

FORESEEABLE AND UNFORESEEABLE CHALLENGES IN IMPLEMENTATION SCIENCE

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YALE SCHOOLS OF MEDICINE



GIFT SUMMER BOOTCAMP

JULY 11, 2024

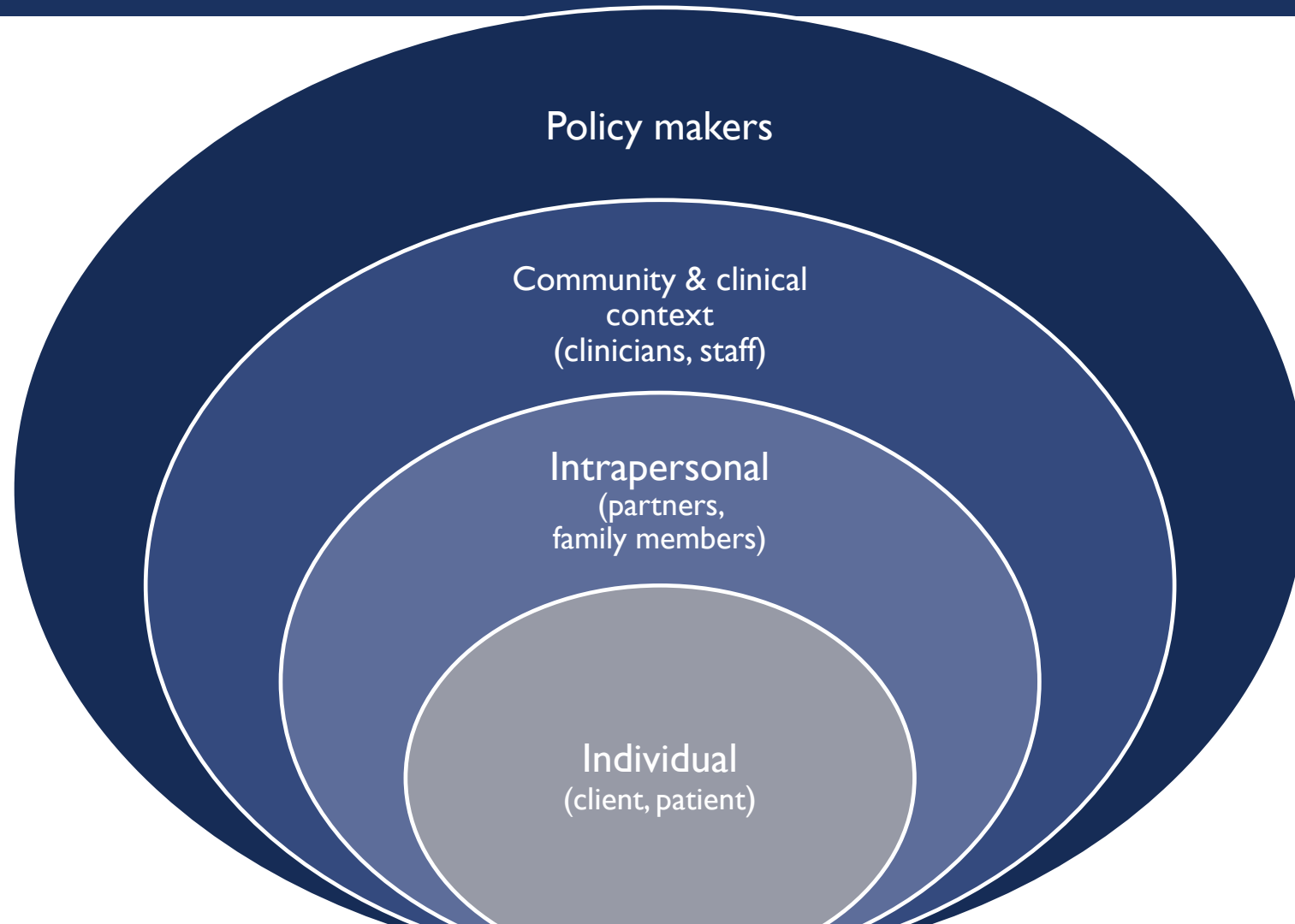
OBJECTIVES

- To describe six key challenges and potential responses

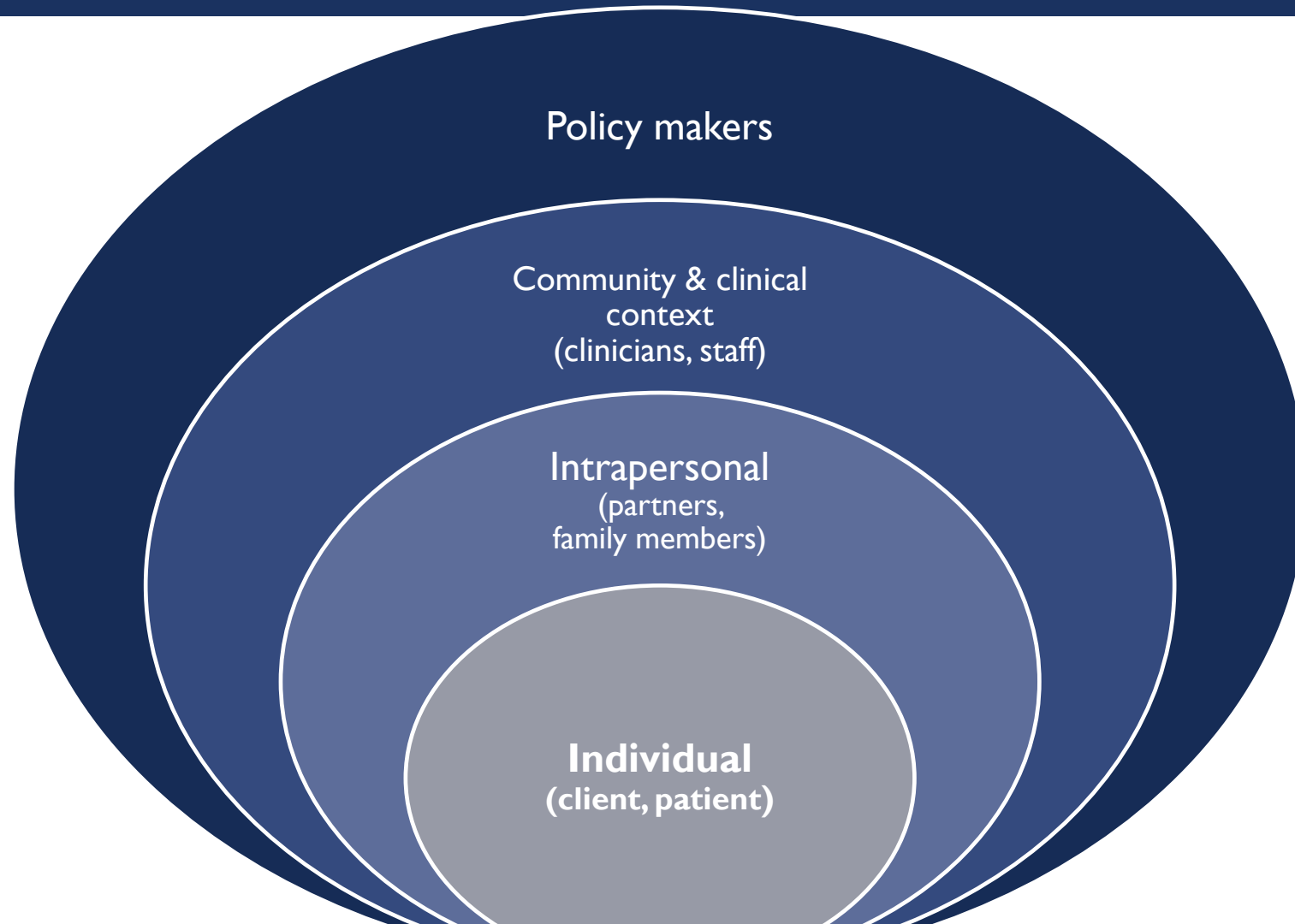


