PROMOTING ADDICTION TREATMENT IN HIV CLINICS INFORMED BY IMPLEMENTATION SCIENCE

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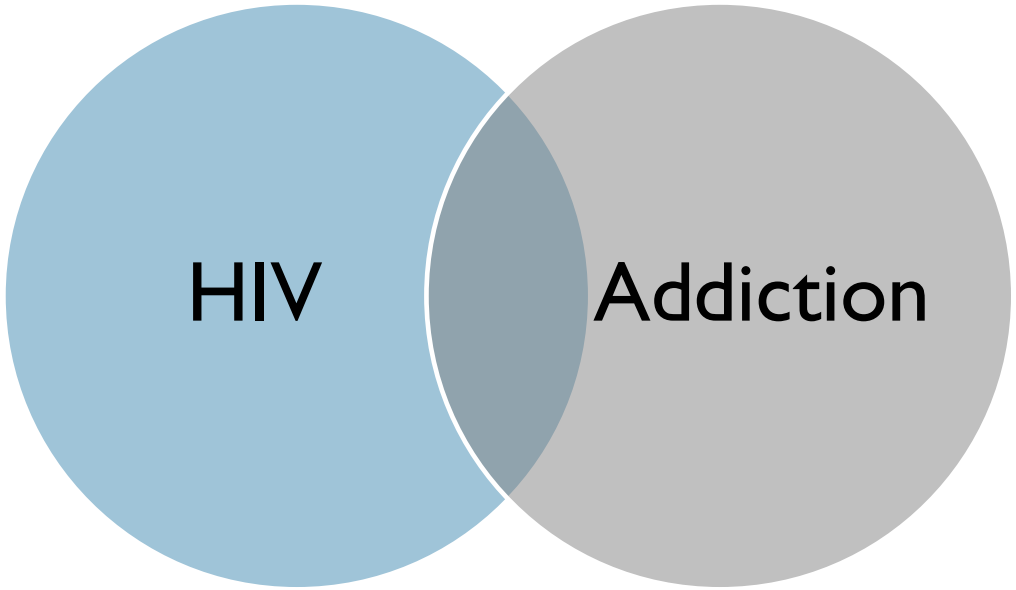
GIFT SUMMER BOOTCAMP

JULY 10, 2024

DISCLOSURES

- No conflicts of interest to disclose
- Funding from National Institutes of Health
- My lens



OUTLINE

What's the problem?

- Epidemiology
- Gaps in treatment services

Integrating addiction and HIV treatment

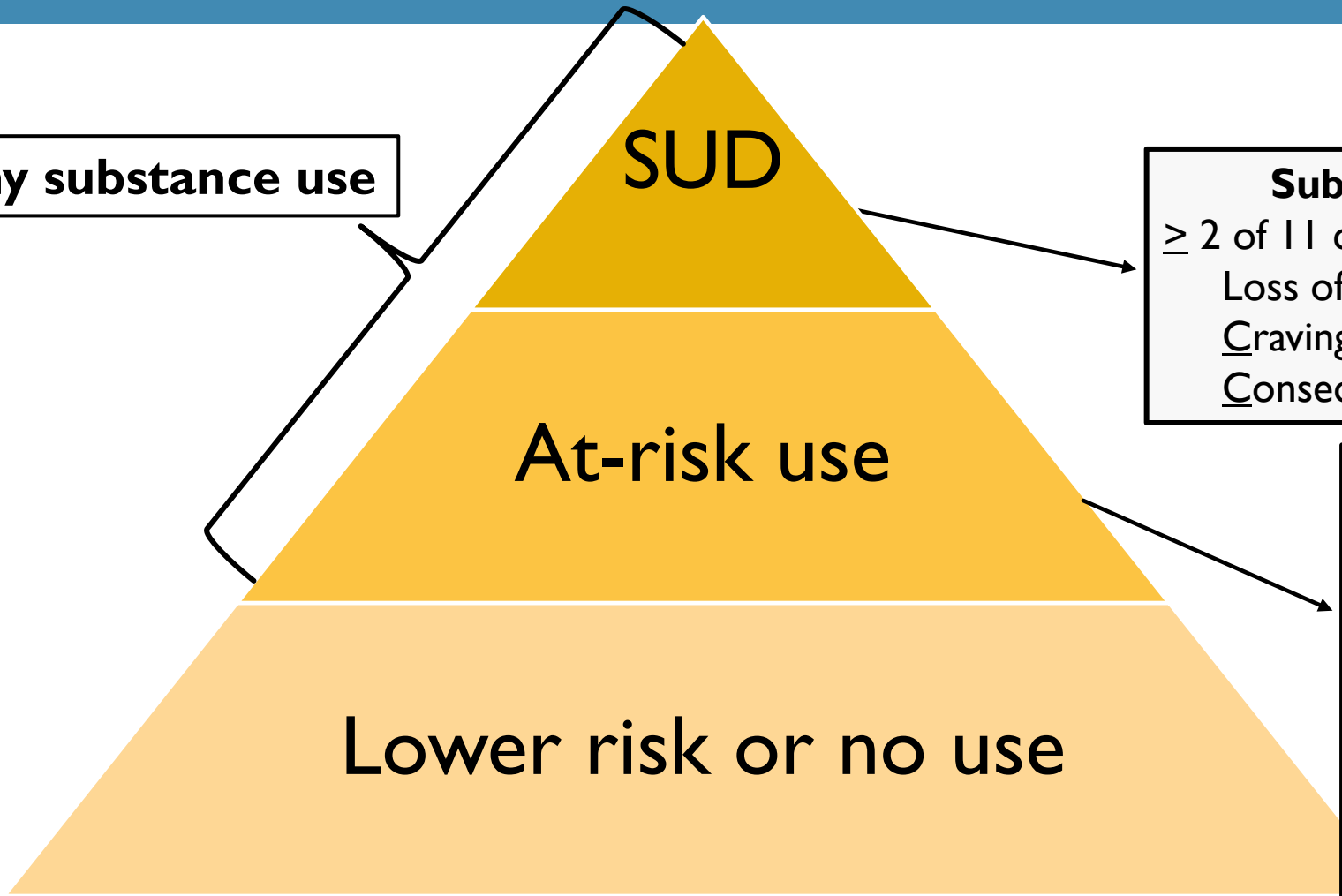
- STEP Trials
- WHAT-IF?
- SMARTTT

Current and future directions

- Mateo…
- Moving beyond HIV clinical settings

UNHEALTHY SUBSTANCE USE

Unhealthy substance use



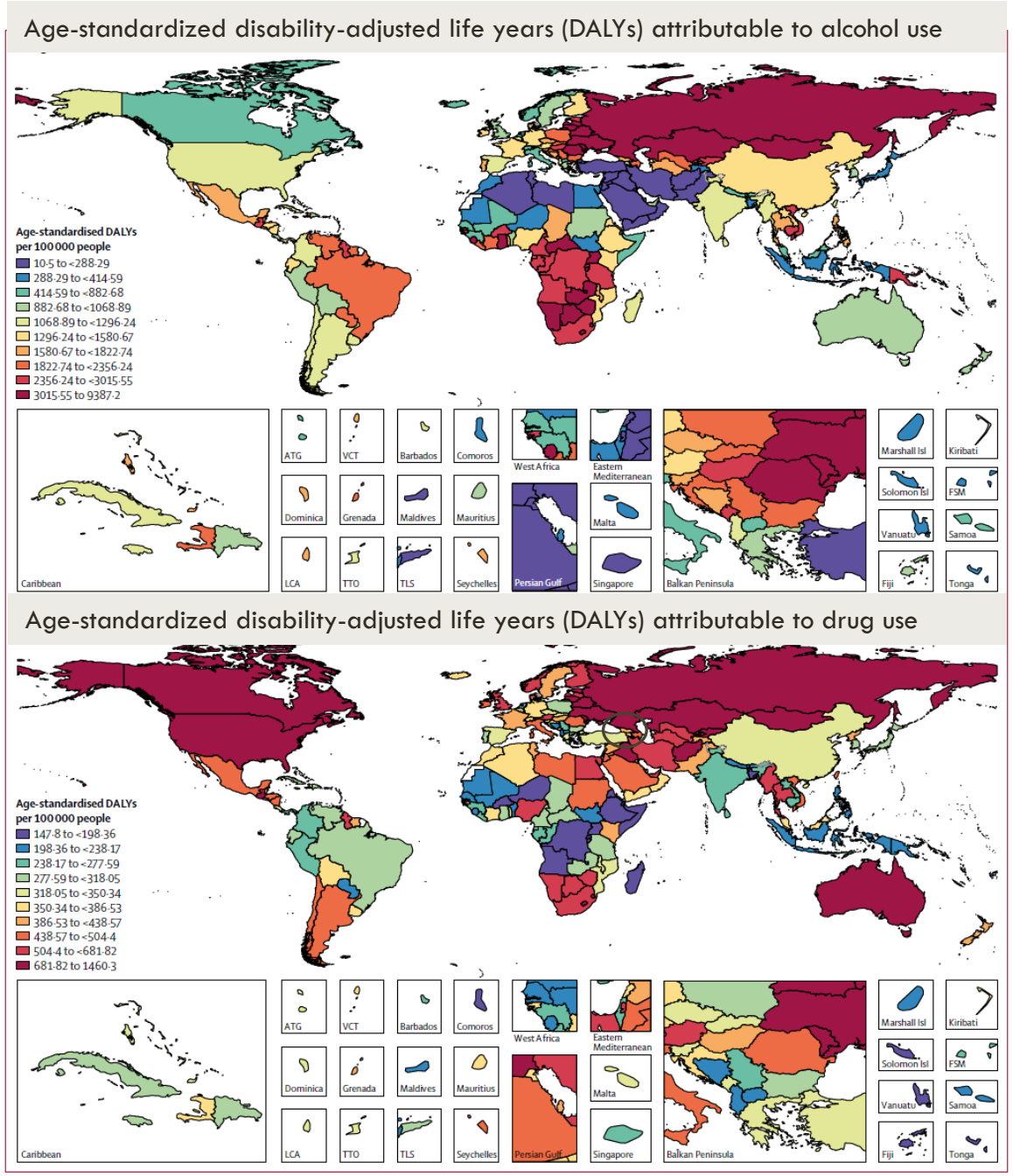
Substance Use Disorder:
≥ 2 of 11 criteria in past year:
- Loss of Control
- Craving, withdrawal, tolerance
- Consequences

