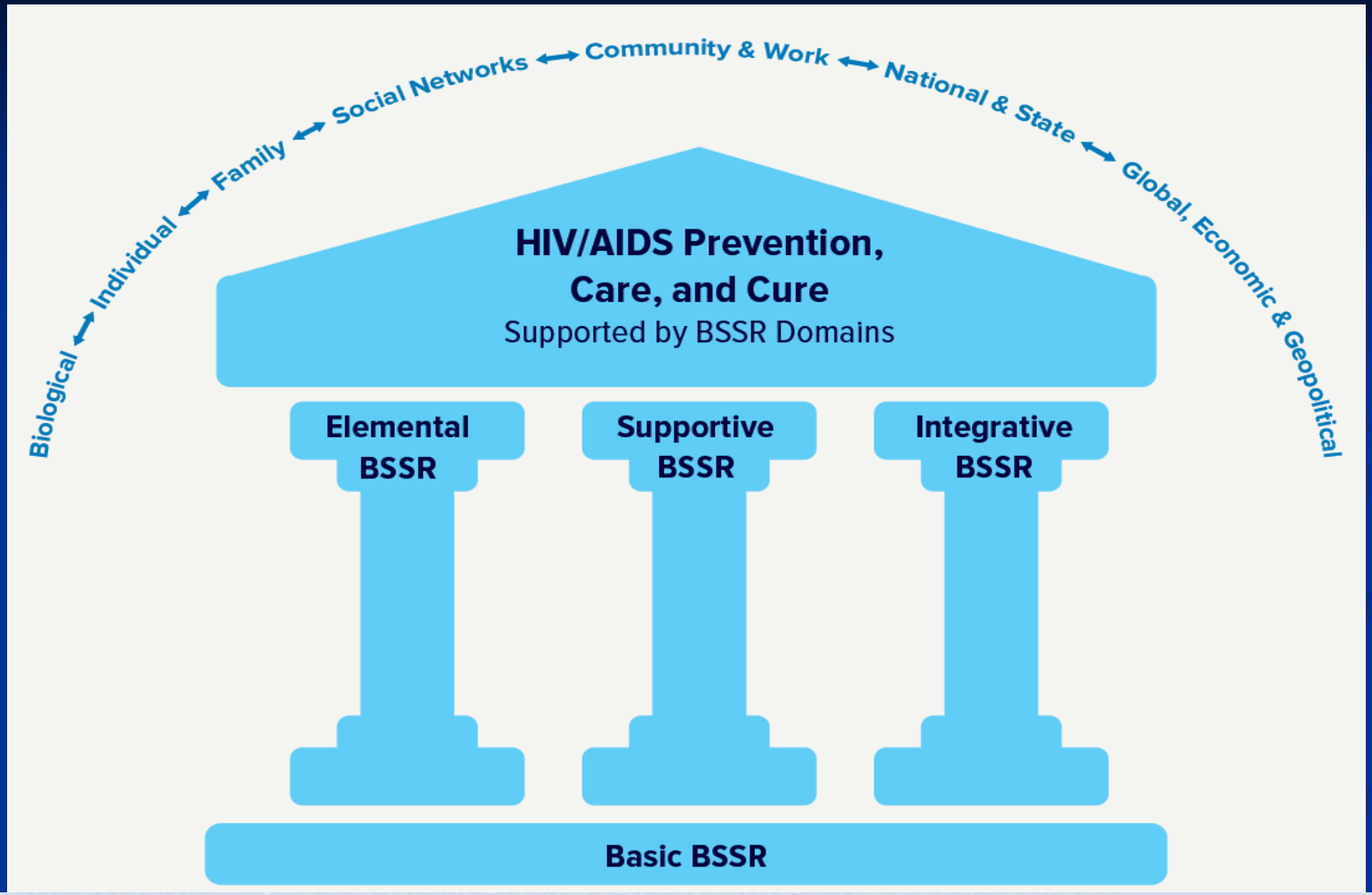
Paul K Drain, Jienchi Dorward, Lauren R Violette, Justice Quame-Amaglo, Katherine K Thomas, Natasha Samsunder, Hope Ngobese, Koleka Mlisana, Pravikrishnen Moodley, Deborah Donnell, Ruanne V Barnabas, Kogieleum Naidoo, Salim S Abdool Karim, Connie Celum, Nigel Garrett