CHALLENGE #1: REACHING TARGET POPULATION

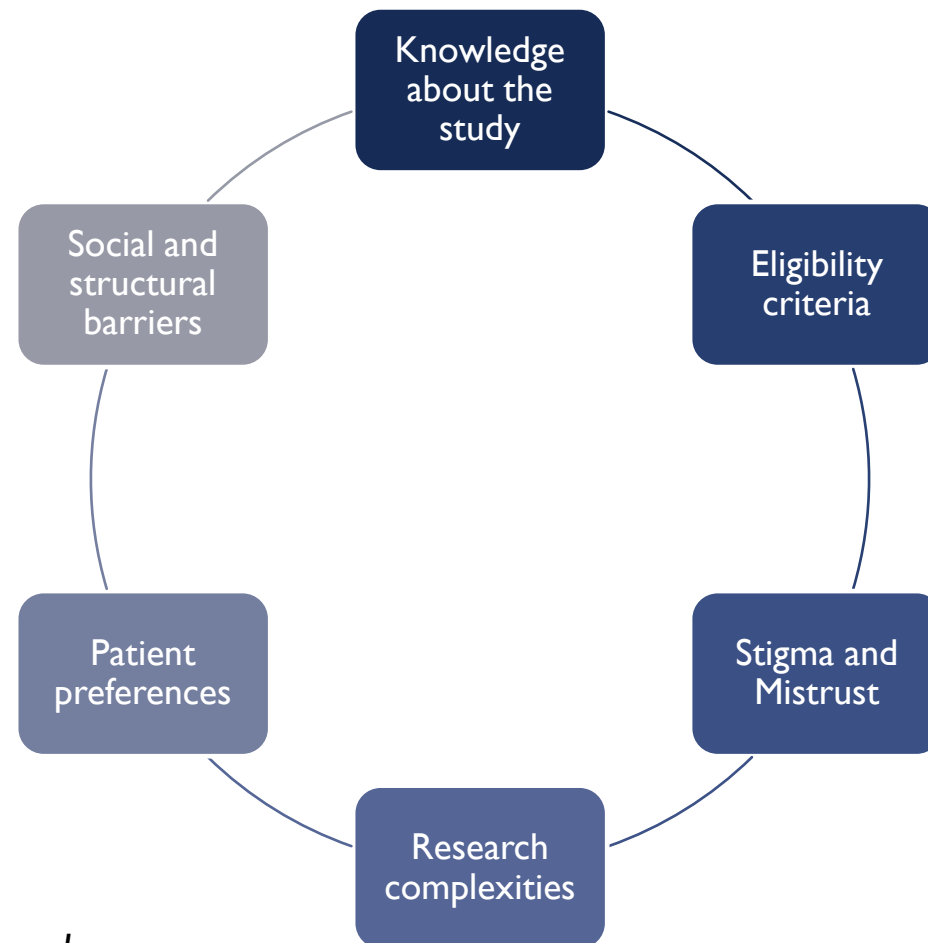
RESPONSE #1: CONSIDER TARGET POPULATION



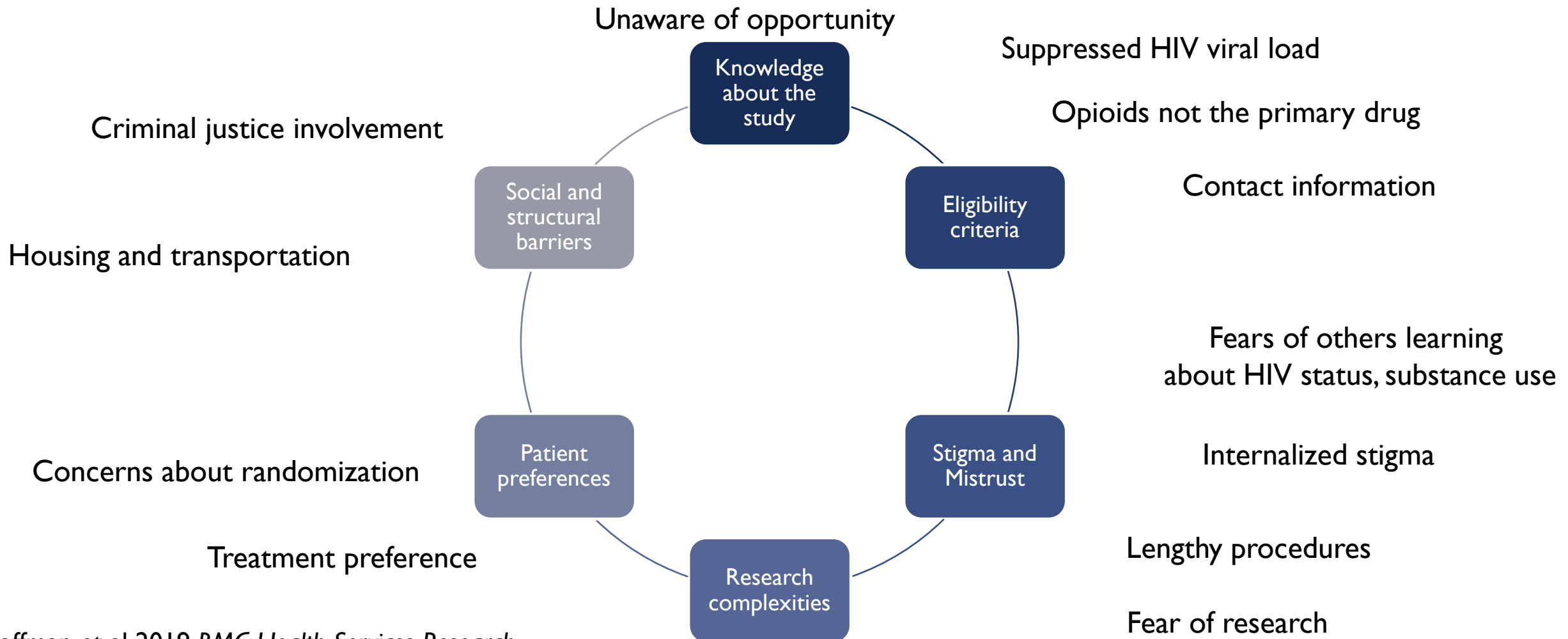
RESPONSE #1: CONSIDER TARGET POPULATION



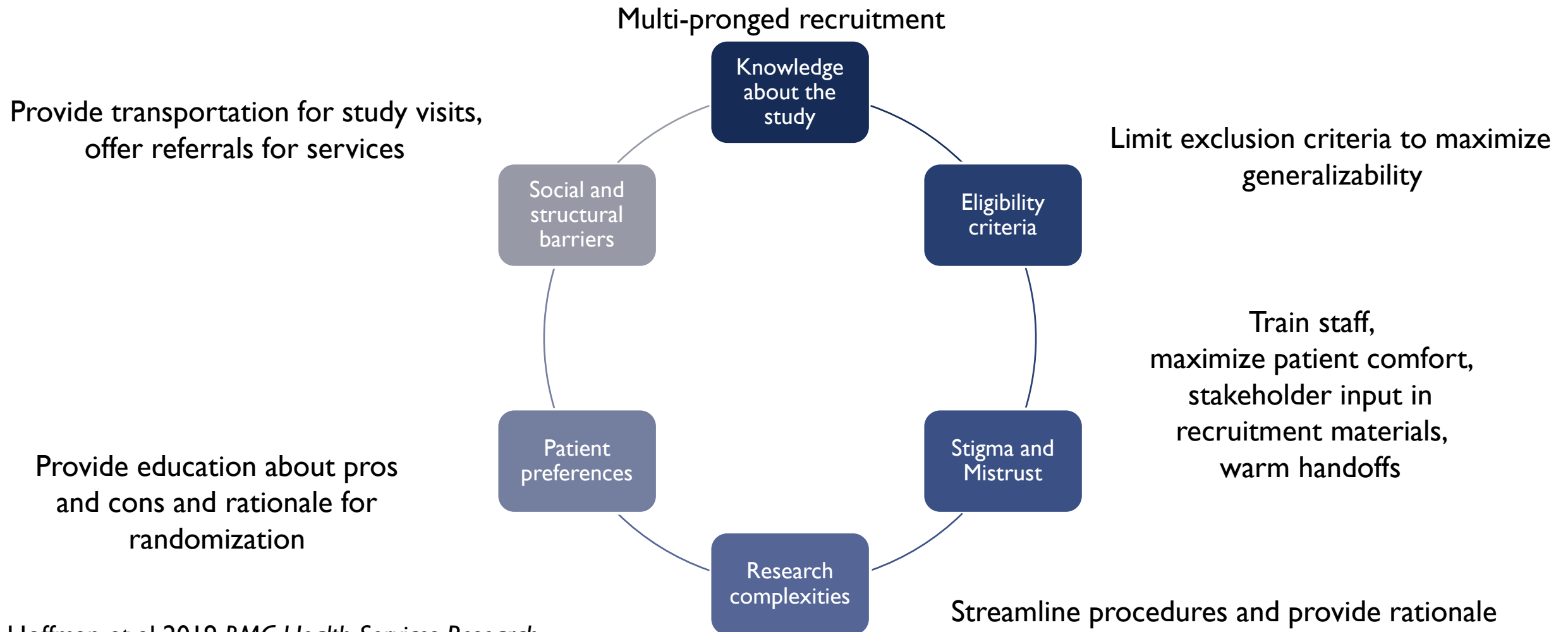
RESPONSE #1: UNDERSTAND BARRIERS TO RECRUITMENT