At-Risk (Risky) Use:
Alcohol:
- Men ≤65 yo:
  - >4 drinks/occasion
  - >14 drinks/week
- Women and men >65 yo:
  - >3 drinks/occasion
  - >7 drinks/week

Drugs: any use

Saitz *NEJM* 2005

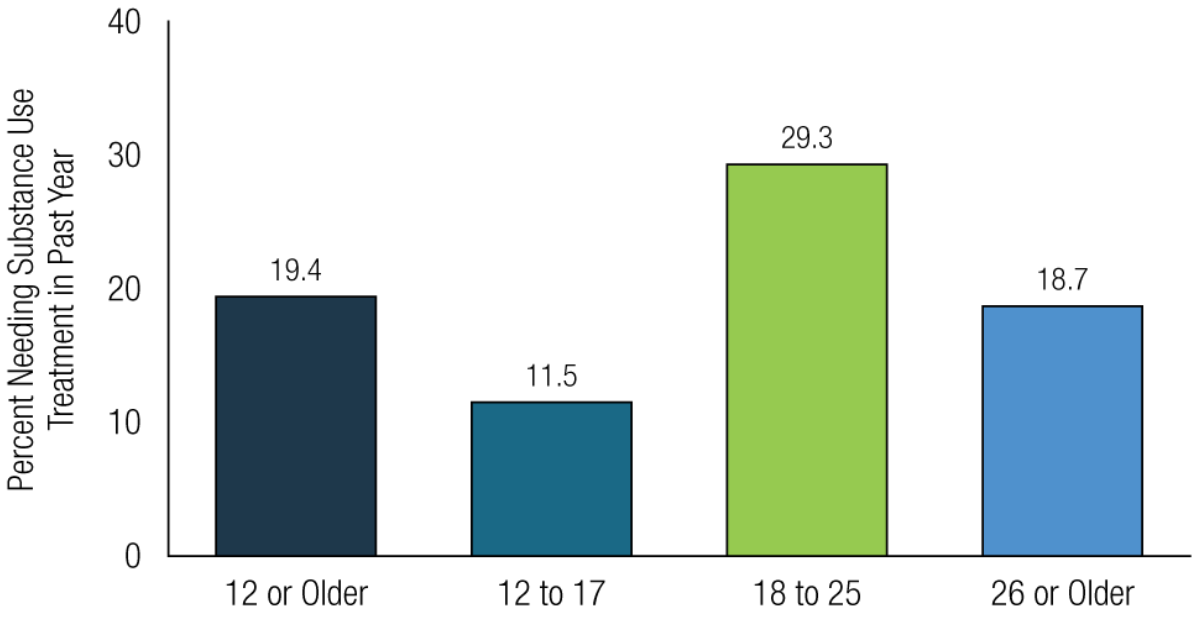
Global burden of disease attributable to alcohol and drug use is significant



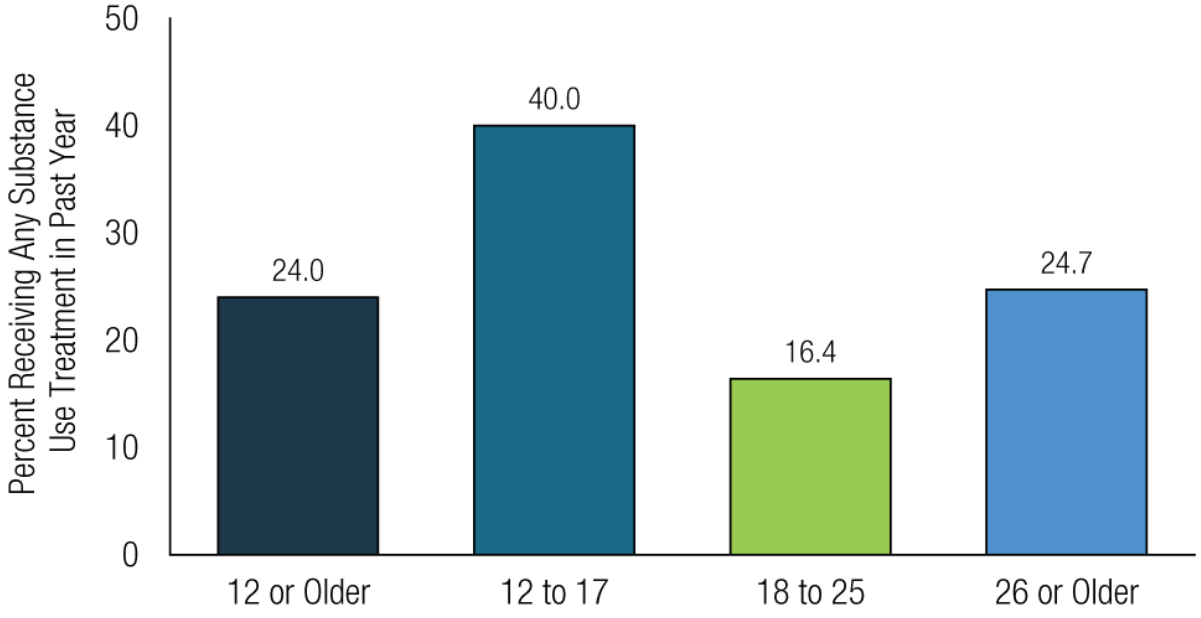
GBD 2016 Alcohol and Drug Use Collaborators *Lancet Psychiatry* 2016

LARGE UNMET NEED FOR SUBSTANCE USE DISORDER TREATMENT
AMONG INDIVIDUALS AGED ≥12 YEARS OLD

Need for substance use treatment, past year



Received any substance use treatment in the past year among those who had a substance use disorder in the past year

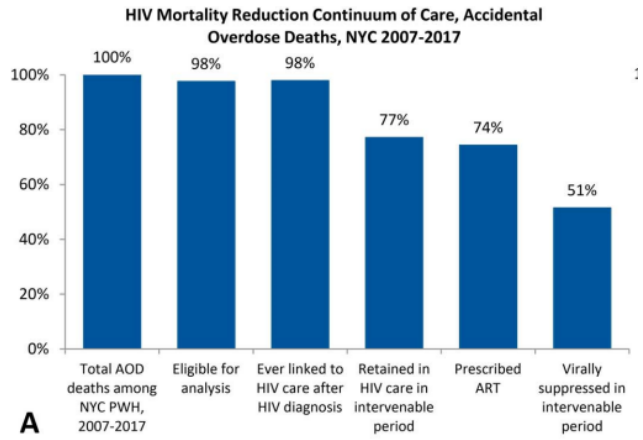


National Survey on Drug Use and Health, 2022

BRIEF REPORT: EPIDEMIOLOGY

Drug Overdose Deaths Among People With HIV in New York City, 2007–2017

Sarah L. Braunstein, PhD, MPH,[a] Rebekkah S. Robbins, MPH,[a] Chitra Ramaswamy, MBBS, DcGO, MPH,[a] and Demetre C. Daskalakis, MD, MPH[b]



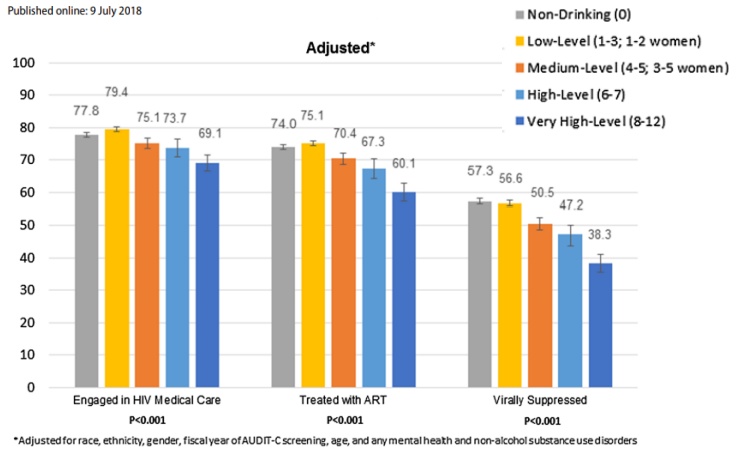
AIDS and Behavior (2019) 23:140–151
https://doi.org/10.1007/s10461-018-2210-6