Financial incentives to promote retention in care and viral suppression in adults with HIV initiating antiretroviral therapy in Tanzania: a three-arm randomised controlled trial

Carolyn A Fahey, Prosper F Njau, Emmanuel Katabaro, Rashid S Mfaume, Nzovu Ulenga, Natalino Mwenda, Patrick T Bradshaw, William H Dow, Nancy S Padian, Nicholas P Jewell, Sandra I McCoy

Frameworks for BSSR in Therapeutics Research

A Framework for BSSR (Gaist & Stirratt , *JAIDS* 2017)



Basic BSSR	Understanding vulnerable populations and risk settings
Elemental BSSR	Improving behavioral and social factor risk reduction
Supportive BSSR	Strengthening biomedical HIV product development and clinical trials
Integrative BSSR	Contributing to effective implementation of combination/multilevel strategies

Supportive BSSR

Support and strengthen the development and clinical testing of biomedical approaches to HIV/AIDS prevention, treatment, and cure

- BSSR information and support need to be considered and incorporated into the planning, implementation, data collection, analysis, and interpretation phases of any clinical trial testing a biomedical product
- Integration of BSSR into all stages of biomedical product development will strengthen clinical trial conduct and help to optimize the ultimate uptake and use of the product or strategy
- Supportive really “essential”

Koblin BA, Andrasik M, Austin J. Preparing for the unexpected: the pivotal role of social and behavioral sciences in trials of biomedical HIV prevention nterventions. J Acquir Immune Defic Syndr. 2013;63(suppl 2):S183–S186.
Rausch DM, Grossman CI, Erbelding EJ. Integrating behavioral and biomedical research in HIV interventions: challenges and opportunities. J Acquir Immune Defic Syndr. 2013;63(suppl 1):S6–S11.

AIDS and Behavior (2019) 23:2146–2154
https://doi.org/10.1007/s10461-018-2358-0

ORIGINAL PAPER

How Biomedical HIV Prevention Trials Incorporate Behavioral and Social Sciences Research: A Typology of Approaches

Amy Corneli[1,2] · Karen Meagher[3] · Gail Henderson[3] · Holly Peay[4] · Stuart Rennie[3]

Approach	Timeline	Objectives	Integration in protocol and consent form(s)	Study population
Formative	Before clinical trial initiation	1. Determine whether the proposed clinical trial is acceptable to the community and meets their needs 2. Inform clinical and non-clinical-related components of the trial 3. Identify strategies for addressing challenges that arose in prior clinical trials	Separate BSSR protocol and consent form(s)	Prospective trial participants Other key stakeholders
Embedded	During clinical trial implementation	1. Provide context for the clinical trial findings 2. Answer separate but related BSSR questions 3. Inform clinical trial procedures in "real time"	Information about the BSSR and clinical study procedures is *integrated into* a single protocol and consent form(s)	Trial participants
Parallel	During clinical trial implementation	1. Provide context for the clinical trial findings 2. Answer separate but related BSSR questions 3. Inform future clinical research and rollout	Separate BSSR protocol and consent form(s)	Trial participants Other key stakeholders
Explanatory	After clinical trial implementation	Explain or provide context for clinical trial findings	Separate BSSR protocol and consent form(s), or amendment to an existing protocol	Trial participants Other key stakeholders
Implications	After clinical trial implementation	Explore the behavioral and social implications of the clinical trial findings and/or participation	Separate BSSR protocol and consent form(s)	Trial participants Other key stakeholders

MTN: Insights on Integrating BSSR

Research process	What are effective practices for conducting social and behavioral research in HIV prevention trials?
Integration	How can social and behavioral research be effectively integrated with clinical research and product development?
Presenting choice	How can researchers offer options and study end user choices among multiple products and adherence support strategies?
Measurement	How can adherence effectively be supported and measured?
Community engagement	How can researchers effectively build relationships with communities, especially with diverse populations and/or in restrictive policy environments?