RESPONSE #1: UNDERSTAND BARRIERS TO RECRUITMENT

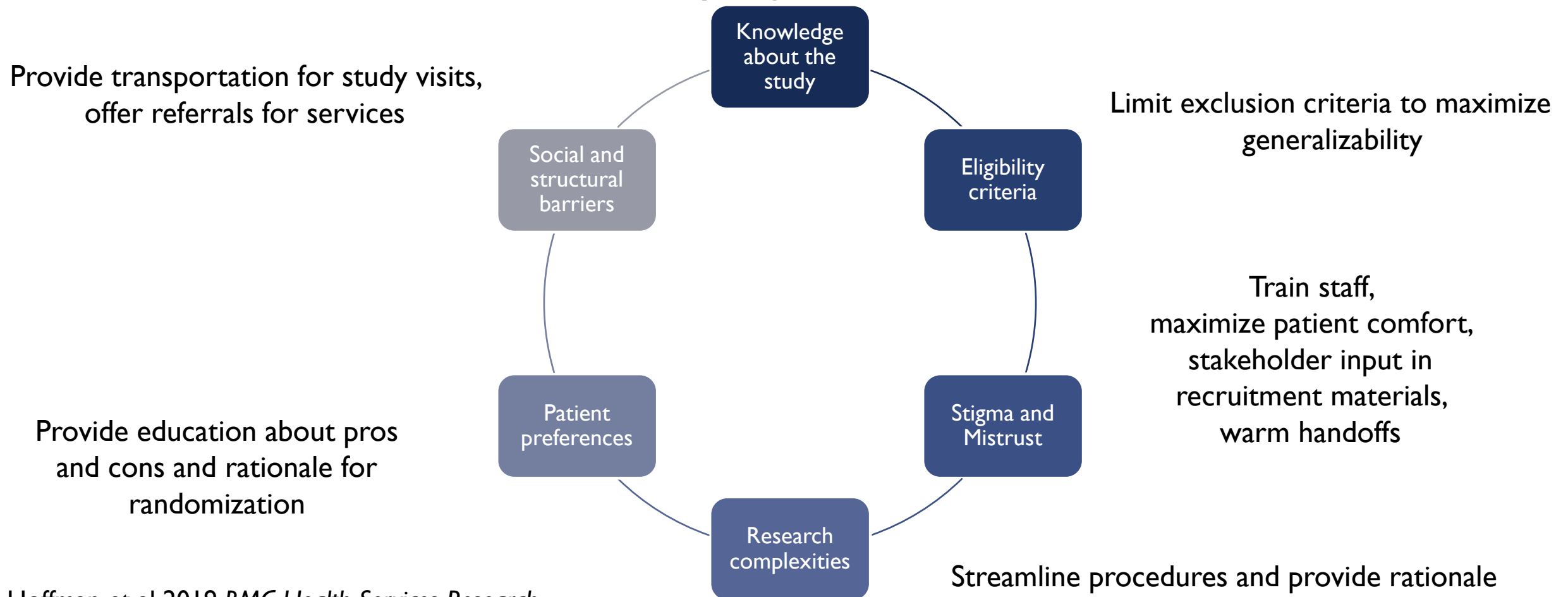


RESPONSE #1: OPTIMIZE RECRUITMENT UPFRONT



RESPONSE #1: OPTIMIZE RECRUITMENT UPFRONT

Multi-pronged recruitment



RESPONSE #1: OPTIMIZE RECRUITMENT UPFRONT



RESPONSE #1: OPTIMIZE RECRUITMENT UPFRONT



SMARTTT
A Smart Approach to
Treating Tobacco Use Disorder

You may be eligible to participate if:

- You are HIV positive
- You are 18 years of age or older
- You smoke cigarettes regularly
- You are **not** currently using nicotine (patches, gum, lozenges, an inhaler or nasal spray), varenicline (Chantix), or bupropion (Zyban or Wellbutrin) regularly

If you decide to take part in this research study:

- We will ask you to meet with a research coordinator for a total of 3 visits
- We will ask you to meet with a clinical pharmacist for a total of 11 visits
- We will ask you to answer questionnaires about your medical and social history, and smoking habits
- The clinical pharmacist will offer counseling to help you reduce your smoking and prescribe medications to help with cravings
- If you are randomly selected to participate in the additional reward program, you can earn additional monetary rewards

Sessions with the research coordinator and clinical pharmacist may occur in-person, by video conference, or by telephone.

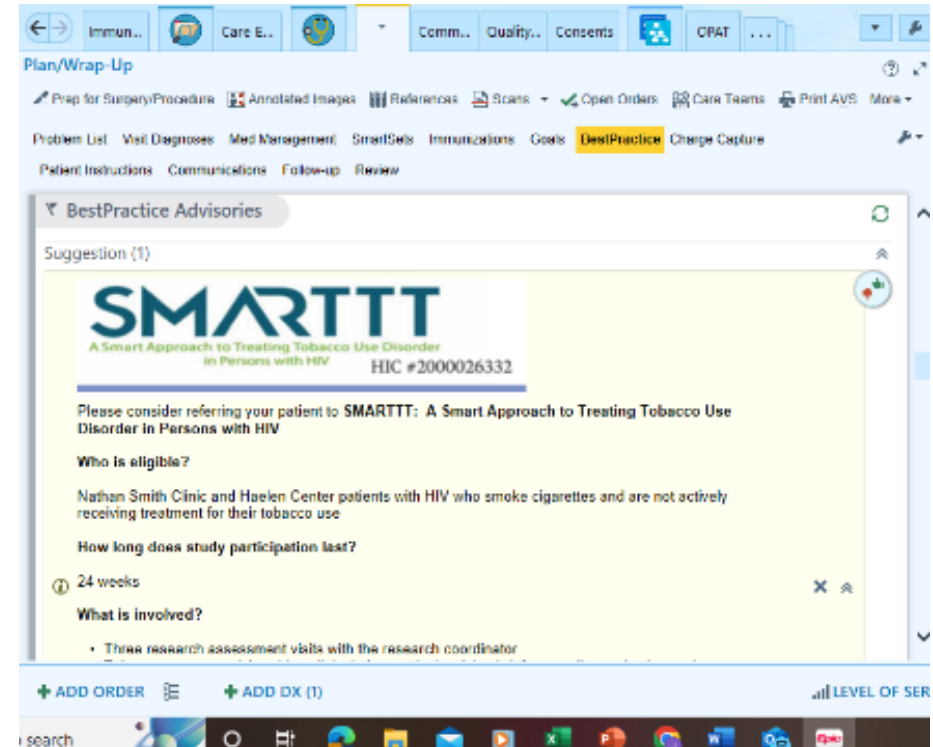
Your participation in this research study is expected to last 6 months, but you may stop participating in this research at any time without any penalty.

You will be compensated for your time.

To find out more about participating in this study, please contact (203) 215-4314.

IRB Approved

Effective Date: 11/8/2022
End Date: 11/7/2023



Plan/Wrap-Up

Prep for Surgery/Procedure Annotated Images References Scans Open Orders Care Teams Print AVS More

Problem List Visit Diagnosis Med Management SmartSets Immunizations Goals **BestPractice** Charge Capture

Patient Instructions Communications Follow-up Review

BestPractice Advisories

Suggestion (1)

SMARTTT
A Smart Approach to Treating Tobacco Use Disorder
in Persons with HIV HIC #2000026332

Please consider referring your patient to **SMARTTT: A Smart Approach to Treating Tobacco Use Disorder in Persons with HIV**

Who is eligible?

Nathan Smith Clinic and Haelen Center patients with HIV who smoke cigarettes and are not actively receiving treatment for their tobacco use

How long does study participation last?

24 weeks

What is involved?