ORIGINAL PAPER

Level of Alcohol Use Associated with HIV Care Continuum Targets in a National U.S. Sample of Persons Living with HIV Receiving Healthcare

Emily C. Williams[1,2] · Kathleen A. McGinnis[3] · E. Jennifer Edelman[4] · Theresa E. Matson[1,5] · Adam J. Gordon[6,7] · Brandon D. L. Marshall[8] · Kendall J. Bryant[9] · Anna D. Rubinsky[10] · Gwen T. Lapham[1,5] · Derek D. Satre[11,12] · Julie E. Richards[2,5] · Sheryl L. Catz[13] · David A. Fiellin[3,4] · Amy C. Justice[3,4] · Katharine A. Bradley[1,2,5,14,15]

Published online: 9 July 2018

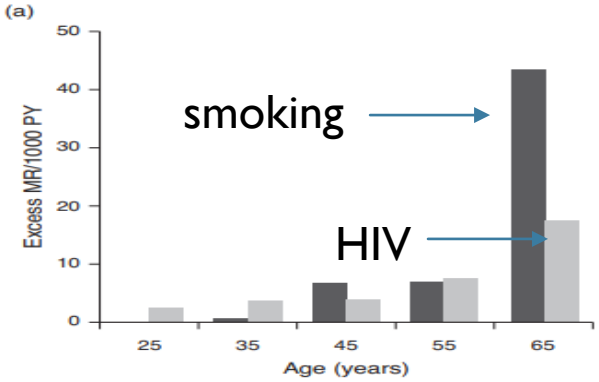


*Adjusted for race, ethnicity, gender, fiscal year of AUDIT-C screening, age, and any mental health and non-alcohol substance use disorders

OPEN

Smoking and life expectancy among HIV-infected individuals on antiretroviral therapy in Europe and North America

Marie Helleberg[a,b], Margaret T. May[c], Suzanne M. Ingle[c], Francois Dabis[d], Peter Reiss[e], Gerd Fätkenheuer[f], Dominique Costagliola[g,h], Antonella d'Arminio[i], Matthias Cavassini[j], Colette Smith[k], Amy C. Justice[l,m], John Gill[n], Jonathan A.C. Sterne[c] and Niels Obel[a,b]



SUBSTANCE USE AMONG INDIVIDUALS WITH HIV IS CAUSE FOR PARTICULAR CONCERN

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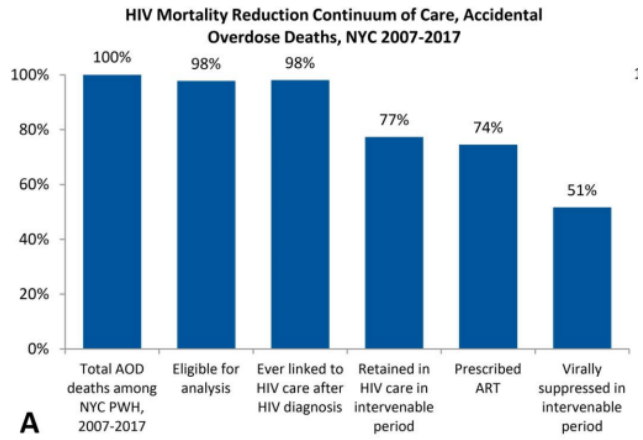

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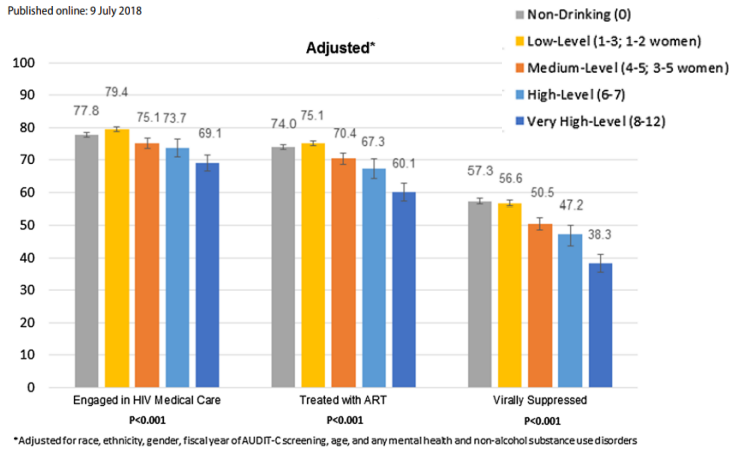

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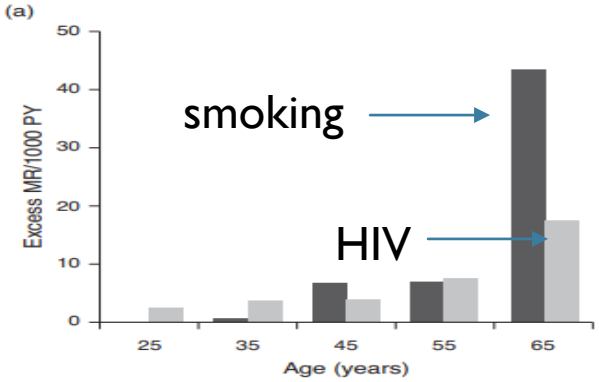

SUBSTANCE USE AMONG INDIVIDUALS WITH HIV IS CAUSE FOR PARTICULAR CONCERN

OUTCOMES ARE IMPROVED WITH INTEGRATED HIV AND OPIOID USE-RELATED CARE

Oldfield et al *AIDS* 2019

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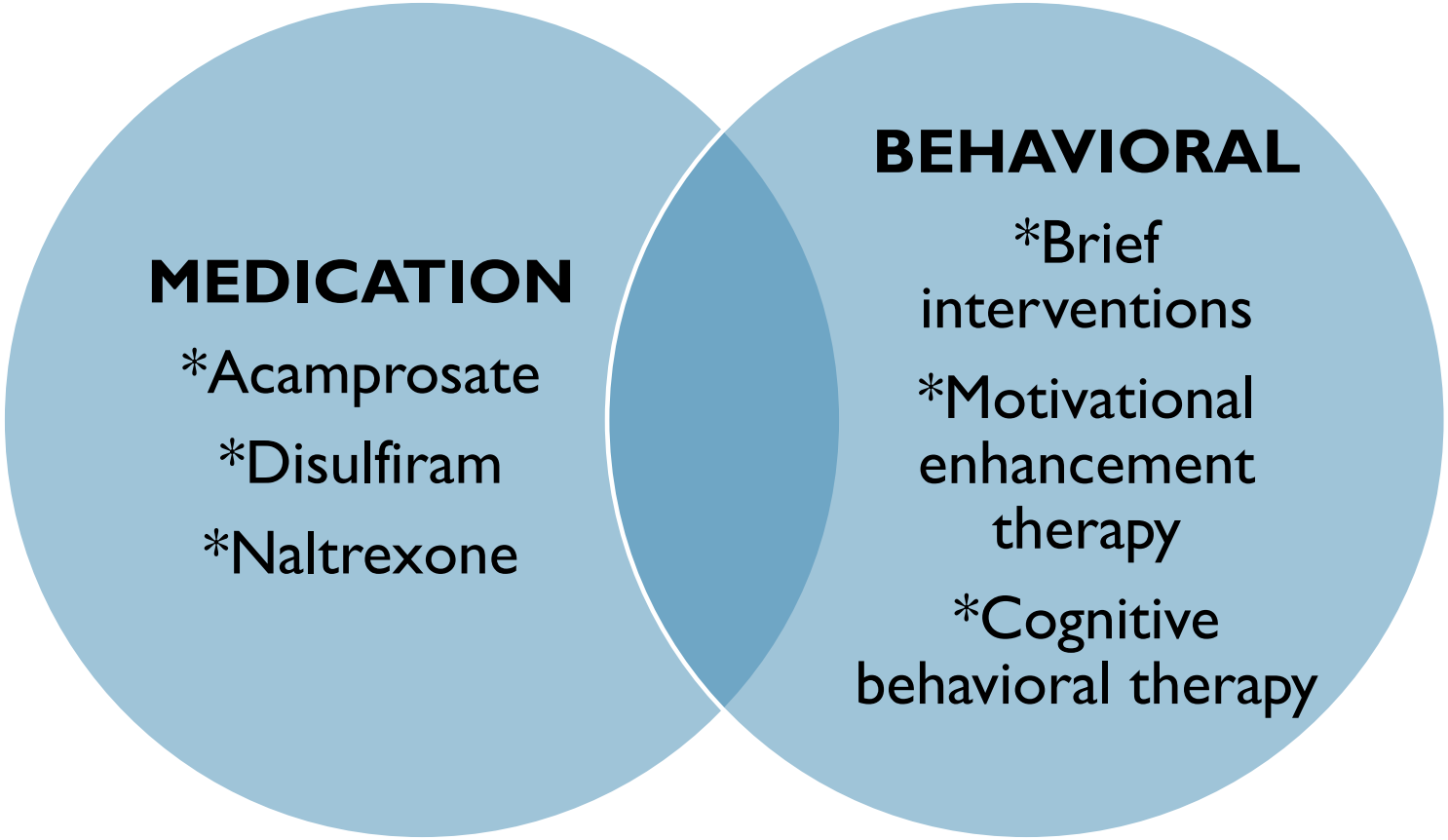
UNHEALTHY ALCOHOL USE: TREATMENT OPTIONS AVAILABLE FOR USE IN HIV CLINICS