Table 1. Possible topics and directions from the application of the BSSR Functional Framework to HIV cure research

Basic BSSR: understanding behavioural and social factors
Defining use of language to define HIV cure research
Understanding community perceptions and knowledge of HIV cure research
Framing expectations around HIV cure research
Examining the construction and management of HIV-related identities
Assessing the social meaning of finding a cure for HIV infection
Understanding views of becoming detectable/undetectable and how the U = U movement shapes desires to engage in HIV cure research
Elemental BSSR: Advancing Behavioural and Social Interventions
Designing counselling and support interventions to address psychological needs related to ATIs
Implementing behavioural risk-reduction strategies during HIV cure and ATI studies to minimize third-party risks (e.g., counselling, PrEP provision, adherence to partner protection measures, HIV testing referral)
Developing and implementing HIV stigma reduction interventions
Supportive BSSR: Strengthening the Design and Outcomes of Biomedically Focused Clinical Trials
Determining desirable target approach and product profiles for sustained antiretroviral (ART)-free HIV cure regimens
Examining acceptability of specific HIV cure research strategies
Assessing PLHIV's (1) willingness to participate in HIV cure research, (2) risk acceptability thresholds for interventions and procedures, (3) barriers and motivators to participation, and (4) acceptability of ATI-related parameters
Understanding HIV cure researchers' and HIV care providers' (1) willingness to refer patients, (2) role of patient-provider relationships, and (3) shared decision making for cure research participation
Improving informed consent processes and understanding of risks and benefits of HIV cure research
Integrating patient-reported measures during the course of HIV cure research participation to examine: (1) factors affecting decisions to participate in research (both accepter and decliner assessments), (2) reports of longitudinal participant experiences (with HIV cure research interventions, ATIs, and study procedures), (3) psychosocial aspects of HIV cure research participation, and (4) participant-centred outcomes
Assessing and supporting adherence to HIV testing and viral load monitoring schedules, as well as ATIs, in cure clinical trial protocols
Integrating strategies to mitigate social impacts and harms during trial participation
Understanding factors affecting or enhancing the engagement and involvement of diverse and under-represented populations in research, such as women and minority groups
Integrative BSSR: Advancing Implementation of Integrated, Combination, and Multi-Disciplinary Approaches
Developing decision tools to help people living with HIV make informed decisions and choices about any available treatment and cure strategies
Testing behavioural interventions to support patient retention and completion of future HIV cure regimens
Anticipating research needs on factors affecting future real-world implementation of HIV cure research strategies, including, but not limited to: (1) infrastructure, staffing and training requirements, (2) monitoring of drug resistance and viral loads, (3) co-morbidities and poly-pharmacy, and (4) intervening factors such as injecting drug use, mental health issues, intimate partner violence, resilience and food security
Developing HIV cure strategies with scalability considerations
Integrating cost-effectiveness research and anticipating performance benchmarks for real-world implementation

Advancing long-acting and extended delivery HIV prevention and treatment regimens through behavioural science: NIH workshop directions

Tia Morton[a], Wairimu Chege[a], Edith Swann[a], Theresa E. Senn[b], Naana Cleland[a], Philip O. Renzullo[a] and Michael J. Stirratt[b]

AIDS 2021, **35**:1313–1317

Table 1. Behavioural and Social Science Research priorities on long-acting and extended delivery regimens for HIV treatment and prevention.

BSSR priority	Overarching goal	Related BSSR topics/methods
Further scientific understanding of end-user needs, desires, and contexts through BSSR to improve LAED product development and testing.	Advance novel LAED regimens that are desirable to end-users to optimize their future use.	Qualitative methods (interviews, focus groups, ethnographic research) Discrete choice surveys with intended end-users Mixed-methods research with clinical trial participants Placebo trials or prototyping studies Community engagement research
Develop tools and approaches to support LAED regimen choice, use and care retention through BSSR.	Support the safe and effective use of proven LAED regimens.	Create decision tools to support person-centred, shared decision-making regarding LAED product initiation and discontinuation Support oral medication adherence during any induction or discontinuation taper period required for LAED regimens Advance care retention interventions to facilitate continuous/sustained use of LAED regimens Understand and address intersectional stigma as a fundamental barrier to care engagement and retention
Advance innovative healthcare delivery models through BSSR to maximize equitable and efficient access to LAED regimens	Maximize the reach and impact of LAED regimens for HIV treatment and prevention.	Understanding provider and care factors Advance provider and workforce training Inform development of innovative healthcare delivery models, including injection clinics, pharmacy-based care, community-based care and telemedicine Geolocation and time-motion analyses on care delivery Integrated care approaches Differentiated care approaches Attending to cost and cost-effectiveness