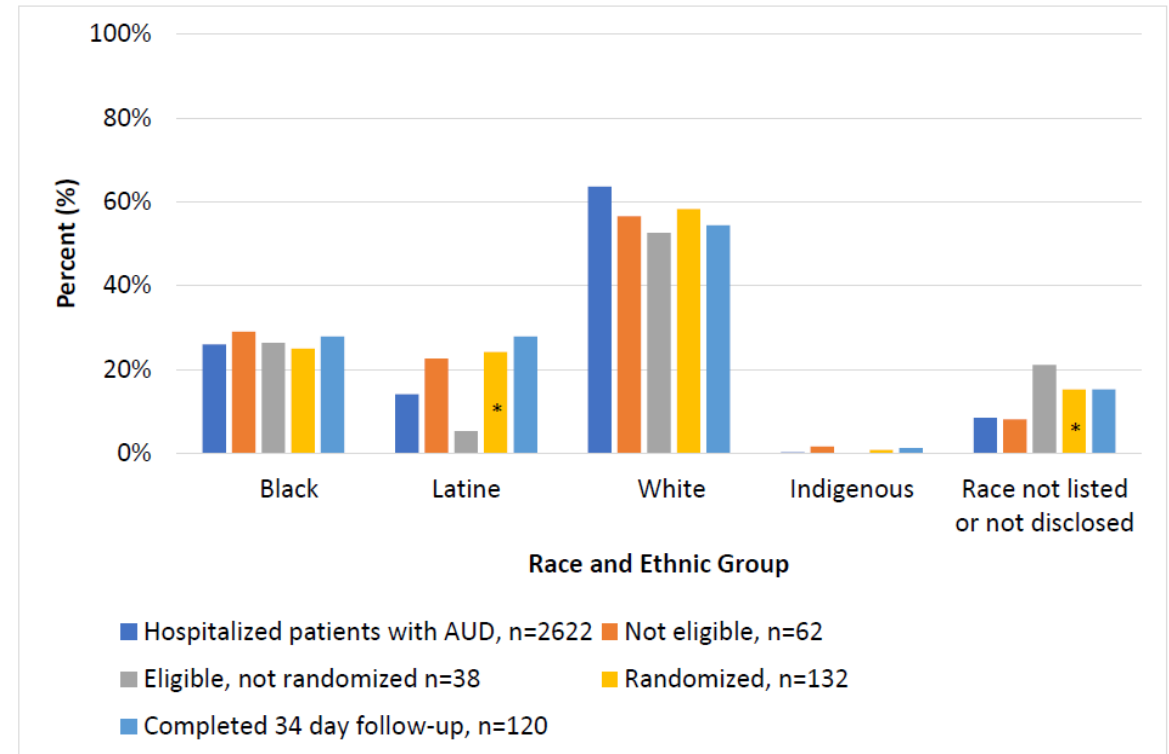
- These research assessment visits with the research coordinator

+ ADD ORDER + ADD DX (1) LEVEL OF SER

RESPONSE #1: MONITOR PROGRESS

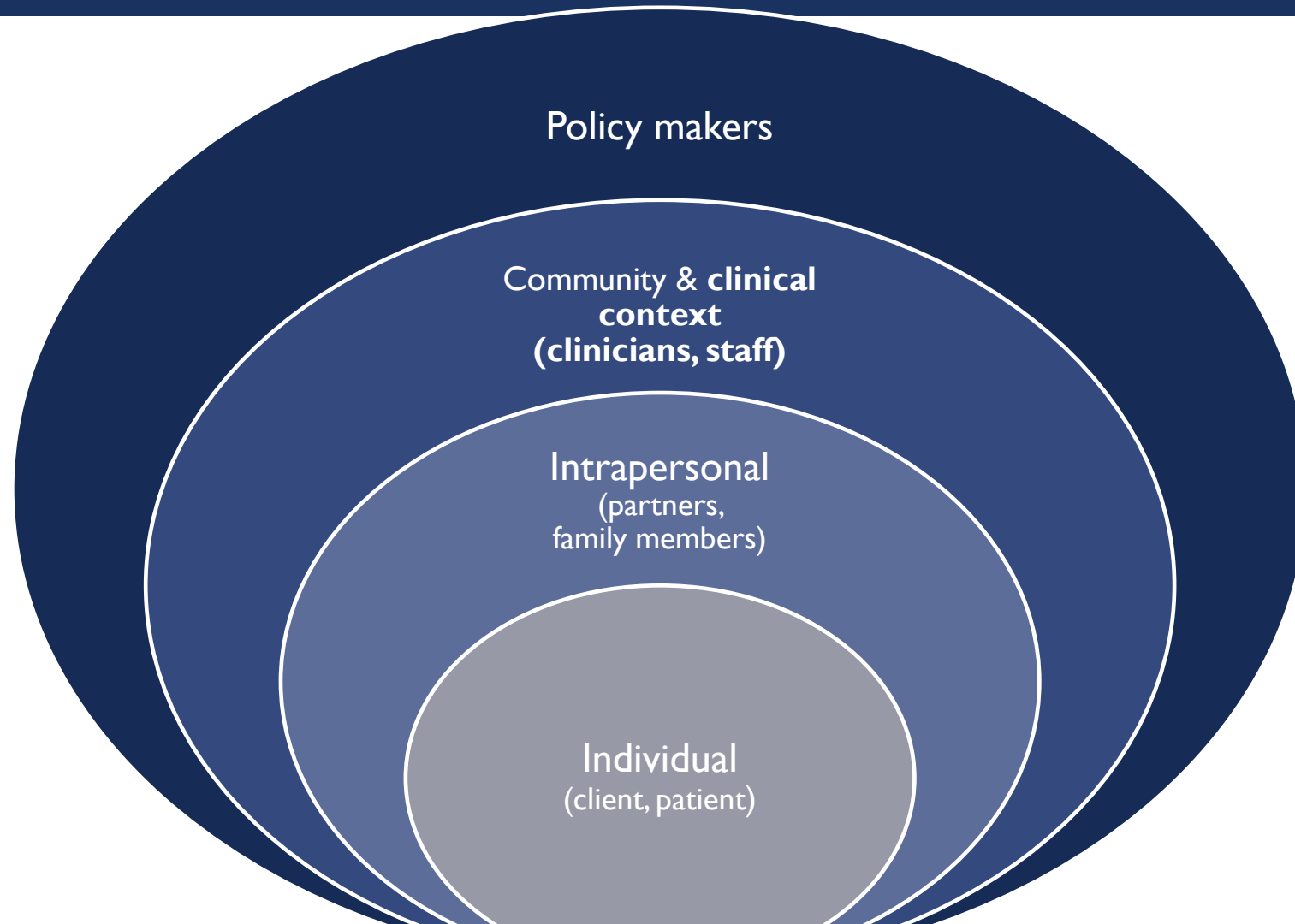
- Define targets
- Understand the underlying denominator (even if imperfect*)
- Monitor
- Refine strategies

Figure 1. Hospitalization and Project ENHANCE recruitment and follow-up experiences by race and ethnic categories

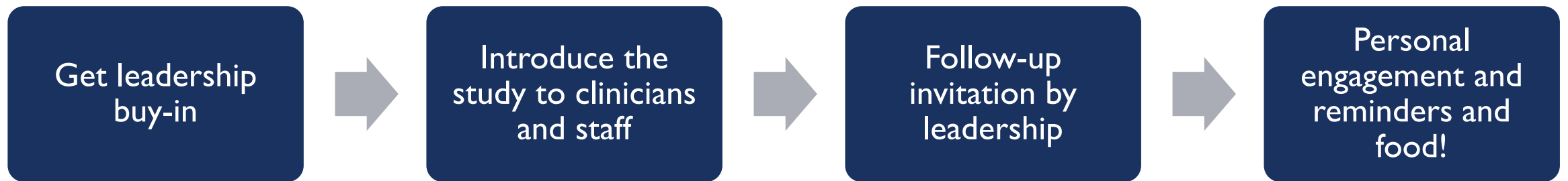


*asterisk indicates $p < 0.005$ for comparison to % of hospitalized patients with AUD within given category.