Jonas *JAMA* 2014; Ray *JAMA Network Open* 2020

Alcoholism: Clinical and Experimental Research

Vol. 36, No. 2
February 2012

Hepatic Safety and Antiretroviral Effectiveness in HIV-Infected Patients Receiving Naltrexone

Jeanette M. Tetrault, Janet P. Tate, Kathleen A. McGinnis, Joseph L. Goulet, Lynn E. Sullivan, Kendall Bryant, Amy C. Justice, and David A. Fiellin; For the Veterans Aging Cohort Study Team

Alcoholism: Clinical and Experimental Research

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February 2012

Hepatic Safety and Antiretroviral Effectiveness in HIV-I

AIDS and Behavior (2019) 23:211–221
https://doi.org/10.1007/s10461-018-2241-z

Jea
Lynn E.

ORIGINAL PAPER

CrossMark

Efficacy of Extended-Release Naltrexone on HIV-Related and Drinking Outcomes Among HIV-Positive Patients: A Randomized-Controlled Trial

E. Jennifer Edelman[1,2,9] · Brent A. Moore[1,3] · Stephen R. Holt[1] · Nathan Hansen[2,4] · Tassos C. Kyriakides[5] · Michael Virata[1] · Sheldon T. Brown[6] · Amy C. Justice[1,3] · Kendall J. Bryant[7] · David A. Fiellin[1,2] · Lynn E. Fiellin[1,2,8]

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ORIGINAL PAPER

CrossMark

Drug and Alcohol Dependence 174 (2017) 158–170

Efficacy of
Outcomes
Trial

E. Jennifer Ede
Michael Virata

ELSEVIER

Contents lists available at ScienceDirect

Drug and Alcohol Dependence

journal homepage: www.elsevier.com/locate/drugalcdep

Full length article

Extended-release naltrexone reduces alcohol consumption among released prisoners with HIV disease as they transition to the community

CrossMark

Sandra A. Springer[a,b,*], Angela Di Paola[a], Marwan M. Azar[a], Russell Barbour[b], Archana Krishnan[c], Frederick L. Altice[a,b,d,e]

Alcoholism: Clinical and Experimental Research

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Efficacy of Outcomes Trial

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Full length article

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Sandra A. Sp
Archana Kri

ADDICTION

SSA Society for the Study of Addiction

RESEARCH REPORT

doi:10.1111/add.13753

Feasibility and safety of extended-release naltrexone treatment of opioid and alcohol use disorder in HIV clinics: a pilot/feasibility randomized trial

Philip T. Korthuis[1], Paula J. Lum[2], Pamela Vergara-Rodriguez[3], Keith Ahamad[4,5], Evan Wood[4,5], Lynn E. Kunkel[1], Neal L. Oden[6], Robert Lindblad[6], James L. Sorensen[2], Virgilio Arenas[3], Doan Ha[1], Raul N. Mandler[7] & Dennis McCarty[1] for the CTN-0055 CHOICES Investigators

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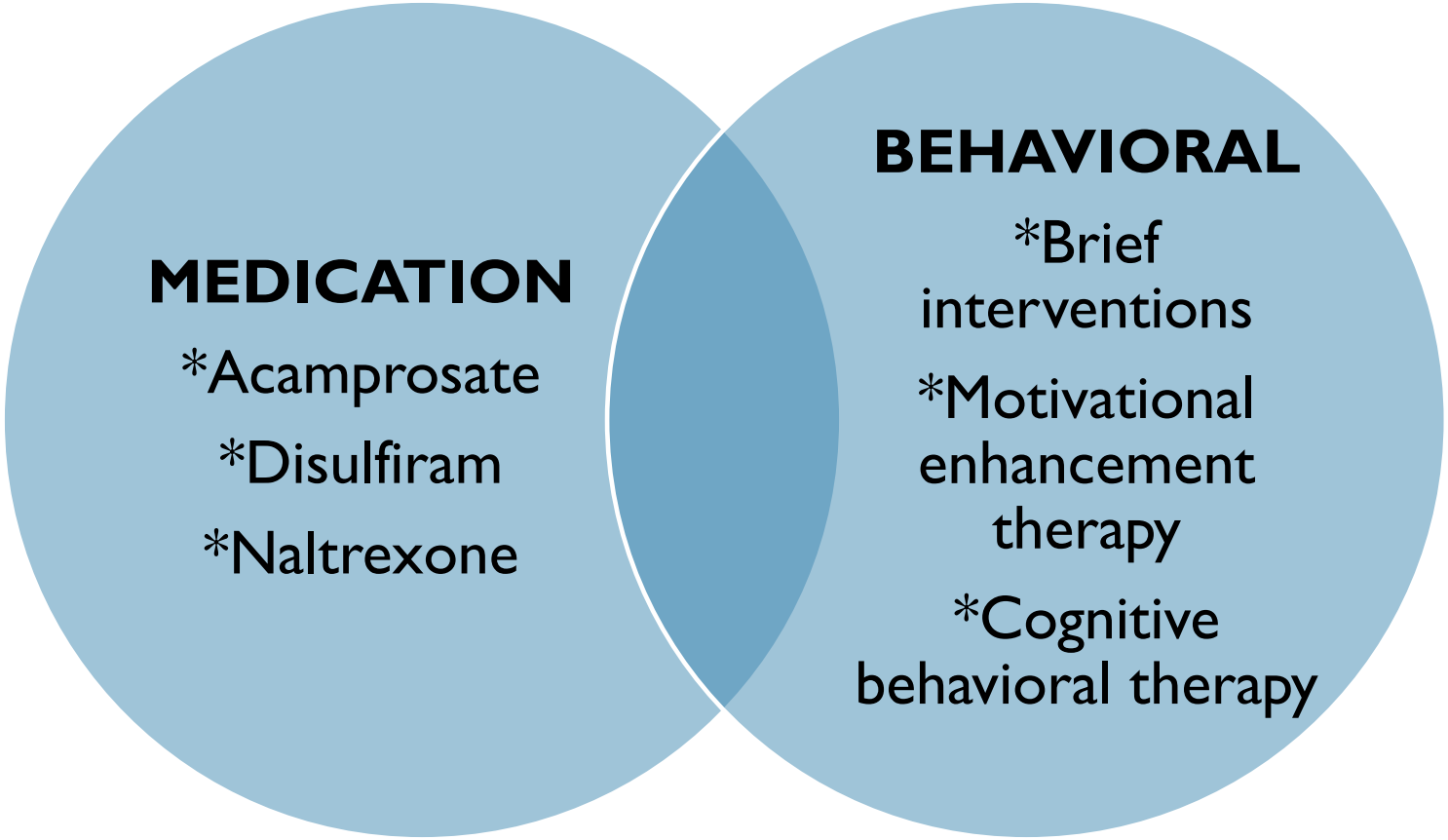
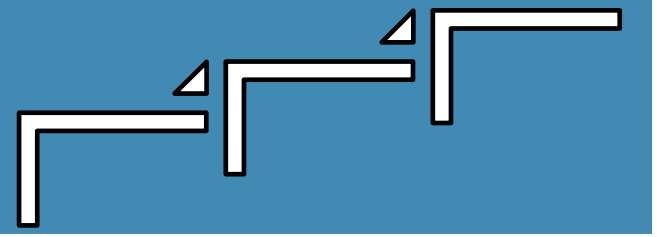


Jonas *JAMA* 2014; Ray *JAMA Network Open* 2020

STEPPED CARE MODELS



- Type of adaptative intervention, flexible, and responsive to patient needs, especially when "one size fits all approach" is not relevant
- Increase intensity of treatment services for individuals unable to reach pre-specified treatment goals
- Previously applied to common conditions (e.g., hypertension, depression, and pain)
- Minimizes demands on patients, which is particularly relevant for non-treatment seeking individuals
- Maximizes use of clinic resources while incorporating different evidence-based practices

EFFORTS TO MOVE THE NEEDLE

STARTING ETHANOL TREATMENT IN PRIMARY CARE TRIALS

STEP Trial

- Three-parallel randomized clinical trials

- To evaluate effectiveness of integrated stepped alcohol treatment (ISAT) for unhealthy alcohol use vs. treatment as usual for patients with HIV and:
  - 1. Moderate alcohol use + liver disease (hepatitis C infection, FIB-4>1.45)
  - 2. At-risk alcohol use
  - 3. Alcohol use disorder

- Five Infectious Disease Clinics within Veterans Health Administration across the United States

Edelman *CCT* 2016; Edelman *ASCP* 2017, 2019; Edelman *JSAT* 2019, Edelman *Lancet HIV* 2019: Funding #U01AA020795 - PI DA Fiellin

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INTEGRATED STEPPED ALCOHOL TREATMENT (ISAT)

STEP Trial

ADDICTION PSYCHIATRIST

Addiction physician management (medications)

PSYCHOLOGIST:

Motivational Enhancement Therapy

SPECIALTY REFERRAL

(detoxification, intensive outpatient program, etc.)