Trial Phase	Ethics	Participant Preferences	Stakeholder Engagement	Heath Communication	Fairness, Equity, Disparities	Health Systems Research	Health Policy Research
3	Insure that IC processes evolve to meet the needs of the broader group of participants who will be involved with phase 3 trials. Perhaps start to study the quality of the IC process	Develop and implement short, standardized methods to assess participants' experiences in trial, both to be able to do CQI and to compare quality across sites	Apply methods developed in earlier phases to implement the kind of broad stakeholder engagement practices across many sites that will be required for multisite phase 3 studies. Study stakeholders to examine and compare engagement across sites.	Implement the communications strategies developed during phases 1 and 2. Compare quality across sites. Test quality improvement interventions.	Phase 3 studies would ideally be done in sufficiently diverse settings to allow reasonably well-powered, a priori subset analyses (e.g., men vs women). Studies of rates of enrollments in different sites that serve different populations could be informative.	If this treatment works, how do we work with health systems to do broader implementation. This includes things like workforce issues.	If this treatment works, what health policy issues are raised, e.g., access, payment, cost, cost effectiveness.

Ira Wilson (2015) Framing HIV CURE related social and behavioral science research

BSSR Methods and Tools

Name, abbreviation	Description
In-depth interview, IDI	Qualitative, open-ended and sometimes unstructured interviews with a single participant to gather detailed information
Focus group discussion, FGD	Qualitative, open-ended and sometimes unstructured interviews with a group of participants to gather detailed information about the group's experiences or perceptions.
(Audio) computer-assisted self-interview, (A)CASI	Structured data collection on a computer or tablet using specialized software. ACASI includes audio prompts, which participants can listen to with headphones.
Discrete choice experiment, DCE	Structured data collection and analysis method that indirectly assesses preference by asking participants to make a series of choices between two alternatives.
Ethnography	An approach to research derived from anthropology, which involves in-depth exploration of social or cultural phenomena using a variety of methods.
Body mapping	An approach to data collection using drawings of the human body to identify or clarify specific anatomical regions or to encourage discussion around health-related topics.
Debrief reports	Structured forms completed after IDIs or FGDs to summarize key information.
Interactive voice response	Automated approach to data collection using pre-recorded questions played during a phone call, with participants recording answers through voice responses or keypad entries.
SMS data collection/SMS CASI	Automated approach to data collection using SMS messaging.
Convergence interviews	Brief, structured interview to gain insight into discrepancies between different adherence data sources.
Counseling session analysis	Analysis of audio-recorded and transcribed counseling sessions.
Pile sorting	Structured qualitative data collection where participants sort cards, containing names of items or attributes, into related piles.
Emoji stickers and opinion tool	During IDIs, participants used emojis to express opinion about the ring and described why these were selected. Probing explored likes, dislikes, and changes in attitudes over time.
Home mapping	Visual data collection; participants draw their home environment to facilitate discussions.
Voting activity	FGD participants vote on their choice of specific options or scenarios.
Market research	Research involving end users to assess their needs and preferences.
Couples interviews	Structured or unstructured interviews with couples.

11/2021 from MTM Team: Kathleen Ridgeway, Ariane van der Straten, Kristine Torjesen, Neeraja Bhavaraju, & Mary Kate Shapley-Quinn

Uses for Supportive BSSR in HIV Therapeutics Research

- Product development
- Product use
- Social context
- Trial design
- Measurement/assessments
- Adherence monitoring and promotion
- Community integration & implementation

Product Development

- Pre-trial biomedical product development is key
- Supportive BSSR can determine preferences for hypothetical products and likely acceptability
- Via qualitative methods such as interviews and focus groups as well as sophisticated quantitative methods such as conjoint analysis and discrete choice experiments.