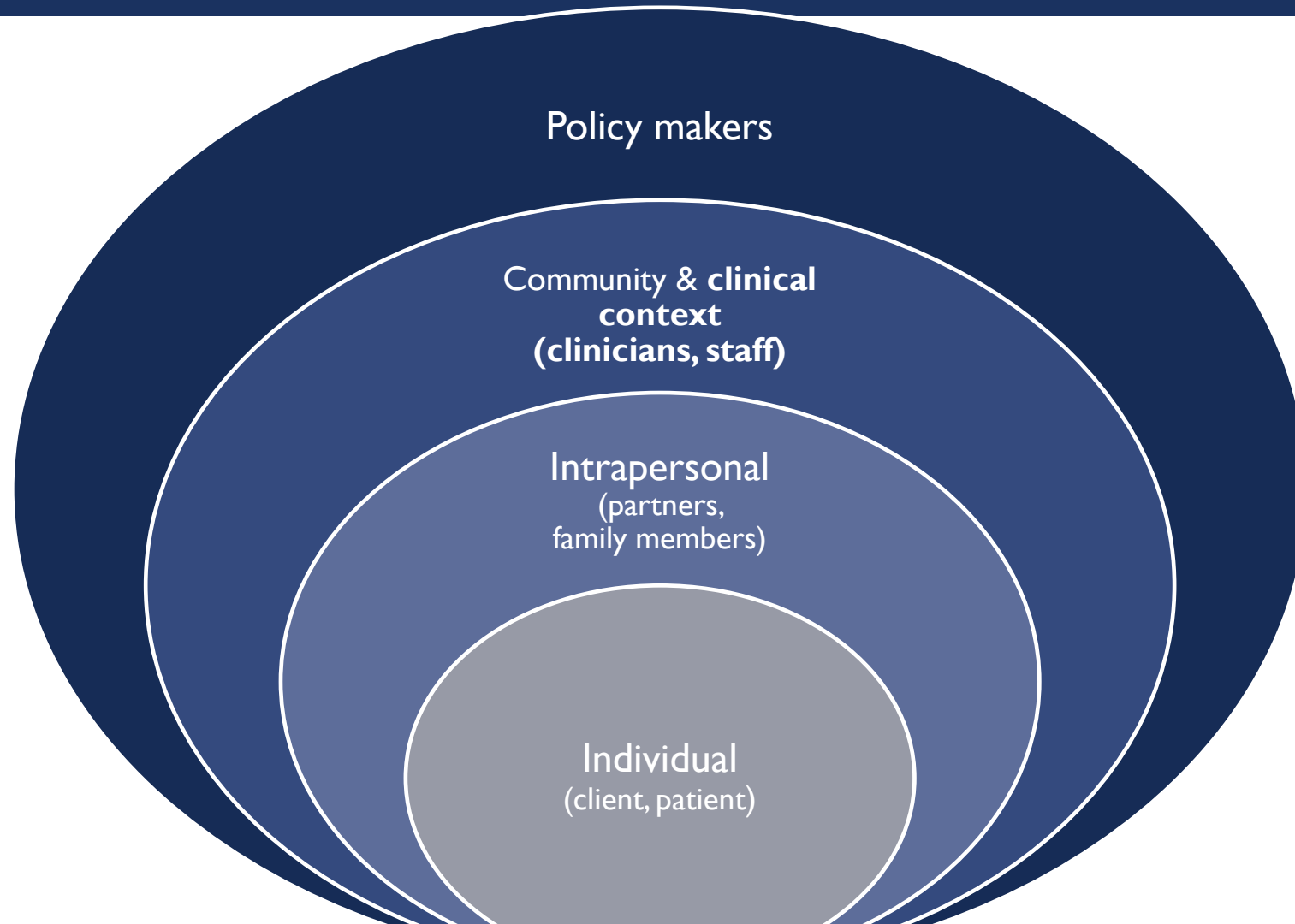
RESPONSE #1: CONSIDER TARGET POPULATION



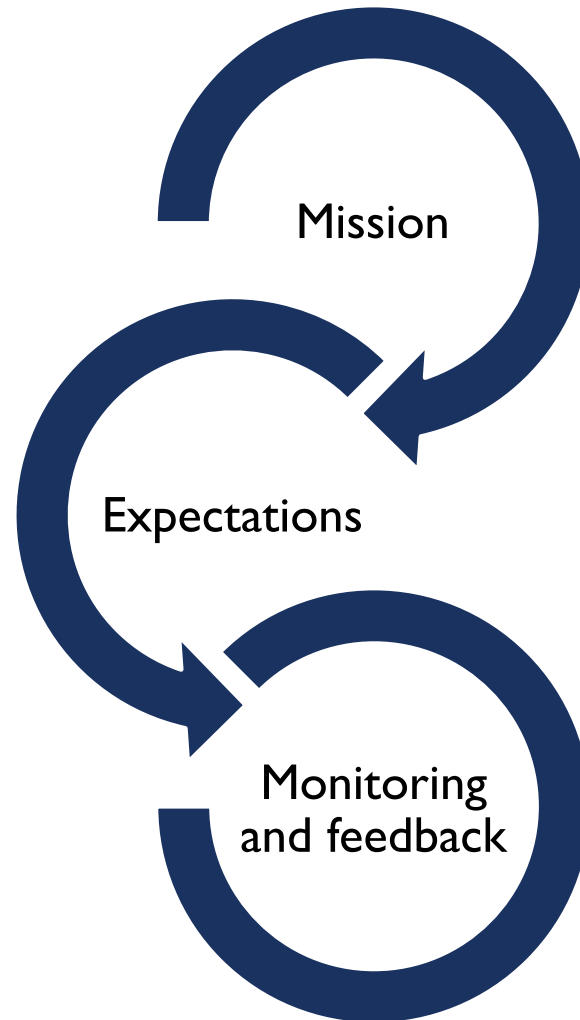
RESPONSE #1: REACHING TARGET PROVIDER POPULATION



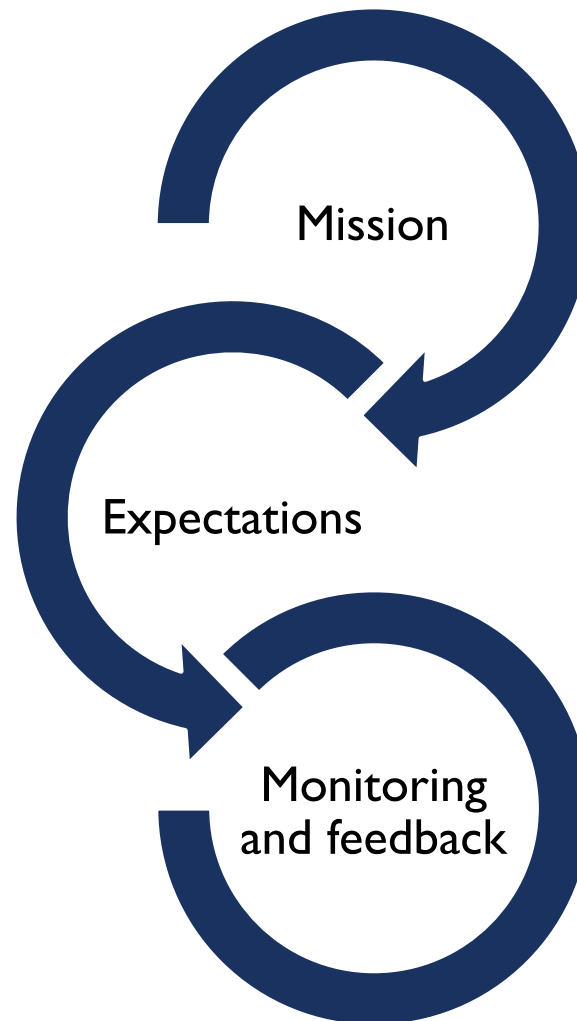
RESPONSE #1: CONSIDER TARGET POPULATION



RESPONSE #1: CONSIDER SITE ALIGNMENT



RESPONSE #1: CONSIDER SITE ALIGNMENT



It is okay to
break-up and
pivot!

CHALLENGE #2: RETENTION

Missing data especially problematic if not missing at random

Threatens validity, reliability and usability of results

CHALLENGE #2: RETENTION

Missing data especially problematic if not missing at random

Threatens validity, reliability and usability of results

Makes Denise very unhappy!

RESPONSE #2: OPTIMIZE RETENTION



Strategies to improve retention in randomised trials (Review)

Gillies K, Kearney A, Keenan C, Treweek S, Hudson J, Brueton VC, Conway T, Hunter A, Murphy L, Carr PJ, Rait G, Manson P, Aceves-Martins M

Gillies K, Kearney A, Keenan C, Treweek S, Hudson J, Brueton VC, Conway T, Hunter A, Murphy L, Carr PJ, Rait G, Manson P, Aceves-Martins M.
Strategies to improve retention in randomised trials.
Cochrane Database of Systematic Reviews 2021, Issue 3. Art. No.: MR000032.
DOI: 10.1002/14651858.MR000032.pub3.