Participants "stepped up" if heavy alcohol use in the prior 14 days at week 4 or week 12 assessment.

Treatment as usual: specialty referral at the discretion of HIV clinician

Edelman *CCT* 2016; *Lancet HIV* 2019

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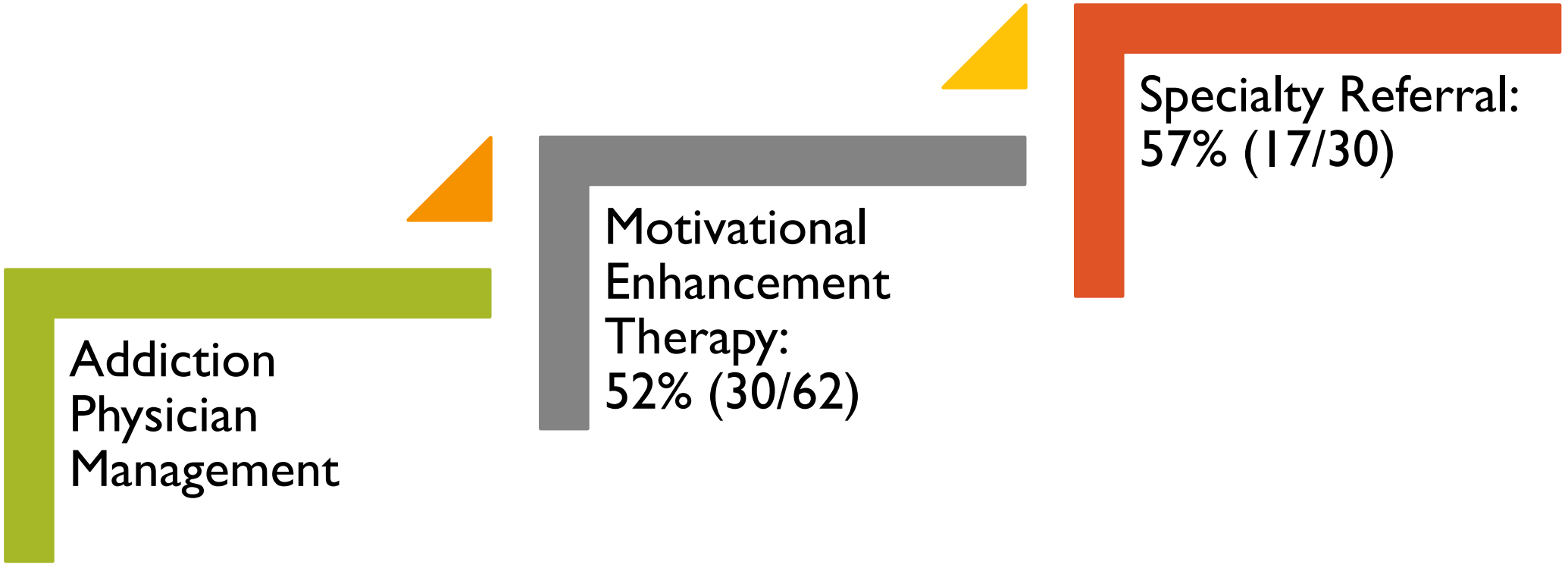
Edelman *CCT* 2016; *Lancet HIV* 2019

BASELINE PARTICIPANT CHARACTERISTICS, N=128

STEP Trial

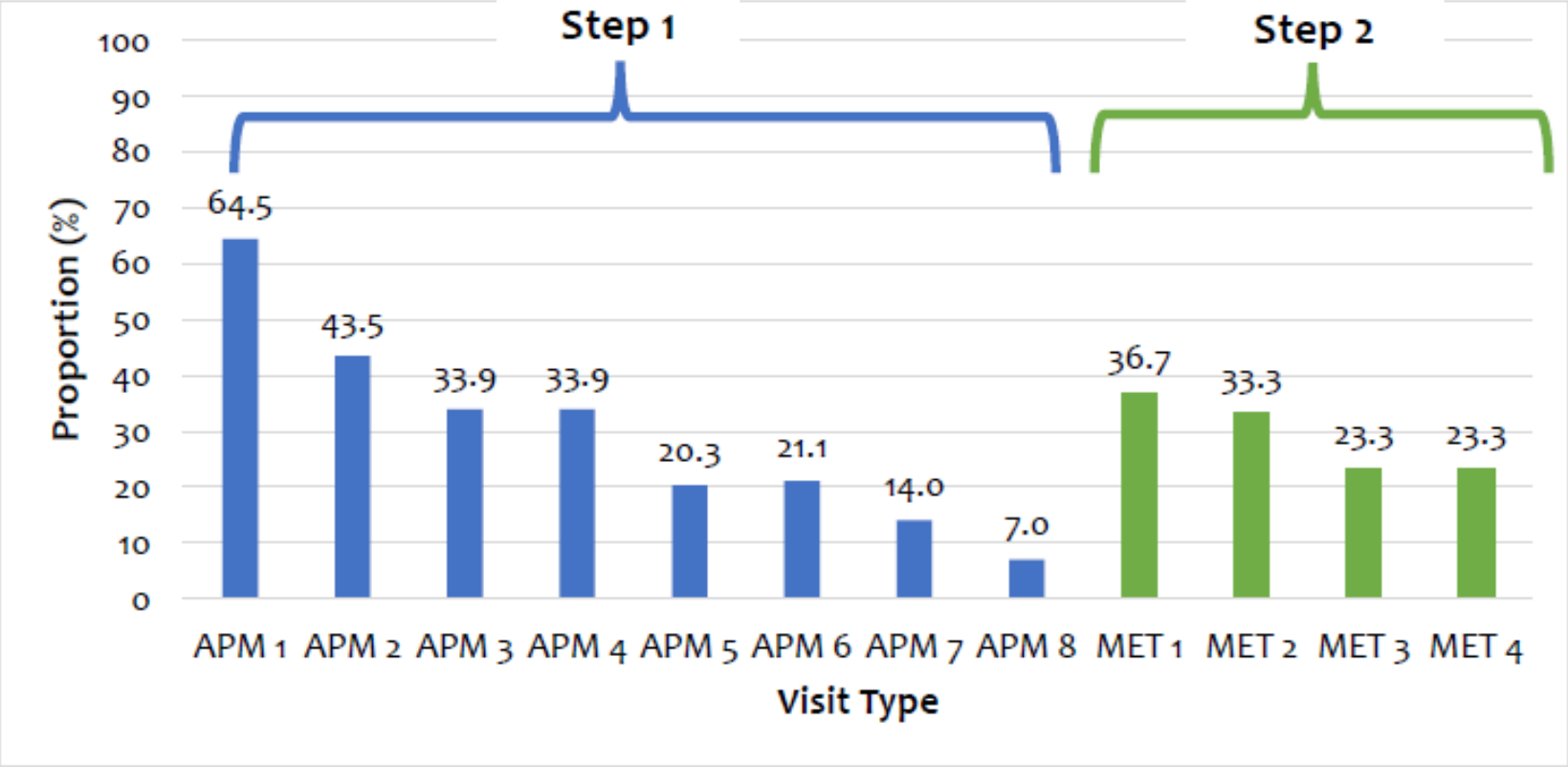
Characteristic	ISAT, N=63	TAU, N=65
Gender, male, %	98%	97%
Age, mean (SD)	56 (9)	52 (12)
Race, %		
White	19%	19%
Black	78%	80%
Other	3%	2%
Ethnicity, Hispanic, %	5%	11%
AUDIT-C, mean (SD)	7 (2)	8 (2)
Drinks per week, mean (SD)	31.3(23.5)	32.8(27.3)
HIV viral load, detectable, %	33%	37%
CD4 cell count, cells/mm^3, median (range)	590 (8 -1450)	496 (16 – 1364)

RECEIPT OF INTEGRATED STEPPED ALCOHOL TREATMENT



Edelman *CCT* 2016; *Lancet HIV* 2019

RECEIPT OF INTEGRATED STEPPED ALCOHOL TREATMENT*



Notes: Denominator based on participants eligible for visit. APM=addiction physician management; MET=motivational enhancement therapy

Edelman *CCT* 2016; *Lancet HIV* 2019

Asterisk (*): indicates among those eligible

RECEIPT OF MEDICATIONS FOR ALCOHOL USE DISORDER

STEP Trial

Medication	Integrated Stepped Alcohol Treatment, N=63	Treatment as Usual, N=65	p value
Disulfiram, %			
Baseline	0	0	
Week 24	3	0	0.24
Week 52	0	0	n/a
Acamprosate, %			
Baseline	0	0	
Week 24	10	0	**0.01**
Week 52	0	0	n/a
Naltrexone, %			
Baseline	0	2	
Week 24	32	8	**<0.001**
Week 52	6	8	1.00