Product Use

- Supportive BSSR Data can yield data on actual product use, potential barriers to be addressed, and acceptability during early stage clinical trials
- Can guide decisions on which products, dosing intervals, and supports are needed

MTN: Insights on Product Development, Use, and Introduction

Acceptability	What factors affect product acceptability, and how does acceptability influence product use? Who influences an end user's acceptability of a product (e.g., partner, family, community), and in what ways?
Adherence	What are the most accurate and reliable measures of product adherence, and how can multiple adherence assessments be triangulated to obtain accurate estimates? What types of support do study participants need to effectively use study products?
Social factors	How do male partners influence women's experience with and use of HIV prevention products? How can male partners better support product use? What roles do peers and family play in product acceptability, use, and continuation?
Contextual factors	For women using vaginal products, how do cultural practices around menstrual cycle management affect product use and acceptability? How does social and cultural context, including community beliefs, practices, and family members, affect trial participants' attitudes about the study and product use?
Sexual behavior	Which approaches can best elicit accurate data about stigmatized sexual behaviors? How can researchers work within norms that discourage explicit language around bodies and sex?
Multipurpose prevention technology (MPT)	What product characteristics influence choices and preferences for an MPT? For women in heterosexual relationships, what role does a male partner play in choosing MPT options?

Community Context

Supportive BSSR can provide systematic data on

- Key populations and communities
- Local environments
- HIV landscape
- Social and historical context

Robust, triangulated, multilevel data, along with ethnographic surveys and participant observations, can yield important insights into complex systems and experiences navigating HIV prevention and care.

Emily Arnold, et al.: *The innovative use of qualitative and mixed methods research to advance improvements along the HIV prevention and care continua*

Trial Design

- BSSR can strengthen the design, implementation, and interpretation of trials
- Early testing of proposed trial procedures with process evaluation to evaluate their feasibility and to identify any operational obstacles
- Qualitative studies of the user experience, such as around the ethics of consent and limiting potential harms in studies of new treatments, exit interviews

How can behavioural science help us design better trials?

Katie Gillies[1*], Jamie Brehaut[2,3], Taylor Coffey[1], Eilidh M. Duncan[1], Jill J. Francis[2,4], Spencer P. Hey[5,6], Justin Presseau[2,3], Charles Weijer[7] and Marion K. Campbell[1]

Example process problem	Recruitment of participants	Sharing results with participants at end of trial
Behavioural specification (identifying the problems)	*Use a framework such as AACTT to specify the key behaviours involved in recruitment for further investigation.*	
	Actions: such as clinician screening patients, providing information, informed consent discussion; **Actor**: clinician responsible for recruitment; **Context**: hospital clinic; **Target** of behaviour: potential trial participants; **Time**: throughout the trial.	**Actions**: identifying whether and how participants wish to receive results, disseminating the result to participant at trial end; **Actor**: Chief Investigator and/or Trial Manager and/or Sponsor; **Context**: trial office; **Target** of behaviour: trial participants; **Time**: end of the trial.
Behavioural investigation (diagnosing the problems)	*Several ways to investigate the problem, which may include:*	
	• Conduct behaviourally focussed interviews with health care professionals (and/or patients) to identify salient theoretical domains important to influence (positively or negatively) trial recruitment. • BCT analysis of site training and/or staff and patient information related to recruitment.	• Survey of stakeholders (trial teams, funders, regulators) to understand the main behavioural (individual, collective, organisational) challenges to sharing trial results with participants at the end of a trial
Behavioural solutions (treating the problems)	*Develop targeted behaviour change solutions that incorporate relevant BCTs identified from the previous stages, which ideally would be evaluated and implemented.*	
	• Potential solutions may include tailored training for staff, restructuring the physical environment, incentives or rewards all of which will depend on the diagnosis phase and acceptability of potential solutions to be implemented.	• Potential solutions may include audit of existing practice with follow up feedback that highlights their practice compared with existing standards and/or against other trial teams, and, reward and threats, again all of which will depend on the diagnosis phase and acceptability of potential solutions to be implemented.