- Outward mail with first class postage, personalized letter
- Self-sampling kits
- Telephone reminders compared to postal reminders
- Prenotification cards compared to no card
- Addition of monetary rewards with prenotification or reminder letters
- Peer-led follow-up strategy compared to usual follow-up
- Optimized information
- Pen at recruitment

As it stands, there is nothing in the evidence base with high certainty evidence that can be applied to trials to improve retention

RESPONSE #2: OPTIMIZE RETENTION

RESEARCH ARTICLE

Retention strategies among those on community supervision in the South: Lessons learned during the COVID-19 pandemic

Breana J. Uhrig Castonguay^{1,2*}, Katherine LeMasters^{2,3}, Chris Corsi², Evan J. Batty⁴, Taylor J. Krajewski^{5,6}, Madelene Travis², Craig Waleed⁷, Carrie B. Oser⁸, Kathryn M. Nowotny⁹, Lauren Brinkley-Rubinstein²

- Collect and track detailed locator information
- Develop strong relationship between research staff and participants
- Minimize barriers to participation
- Be persistent, creative, and flexible in retention efforts
 - Retention bonuses
 - Contact payments
 - Study branded materials – backpack, magnets, snacks, etc.
 - Contact different times of day and by different methods
 - Mail personalized letters
 - Confirm and share phone number at study enrollment
 - Retention journal
- Hold standing retention meetings

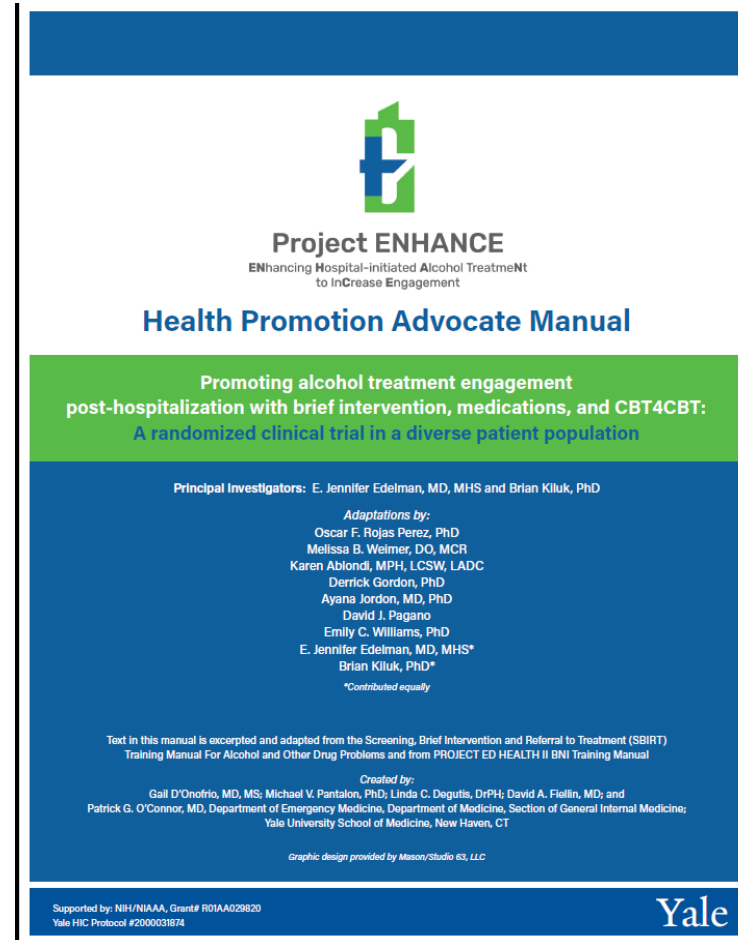
CHALLENGE #3: STAFFING

- New contexts may require extra training for experienced coordinators
- “Interventionist” buy-in may be variable
- Life happens – sickness, vacation, job transitions!



RESPONSE #3: PREVENT AND PREPARE FOR STAFFING

- Detailed manuals (MOPs), update as you go
- Checklist for onboarding new staff
- Record training sessions + couple with role play/quizzes
- Participate in staff selection as possible and assess “buy-in” and address concerns
- Build in back-up with cross-training



The image shows the cover of a manual titled "Health Promotion Advocate Manual". At the top is a blue header bar. Below it is a white section containing the Project ENHANCE logo, which is a green and blue stylized cross. The text reads "Project ENHANCE" and "ENhancing Hospital-initiated Alcohol Treatment to InCrease Engagement". Below this is the title "Health Promotion Advocate Manual" in blue. A green horizontal bar contains the text "Promoting alcohol treatment engagement post-hospitalization with brief intervention, medications, and CBT4CBT: A randomized clinical trial in a diverse patient population". The bottom section is blue and lists the Principal Investigators: E. Jennifer Edelman, MD, MHS and Brian Kiluk, PhD. It also lists Adaptations by: Oscar F. Rojas Perez, PhD; Melissa B. Welmer, DO, MCR; Karen Ablondi, MPH, LCSW, LADC; Derrick Gordon, PhD; Ayana Jordan, MD, PhD; David J. Pagano; Emily C. Williams, PhD; E. Jennifer Edelman, MD, MHS*; and Brian Kiluk, PhD*. A note says "*Contributed equally". At the bottom, it states "Text in this manual is excerpted and adapted from the Screening, Brief Intervention and Referral to Treatment (SBIRT) Training Manual For Alcohol and Other Drug Problems and from PROJECT ED HEALTH II BNI Training Manual". It also lists "Created by:" Gail D'Onofrio, MD, MS; Michael V. Pantalon, PhD; Linda C. Degutis, DrPH; David A. Fiellin, MD; and Patrick G. O'Connor, MD, Department of Emergency Medicine, Department of Medicine, Section of General Internal Medicine; Yale University School of Medicine, New Haven, CT. At the very bottom, it says "Graphic design provided by Mason/Studio 63, LLC".

Project ENHANCE
ENhancing Hospital-initiated Alcohol Treatment
to InCrease Engagement

Health Promotion Advocate Manual

Promoting alcohol treatment engagement
post-hospitalization with brief intervention, medications, and CBT4CBT:
A randomized clinical trial in a diverse patient population

Principal Investigators: E. Jennifer Edelman, MD, MHS and Brian Kiluk, PhD

Adaptations by:
Oscar F. Rojas Perez, PhD
Melissa B. Welmer, DO, MCR
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Yale University School of Medicine, New Haven, CT

Graphic design provided by Mason/Studio 63, LLC

Supported by: NIH/NIAAA, Grant# R01AA029820
Yale HIC Protocol #2000031874

Yale

CHALLENGE #4:
INTERVENTIONISTS
DO NOT ALWAYS
FOLLOW
PROTOCOL



RESPONSE #4: FACILITATE PROTOCOL ADHERENCE AND BUILD IN FIDELITY MONITORING AND LEARNING COLLABORATIVES

The screenshot displays a medical chart review interface. At the top, there are navigation tabs: SnapShot, Chart Review (selected), Review Flowsheets, Results Review, Synopsis, History, Allergies, Problem List, Medications, Immunizations, and Demographics. Below this is a sub-menu for 'Chart Review' with tabs: Encounters (selected), SnapShot, Surgeries, Consents, Notes, Media, Results Review, Labs, Micro, Genomics, Path, and Blood Bank. A toolbar contains various actions: Preview, Refresh (6:50 AM), Select All, Deselect All, Review Selected, Side-by-Side, Lifetime, Flowsheet, Route, and Load Record. A filters section includes checkboxes for Default filter, Me, Infectious Diseases, Yale Center for Infection, Admissions, Telephone Encounters, Exclude Scan Doc, and Phone. A yellow warning banner states: 'Not all records have been loaded and sorted. Load remaining records to sort all records.' Below this is a table with columns: B..., S..., When, Type, Enc Detail, With, Description, and Status. One row is visible for 12/15/2023, Clinical Support, PHARMACY RET..., Inf Disease - Thayer, B, Tobacco use disorder..., and Signed. Below the table is a 'Progress Notes' section for Thayer, Bailey, PharmD (F). The note title is 'SMARTTT: Follow-Up Visit (Weeks 13 to 24) - Med and CM'. The text includes: Research Coordinator: Renee Capasso; Clinical Pharmacist: Bailey Thayer, PharmD; 11/3/2023; Patient randomization group: Group 2C: NRT and CM+ (Intensified, Weeks 13-24) Note: only for those previously in Group 1A; Visit Number: Week 20 (Visit 9); Yale ID 120. A red note states: 'This visit was recorded and the recording was shared with the coordinating center: no - completed via telehealth'. The note is structured into two steps: Step 1: Introduction, and Step 2: Review tobacco use with the patient. Step 1 includes: Re-Introduction of clinical pharmacist and explanation of role to the patient; and Discuss goals of sessions are to help the patient stop smoking by using medications and by having the opportunity to earn rewards. Step 2 includes: Patterns of tobacco use: Has the patient smoked even a puff in the last 7 days? none; Current nicotine use is: none; Patient reports she cannot recall exact quit date but believes it was around 11/28/23. Baseline nicotine use: 10+ newport menthols; A breath CO test was not performed at the visit today given tele health; # of draws this week and corresponding prizes (if applicable): 5. Prizes listed: Prize 1: medium \$20, Prize 2: medium \$20, Prize 3: medium \$20, Prize 4: medium \$20, Prize 5: medium \$20, TOTAL = \$100. Does the patient smoke marijuana? yes. Patient's stressors and triggers of use: Patient reports the following triggers: First one in the morning.