Edelman *CCT* 2016; *Lancet HIV* 2019

SELF-REPORTED DRINKING OUTCOMES, PAST 30 DAYS

STEP Trial

Figure a. Drinks per week

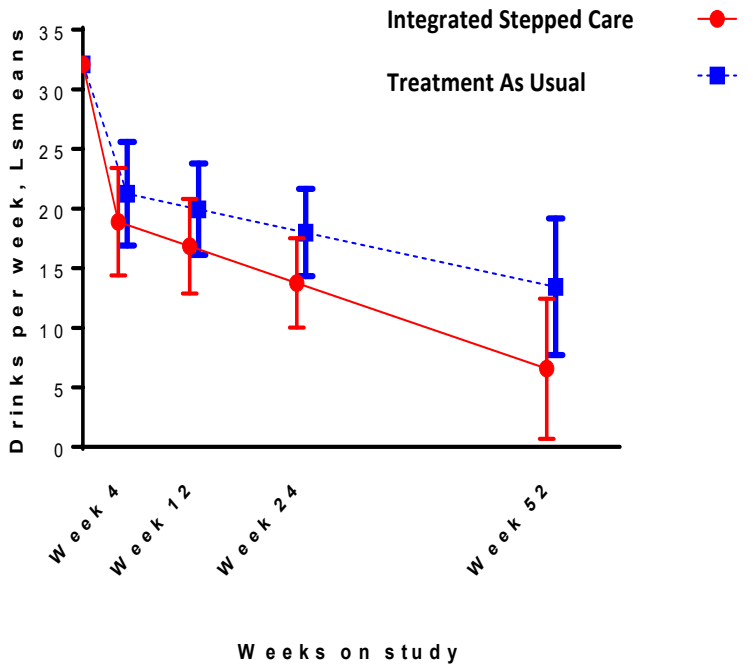
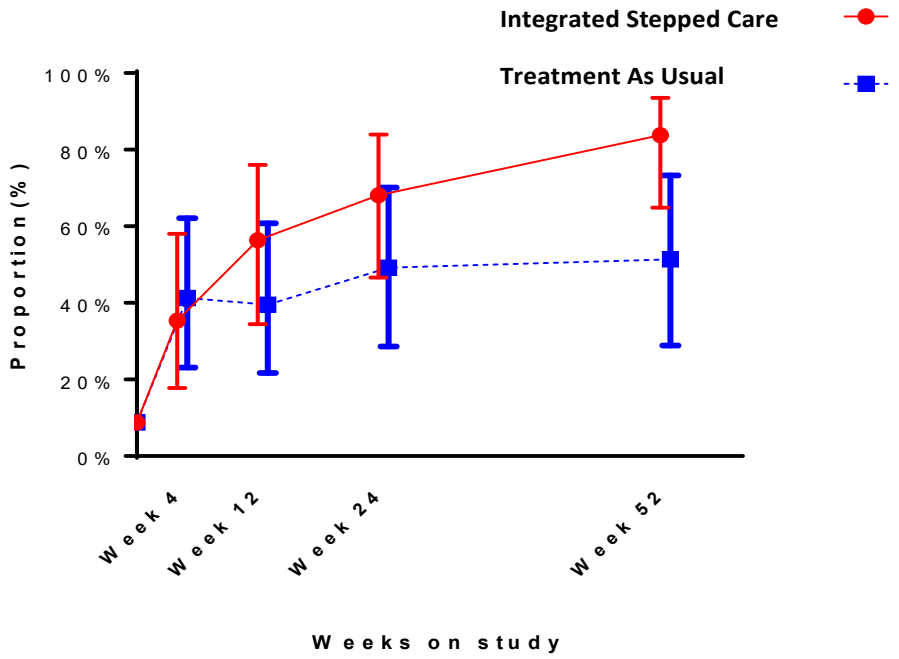


Figure b. Proportion with no heavy drinking days*



Adjusted mean difference (95% CI)
Week 24: -4.2 (-9.4, 0.9)
Week 52: -6.9 (-15.0, 1.3)

Adjusted odds ratio (95% CI)
Week 24: 2.2 (0.8, 6.1)
Week 52: **4.9 (1.5, 15.8)**

Edelman *CCT* 2016; *Lancet HIV* 2019

MOVING INTEGRATED STEPPED ALCOHOL TREATMENT INTO PRACTICE

HIV and alcohol use disorder: we cannot ignore the elephant in the room

Roberta Agabio, Lorenzo Leggio

Lancet HIV Vol 6, August 2019

"The study… is of great importance for the HIV field and beyond because it clearly addresses the current need to improve the way alcohol use disorder is treated, in the context of HIV and in general."

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Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents with HIV

Developed by the HHS Panel on Antiretroviral Guidelines for Adults and Adolescents—A Working Group of the NIH Office of AIDS Research Advisory Council (OARAC)

Data on the use of disulfiram and acamprosate among people with HIV are lacking. Notably, integrating treatment for AUD with treatment for HIV has been shown to increase the number of patients who receive alcohol treatment medication, counseling, and formal outpatient alcohol treatment services. Integrating these treatments also may improve the likelihood that a patient will achieve viral suppression on ART. A randomized controlled trial of 128 individuals with HIV and AUD compared an integrated stepped-care model of alcohol treatment in Veterans Administration HIV clinics to treatment as usual. At the end of treatment (24 weeks), integrated stepped care resulted in more participants' receiving pharmacotherapy for AUD and participating in counseling. Although differences in alcohol use and viral suppression were not seen at 24 weeks, at 52 weeks, integrated stepped care was associated significantly with an increased number of alcohol-abstinent days, a decrease in the number of drinks per drinking day, and a decreased number of heavy drinking episodes. In addition, the patients in the stepped care group had increased odds of achieving viral suppression (odds ratio [OR] 5.58; 95% confidence interval [CI], 1.11–27.99).[47]

STEP TRIALS: EXPERIENCES AND LESSONS LEARNED

- Lends support for integrated, stepped alcohol treatment models in HIV clinical settings
- Low patient motivation to address alcohol use or enter a study
- Integrated stepped care alcohol treatment may be enhanced with addition of incentives

Agabio, Leggio *Lancet HIV* 2019; Edelman *CCT* 2023, Funding #U01AA020795 - PI DA Fiellin)

EFFORTS TO MOVE THE NEEDLE

NEED TO IMPLEMENT EVIDENCE-BASED TREATMENTS ACROSS THE SPECTRUM OF SUBSTANCE USE IN HIV CLINICS

Substance	Medication	Counseling
Tobacco	• Bupropion • Nicotine replacement therapy • Varenicline	• Brief intervention
Alcohol	• Acamprosate • Disulfiram • Naltrexone (oral and injectable)	• Brief intervention (at-risk alcohol use only) • Cognitive behavioral therapy • Motivational enhancement therapy
Opioid	• Buprenorphine • Naltrexone (injectable)	• Cognitive behavioral therapy • Motivational enhancement therapy • Drug counseling

IMPLEMENTATION STRATEGIES: IMPLEMENTATION FACILITATION

Component	Description
External facilitator	Outside content expert who assists site
Local champion	Local site stakeholder who promotes change
Provider education and academic detailing	Provision of unbiased peer education
Stakeholder engagement	Aligning goals of implementation effort and those impacted
Tailor program to site	Addressing site specific needs
Performance monitoring and feedback	Assess implementation of screening and treatment efforts to inform site of results
Formative evaluation	Quantitative and qualitative determination of impact
Establish a learning collaborative	Shared learning opportunities tailored to stakeholders
Program marketing	Efforts designed to increase attention to availability of on-site addiction treatment services

Primary care practices are 2.76 (95% CI, 2.18-3.43) times more likely to adopt evidence-based guidelines through implementation facilitation

Baskerville *Annals Family Med* 2012

WORKING WITH HIV CLINICS TO ADOPT ADDICTION TREATMENT USING IMPLEMENTATION FACILITATION

- **Aim 1**. To use mixed-methods to identify barriers and facilitators to the integration of addiction treatments to tailor an Implementation Facilitation for each clinic.

- **Aim 2**. To assess the impact of Implementation Facilitation on implementation outcomes, including organizational and provider readiness; provision of addiction treatments; and changes in organizational models.