Fig. 1 Trial lifecycle highlighting example trial processes and potential application of the behavioural science approach

Measurement /Assessments

Of behavioral and psychosocial factors

Often necessary for eligibility or to elucidate findings, especially with null findings or intergroup differences

Ex: Mental health (depression, anxiety, PTSD

Quality of Life

Adherence (need to document adherence to determine safety and efficacy)

Need psychometrically sound measures – i.e., valid and reliable for the population under study

Harmonization across studies for better comparison across protocols

Adherence Monitoring & Promotion

BSSR can provide strategies for improving product adherence in trials and strengthening adherence through monitoring and feedback approaches

Gaist & Stirratt: *Brief BSSR theory-based adherence counseling is an essential component of any clinical trial protocol*

Evidence-based counseling interventions have more favorable outcomes than non-specific counseling or supportive counseling

Training of counselors:

- Research shows that workshops are not sufficient to change counselor behavior long-term, with initial gains in new skills diminishing after a couple of months
- Coaching and counselor support help maintain and gain new skills
- Fidelity monitoring is critical to ensure that key components of the interventions are delivered so the interventions retain their efficacy.

Community Integration & Implementation

- Community member perspectives are essential to trial success
- They can provide insight into subjective, multifaceted, complex, and contested realities within the daily lives of PLWH
- Critical to recruitment

  Increasing BIPOC participation in clinical trials through community engagement and recruitment goal establishment. **Andrasik et al. (2021)** PMID: 34665829

- Critical to addressing disparities in efficacy and uptake

BSSR to Support Adoption/Implementation

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

Social-Behavioral Sciences (SBS) in IMPAACT

Presented by: Graeme Hoddinott, Jessica Haberer, Yael Hirsch-Moverman, Nishi Suryavanshi, Nicole Montañez

26 January 2022

Summary: Supportive *("Essential")* BSSR

Gaist & Stirratt, 2017

- *When used from planning stages to interpretation of outcomes, BSSR can improve development and clinical testing of biomedical products*
- *BSSR facilitates selection of the most acceptable products and identification of adherence support approaches to ensure proper proof-of-concept testing*
- *Helps plan for and better execute biomedically centered intervention and product-oriented research*

Barriers to BSSR in Therapeutics

- Ignorance (see no need because premise or value not well articulated)
- Traditional pharma focus on “compliant subjects”
- Active, blanket refusal/dismissal (“don’t want to waste time asking participants questions”)
- Avoidance of unwanted findings (study/regimen burden may actually be too high)
- Restrictive funding structures (no $$ for qualitative interviewers or analysis)
- Insufficient BSSR expertise on team
- Reluctance to further delay trial time lines (want to avoid protocol “creep” and cost increases)

Strategies to Surmount Barriers

- Continue to conduct impactful BSSR studies
- Publicize advantages of BSSR-informed trials
- Form interdisciplinary teams
- Support harmonization among the major DAIDS networks
- Lobby NIH to require incorporation of relevant BSSR into therapeutics trials and networks
- Propose BSSR investigations within the networks

Long-acting Injectable ART

UW Project PREFER – A discrete choice experiment (DCE) of patient preferences for long-acting ART

(R01 MH121424, MPI Graham/ Simoni)

- Conducted 12 key informant interviews to refine attributes and levels based on the full range of products in the pipeline
- DCE design features choices between either of two hypothetical LA options and current daily oral ART
- Developed and pilot tested a survey and DCE with 50 participants in Seattle
- Conducting full DCE with 350 participants in Seattle and 350 participants in Atlanta
- Will analyze final data to identify patient preferences that may predict uptake and associations with those preferences
- Will repeat process in Kenya in 2022-2024

UW Project PREFER – A discrete choice experiment (DCE) of patient preferences for long-acting ART

(R01 MH121424, MPI Graham/ Simoni)