RESPONSE #4:
 FACILITATE
 PROTOCOL
 ADHERENCE AND
 BUILD IN
 FIDELITY
 MONITORING
 AND LEARNING
 COLLABORATIVES

SMARTTT: Adherence measures for rating recordings

Recording # _____ Session # _____
 Date: ____/____/____
 Clinical pharmacist: _____
 Participant ID: _____

Rater: _____
 Start time: _____
 Stop time: _____
 Session duration: ____ min.

1. To what extent did the clinical pharmacist discuss self-report of tobacco use?

Quantity: 1.....2.....3.....4.....5.....6.....7
 Not at all Negligible Infrequent Somewhat Quite a bit Considerable Extensive
 Quality: 1.....2.....3.....4.....5.....6.....7
 Very poor Poor Barely acceptable Acceptable Good Very Good Excellent

2. Did the clinical pharmacist state how many draws were earned at this session?

Quantity: 1.....4.....7
 No Patient drew, but Yes
 # was unclear
 Quality: 1.....2.....3.....4.....5.....6.....7
 Very poor Poor Barely acceptable Acceptable Good Very Good Excellent

3. Did the clinical pharmacist state how many draws would be earned at the next session if the patient is abstinent from tobacco?

Quantity: 1.....4.....7
 No Draws mentioned Yes
 but # was unclear
 Quality: 1.....2.....3.....4.....5.....6.....7
 Very poor Poor Barely acceptable Acceptable Good Very Good Excellent

4. To what extent did the clinical pharmacist assess the patient's desire for rewards

Quantity: 1.....2.....3.....4.....5.....6.....7
 Not at all A little Infrequent Somewhat Quite a bit Considerable Extensive
 Quality: 1.....2.....3.....4.....5.....6.....7
 Very poor Poor Barely acceptable Acceptable Good Very Good Excellent

5. To what extent did the clinical pharmacist express enthusiasm for the patient's reward earnings?

Quantity: 1.....2.....3.....4.....5.....6.....7
 Not at all A little Infrequent Somewhat Quite a bit Considerable Extensive
 Quality: 1.....2.....3.....4.....5.....6.....7
 Very poor Poor Barely acceptable Acceptable Good Very Good Excellent

RESPONSE #4:
FACILITATE
PROTOCOL
ADHERENCE AND
BUILD IN
FIDELITY
MONITORING
AND LEARNING
COLLABORATIVES

- Build in structures to facilitate protocol adherence and with input (or even better created) by the interventionists from the beginning
- Address any potential biases up front, invite questions
- Regular calls with site interventionists and coordinating center team to review:
 - fidelity monitoring findings and give feedback
 - discuss shared experiences and co-learning
 - insights into challenges with intervention delivery
- Use lessons learned to inform future implementation work
- Turn gaps into advocacy

RESPONSE #4: PROTOCOL GAPS AS OPPORTUNITIES TO ADVOCATE

ORIGINAL RESEARCH

Discordance Between Insurance Coverage of Antiviral Medications and Nicotine Replacement Therapy Among Individuals With Human Immunodeficiency Virus Who Smoke

Steven L. Bernstein, MD, Jessica E. Yager, MD, MPH, Keith Sigel, MD, PhD, Elizabeth Porter, MBA, Tina Do, PharmD, MS, Erika Payne, PharmD, Krysten Bold, PhD, David Ledgerwood, PhD, and E. Jennifer Edelman, MD, MHS

Introduction: Tobacco contributes to the leading causes of morbidity and mortality among persons with human immunodeficiency virus (PWHs). Nonetheless, medications for tobacco use disorder are widely underused, particularly among PWHs. We sought to characterize the extent to which insurance barriers impacted access to medications for tobacco use disorder and, in comparison, to access to antiretroviral therapy (ART).

This may undermine the efficacy of antivirals. Mandated insurance coverage of nonprescription NRT may improve the health of PWHs who smoke.

Key Words: smoking cessation, HIV, antiviral medication, insurance coverage, tobacco use disorder, tobacco free

(*J Addict Med* 2024;00: 00–00)

STATE OF CONNECTICUT
DEPARTMENT OF PUBLIC HEALTH



Manisha Juthani, MD
Commissioner

Ned Lamont
Governor
Susan Bysiewicz
Lt. Governor

TB, HIV, STD, and Viral Hepatitis Section

November 8, 2022

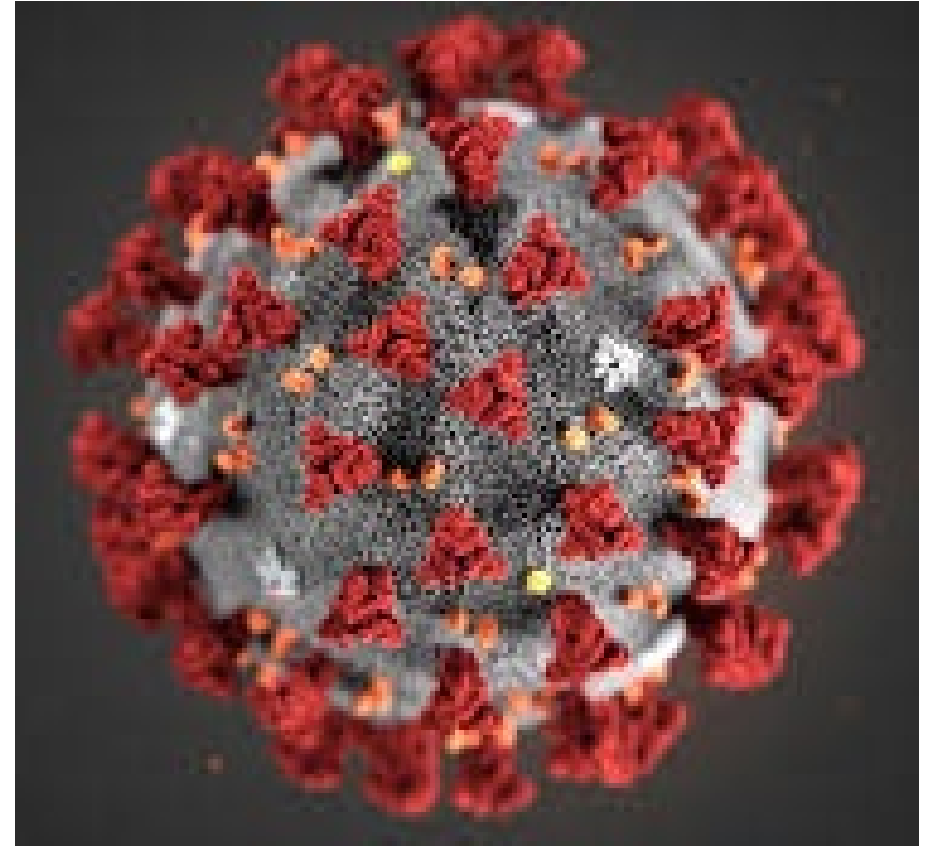
Dear Ryan White and HIV Care Providers,

The Connecticut AIDS Drug Assistance Program (CADAP) Clinical Advisory Board convened on October 27th, 2022 and reviewed the CADAP formulary, formulary addition requests, and prior authorization criteria. The Clinical Advisory Board voted by consensus to approve the following additions to the CADAP formulary:

Formulary Additions Effective November 7, 2022

Nicotine Replacement Therapy/Substance Use Treatment	Diabetes Treatments	Respiratory	Ophthalmic
Nicotine Patches	Glimepiride	Spiriva Handihaler	Xiidra
Nicotine Lozenges	GLP-1 Agonists • Victoza • Bydureon Bcise • Ozempic	Albuterol Nebulized Solution	Restasis
Nicotine Gum	SGLT-2 Inhibitors • Invokana, Invokamet, Invokamet XR • Jardiance, Synjardy, Synjardy XR • Farxiga, Xigduo XR • Steglatro, Segluromet	Symbicort Advair HFA	Alphagan P

CHALLENGE #5: UNEXPECTED DISRUPTIONS



RESPONSE #5: STAY MISSION DRIVEN



Be realistic



Use infrastructure to gain relevant insights



Revisit ability to meet recruitment targets and impact on study goals



Modify protocol as needed, publish protocol papers



Report transparently and capture systematically (clinicaltrials.gov, FRAMES)



Engage stakeholders – funders, team members



Get external input (e.g., data safety monitoring board)


RESPONSE #5: STAY MISSION DRIVEN

AIDS and Behavior (2022) 26:2099–2111
<https://doi.org/10.1007/s10461-021-03556-7>

ORIGINAL PAPER




Experiences with Telemedicine for HIV Care During the COVID-19 Pandemic: A Mixed-Methods Study

Dini Harsono¹  · Yanhong Deng² · Sangyun Chung² · Lydia A. Barakat³ · Gerald Friedland^{1,3,8} · Jaimie P. Meyer^{1,3,4} · Elizabeth Porter⁵ · Merceditas Villanueva^{1,3} · Michael S. Wolf⁶ · Jessica E. Yager⁷ · E. Jennifer Edelman^{1,5}

AIDS and Behavior
<https://doi.org/10.1007/s10461-023-04170-5>

ORIGINAL PAPER

Prevalence and Correlates of Physical Inactivity Among Individuals with HIV During the First COVID-19 Wave: A Cross-sectional Survey

Dini Harsono¹  · Yanhong Deng² · Sangyun Chung² · Lydia A. Barakat³ · Gerald Friedland^{1,3,4} · Merceditas Villanueva^{1,3} · Jessica E. Yager^{1,6} · Marissa Justen⁷ · E. Jennifer Edelman^{1,5}

Accepted: 8 September 2023
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RESPONSE #5: STAY MISSION DRIVEN

Table 4
Protocol modifications due to COVID-19.