Edelman et al. *CCT* 2020; Funding #R01DA041067 - PI DA Fiellin

METHODS

- Conducted from July 2016 through July 2020
- Randomized clinical trial with hybrid type 3 implementation-effectiveness approach to evaluate the impact of Implementation Facilitation on implementation and effectiveness outcomes
- In four HIV clinics in US Northeast
- Stepped wedge design

Clinic 4	Control	Control	Control	Control	IF	Evaluation	Maintenance
Clinic 3	Control	Control	Control	IF	Evaluation	Maintenance	Maintenance
Clinic 2	Control	Control	IF	Evaluation	Maintenance	Maintenance	Maintenance
Clinic 1	Control	IF	Evaluation	Maintenance	Maintenance	Maintenance	Maintenance
Time Point	**Baseline**	**6 months**	**12 months**	**18 months**	**24 months**	**36 months**	**48 months**

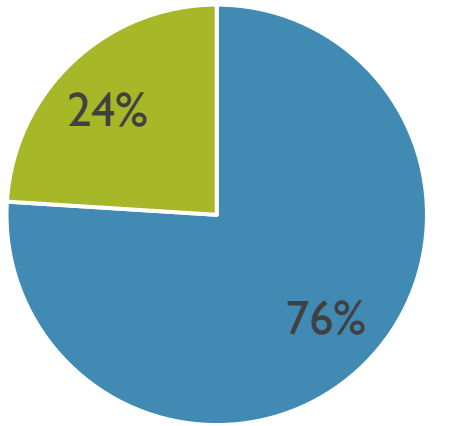
Edelman et al. *CCT* 2020; Funding #R01DA041067 - PI DA Fiellin

PROMOTING ACTION ON RESEARCH IMPLEMENTATION IN HEALTH SERVICES FRAMEWORK (PARIHS)

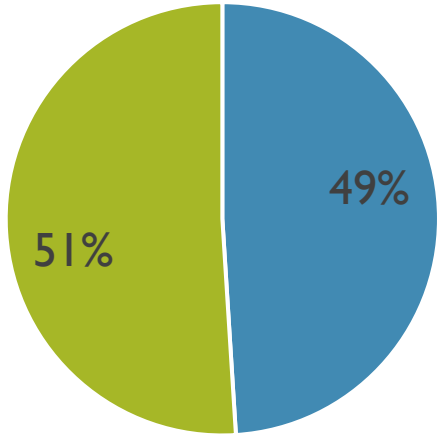
Stetler CB et al. *Implementation Science* 2011; Harvey G and Kitson A. *Implementation Science* 2016.

READINESS TO PRESCRIBE OR REFER FOR MEDICATIONS FOR ADDICTION TREATMENT, BY SUBSTANCE USE DISORDER (N=71)

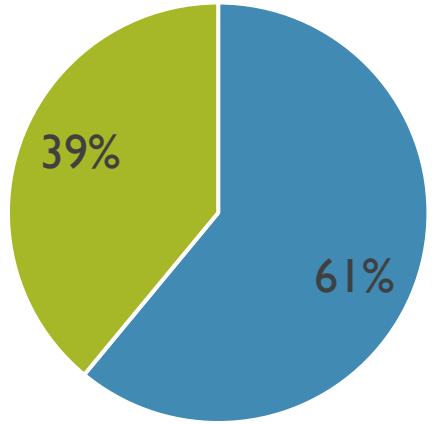
Tobacco use disorder



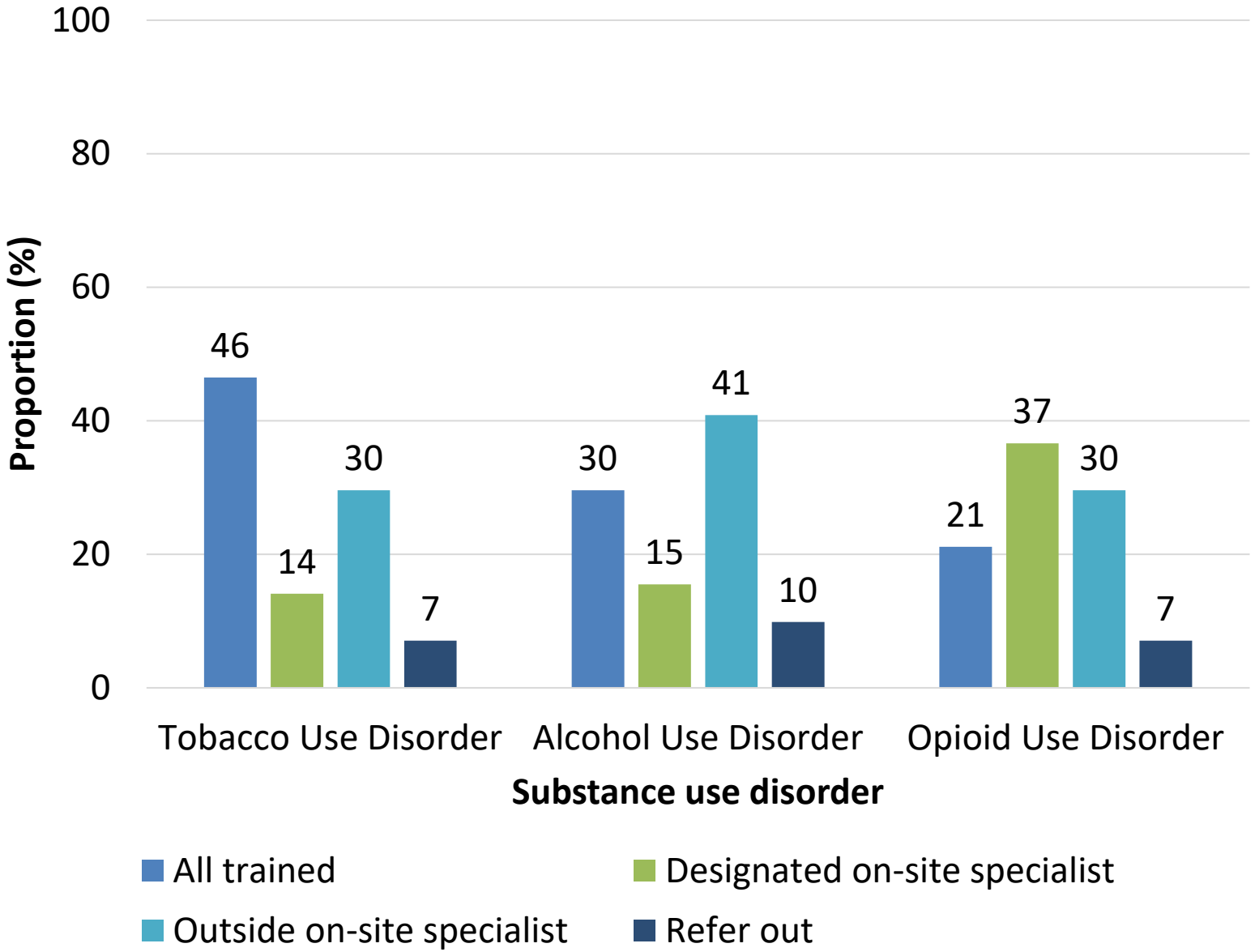
Alcohol use disorder



Opioid use disorder



Edelman et al. *JAIDS* 2021



PREFERRED MODEL FOR PROVIDING TREATMENT

"IN YOUR OPINION, WHICH APPROACH DO YOU THINK WOULD BE MOST FEASIBLE TO IMPROVE TREATMENT FOR [OPIOID/ALCOHOL/TOBACCO] USE DISORDER?"

Edelman et al. *JAIDS* 2021

TOBACCO USE DISORDER TREATMENT IN HIV CLINICS

Facilitators (+)

- Major threat to health
- Dedicated staff for smoking cessation treatment

Barriers (-)

- De-prioritized relative to other issues
- Variable patient motivation and treatment response
- Concern about pills and side effects, preferred patches

Morford et al. *JSAT* 2022; Edelman et al. *JAIDS* 2021

IMPACT OF IMPLEMENTATION FACILITATION ON PROMOTING PROVISION MEDICATIONS FOR ADDICTION TREATMENT IN HIV CLINICS

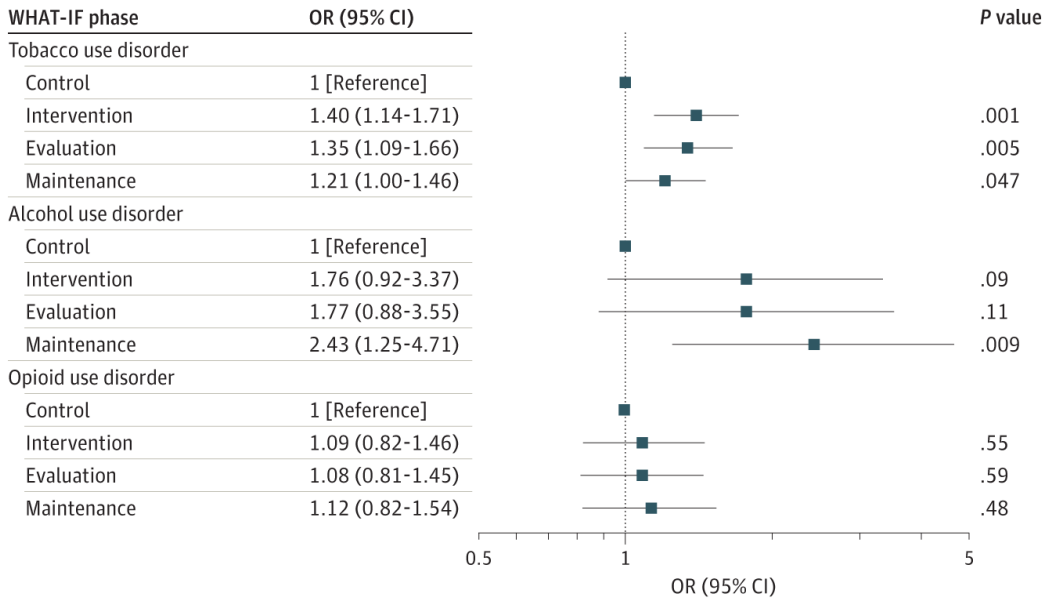


Table 2. Provision of Medications for Addiction Treatment Among Treatment-Eligible Patients Across All Sites by Study Period, Results From Generalized Estimating Equation

	Provision of MOUD[a]		Provision of MAUD		Provision of MTUD	
Study period	Patients, No. (%) [95% CI]	*P* value	Patients, No. (%) [95% CI]	*P* value	Patients, No. (%) [95% CI]	*P* value
Control	243 (27) [22-32]	Reference	251 (8) [5-12]	Reference	810 (33) [30-36]	Reference
Intervention	117 (28) [22-35]	.55	122 (13) [8-21]	.09	444 (41) [37-46]	.001
Evaluation	135 (28) [22-35]	.59	112 (13) [8-21]	.11	471 (40) [36-45]	.005
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Abbreviations: MAUD, medications for alcohol use disorder; MOUD, medications for opioid use disorder; MTUD, medications for tobacco use disorder.