	Option A	Option B	Option C - your current HIV regimen
Treatment type - How do I take this treatment?	Long-acting oral pills 	Injections under the skin 	
Location - Where would I get this treatment?	Home	Local pharmacy	
Frequency - How often would I get this treatment?	Once a week	Once a month	
Pain - How much pain would I feel?	None	Mild	
Pre-treatment time undetectable - How long would I need to be undetectable on daily pills before starting this treatment?	3 months	None	
Pre-treatment negative reaction testing - Would I need to take daily pills to check for negative reactions before starting the treatment?	Needed	Not needed	
Late dose leeway - How late can I be for a dose of this treatment and still remain undetectable?	1 week	1 week	
Which do you prefer?	○	○	○

Interventions to Support Adherence to Long-Acting Injectable ART

Michael Stirratt, Ph.D.
Senior Behavioral Scientist
NIMH Division of AIDS Research

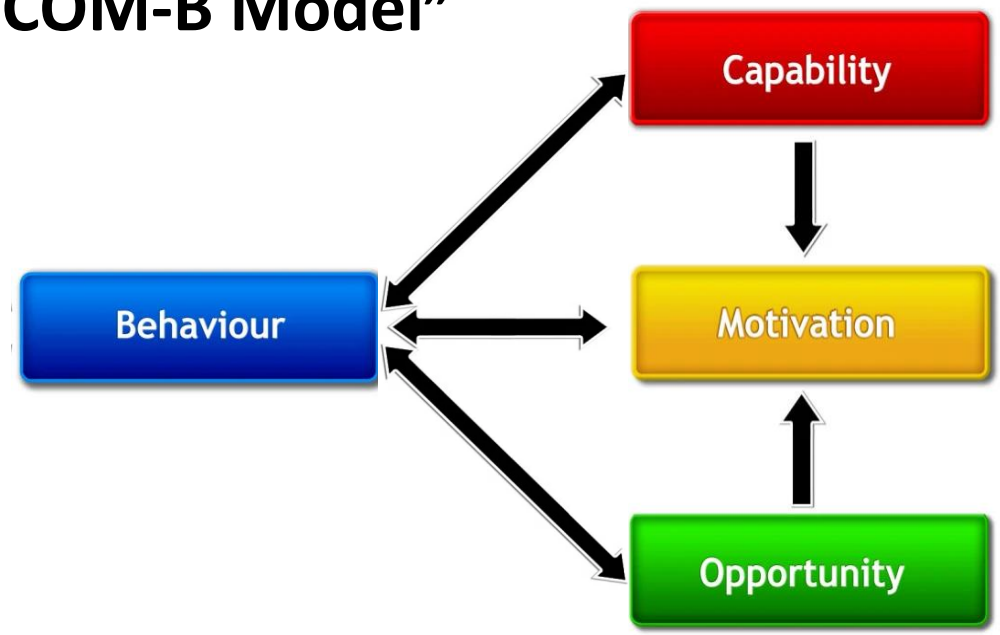
Jane M. Simoni, Ph.D.
Chair, ACTG Behavioral Science Sub-Committee
University of Washington

ACTG ARTS TSG Presentation

March 7, 2023

The science of behavior change: Use theory to guide interventions

"COM-B Model"



Michie 2011 Implement Sci

Examples of intervention targets/approaches

Education/Information
Skills training
Mental health

Monitoring/feedback
Conditional incentives
Motivational interviewing

Housing
Transportation
Stigma reduction

Principles for Reaching the "Hardly Reached"

Offer multiple forms of support in combination:

"Monotherapy" is not effective for ART, and the same is true with behavioral support.

Meet deeper needs:

People with adherence and care retention challenges often have comorbid concerns including issues with mental health, substance use, and housing.

Options for combination support

Strategy	Approaches	Resources (staffing; cost)
Use standard tools	Regularly updated contact info/locator forms Appointment reminders and travel reimbursement	Low
Enhance motivation	Rapid point-of-care feedback on VL or drug levels Conditional financial incentives for appt attendance (lottery)	Medium
Meet "deeper needs"	Case management services Outreach workers for regular contact, patient navigation & no-show follow-up	High
Pioneer community-based care delivery	Community-based delivery of long-acting ART (via home visits, mobile vans, or socially-oriented "adherence clubs")	High

Thank You


Jane Simoni
jsimoni@uw.edu