	Original protocol	Proposed COVID-19 modifications
Consent Assessments	<ul style="list-style-type: none"> • In-person • In-person; • Clinical pharmacist collects eCO if relevant for a CM visit; otherwise research coordinator collects eCO if assessment visit 	<ul style="list-style-type: none"> • In-person or telephone-based • In-person, using coVita OneBreath™ piece; • Participant is remote with videoconference and Covita iCO smokerylzers; • Participant in clinic using videotechnology to have visit with research coordinator located remotely; clinic staff facilitate eCO collection
Intervention visits	<ul style="list-style-type: none"> • In clinic with clinical pharmacists 	<ul style="list-style-type: none"> • In-clinic with study physician or research coordinator; • Participant in clinic using videotechnology to have visit with clinical pharmacist remotely • Participant on videoconference and remote
Contingency management	<ul style="list-style-type: none"> • Fishbowl with participant draws 	<ul style="list-style-type: none"> • In person- participant or research team member draws with gloves • Participant on videoconference and watches clinical pharmacist draw from fishbowl
Gift cards and CM rewards	<ul style="list-style-type: none"> • Gift cards given directly and immediately after rewards earned 	<ul style="list-style-type: none"> • Mail gift cards or reloadable debit card

Among 320 (632) PWH who smoke and are receiving care in one of three health systems HIV clinics:

- **Aim 1.** To identify the optimal adaptive intervention to promote confirmed smoking reduction (eCO-confirmed abstinence).
- **Aim 2.** To identify the impact of various tobacco treatment regimens (NRT, oral meds, CM) on HIV-related biomarkers over time, including promoting improvements in: 1) CD4 count; 2) HIV viral load suppression; and 3) VACS Index scores.

Among key stakeholders, including participants, clinicians, staff, and leadership at each site:

- **Aim 3.** To conduct an implementation-focused evaluation of a clinical pharmacist-delivered intervention involving nicotine replacement therapy, oral tobacco treatment medication, and contingency management

RESPONSE #5: TRACK AND REPORT SYSTEMATICALLY

Wiltsey Stirman et al. *Implementation Science* (2019) 14:58
<https://doi.org/10.1186/s13012-019-0898-y>

Implementation Science

DEBATE

Open Access

The FRAME: an expanded framework for reporting adaptations and modifications to evidence-based interventions


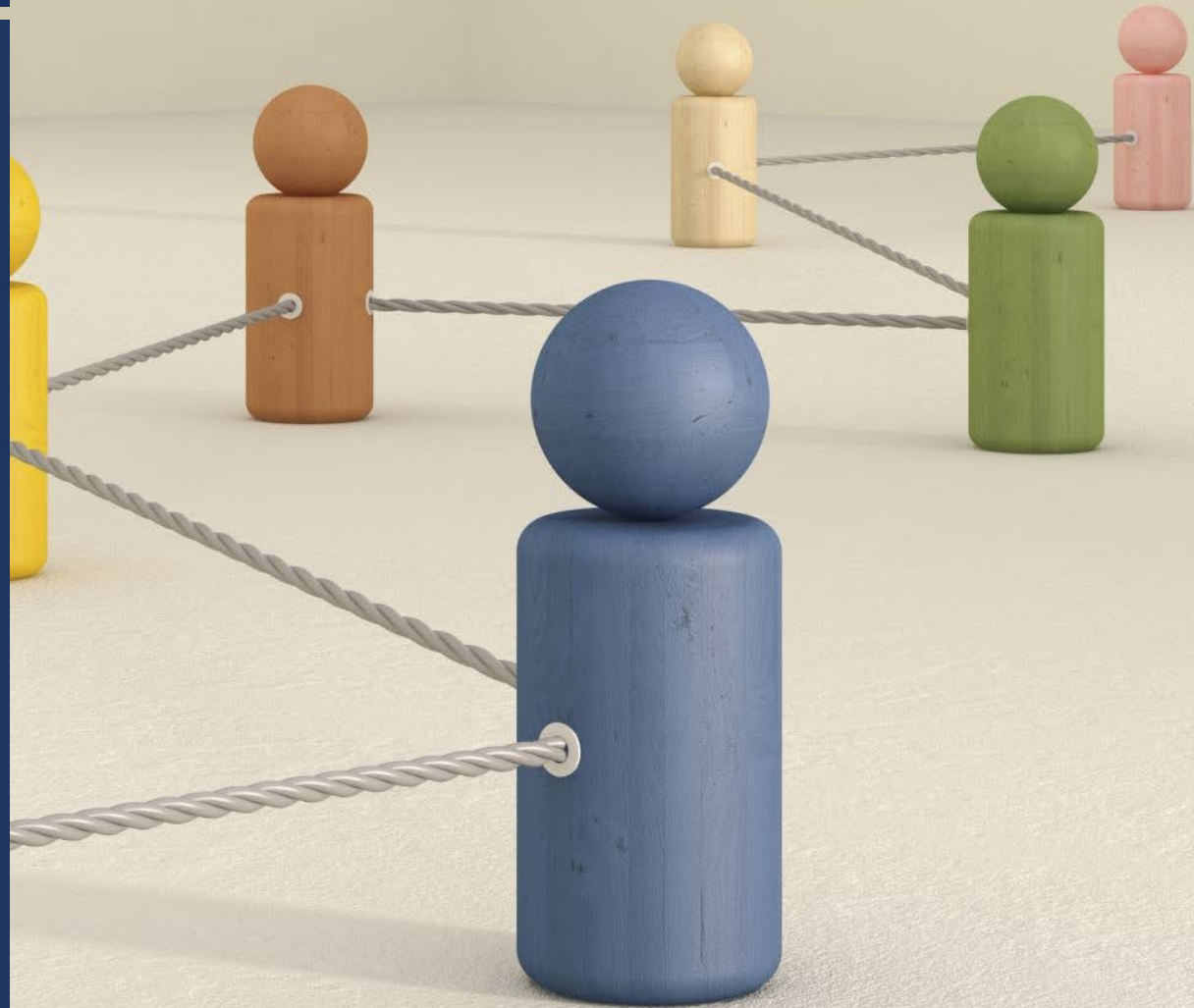
Shannon Wiltsey Stirman^{1*} , Ana A. Baumann² and Christopher J. Miller^{3,4}



Table 1. Project ENHANCE protocol modifications by FRAME domains

What was the level of the modification?	What was modified?	When was the modification made?	Why was the modification made?	What was the modification?
Recipient	Entry criterion	Prior to study launch	Minimize risk of excluding individuals most likely to be impacted by structural racism	Narrowed exclusion criteria from <i>anticipated being unable to complete assessments for any reasons including incarceration to excluding if specifically currently in jail, prison or other overnight facility as required by court of law and/or is considered a prisoner under local law or is under current terms of civil commitment or guardianship</i>
	Recruitment strategies	Prior to study launch and refined iteratively	Optimize recruitment of eligible participants across ethnic and racial groups and improve enrollment/approach ratio	<i>Epic-based reports of potentially eligible participants for research coordinator-driven screening in pairing with routine, clinically-driven AUDIT-C* screening and CIWA** protocols.</i>

CHALLENGE #6:
COMMUNITY
MISTRUST



RESPONSE #6: COMMUNICATE AND SHARE RESOURCES AND KNOWLEDGE



CREATE OPPORTUNITIES FOR
MUTUAL LEARNING



SHARE RESOURCES, INCLUDING
FUNDING



BE PRESENT AND
COMMUNICATE



INVITE TO PARTICIPATE IN
DISSEMINATION ACTIVITIES AND
SHARE FINDINGS WITH
PARTICIPANTS AND PARTNERS

SUMMARY

- Research is messy, there will be challenges along the way
- Build in mini-PDSA cycles within research processes and use this to iterate processes and inform next steps
- Sharing these experiences
- Celebrate successes!