[a] MOUD exclusively included buprenorphine products.

Edelman et al. *JAMA Network Open 2022*

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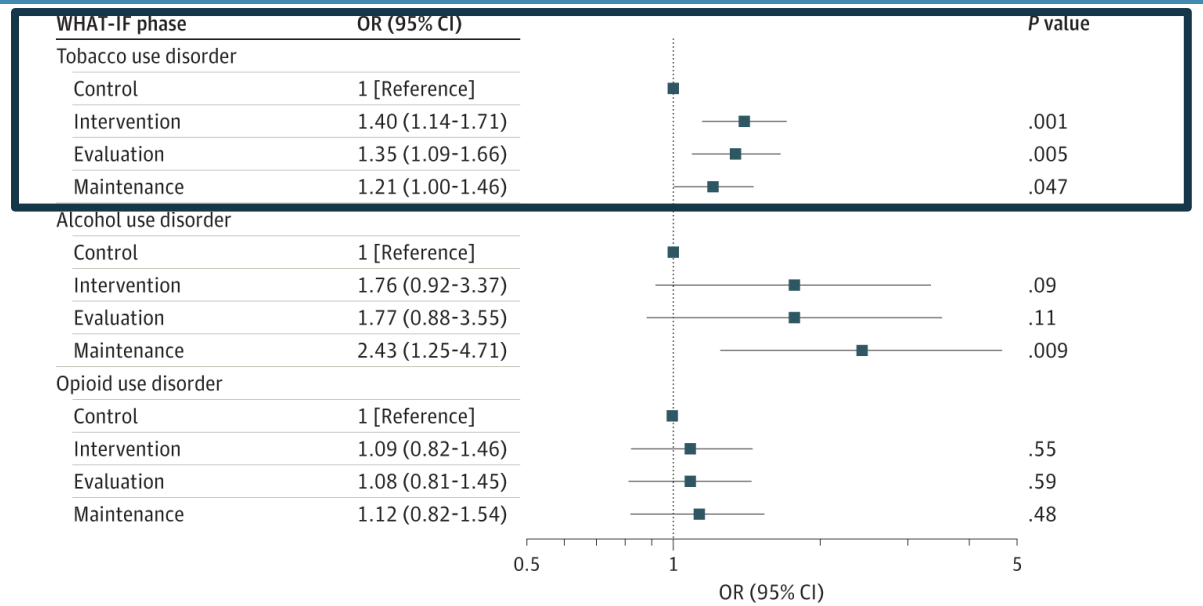

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Edelman et al. *JAMA Network Open 2022*

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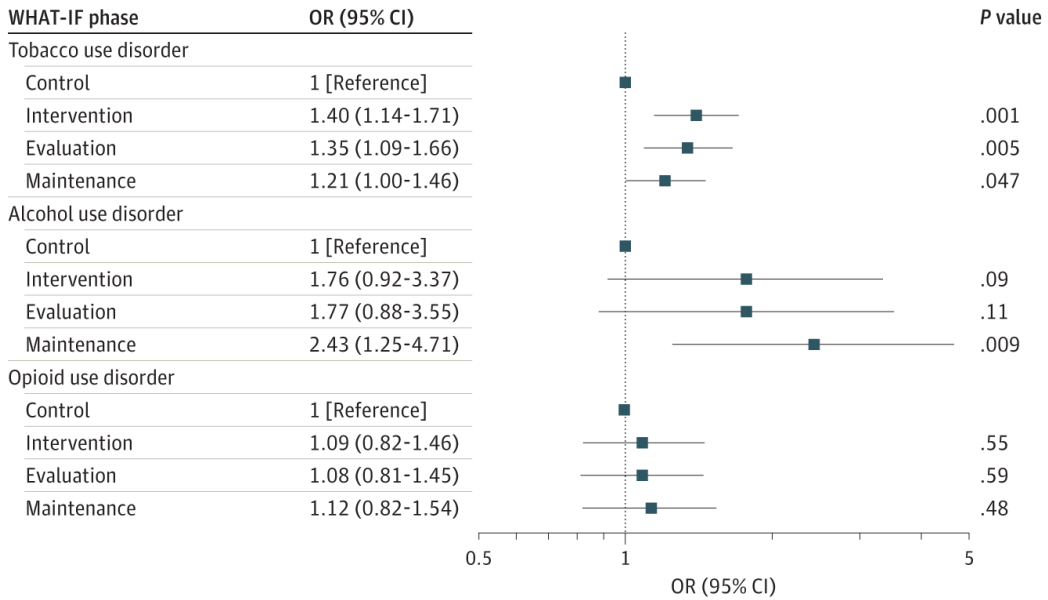

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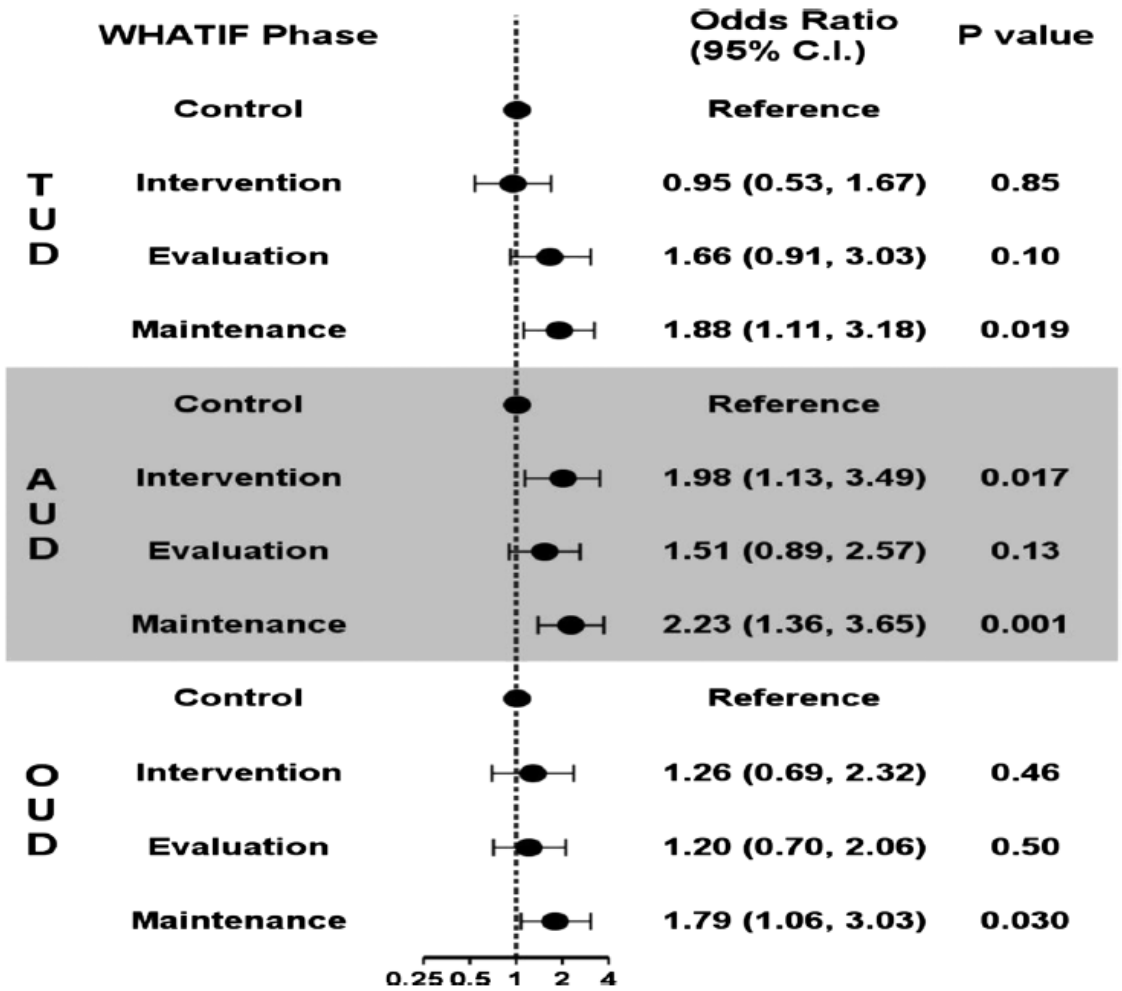
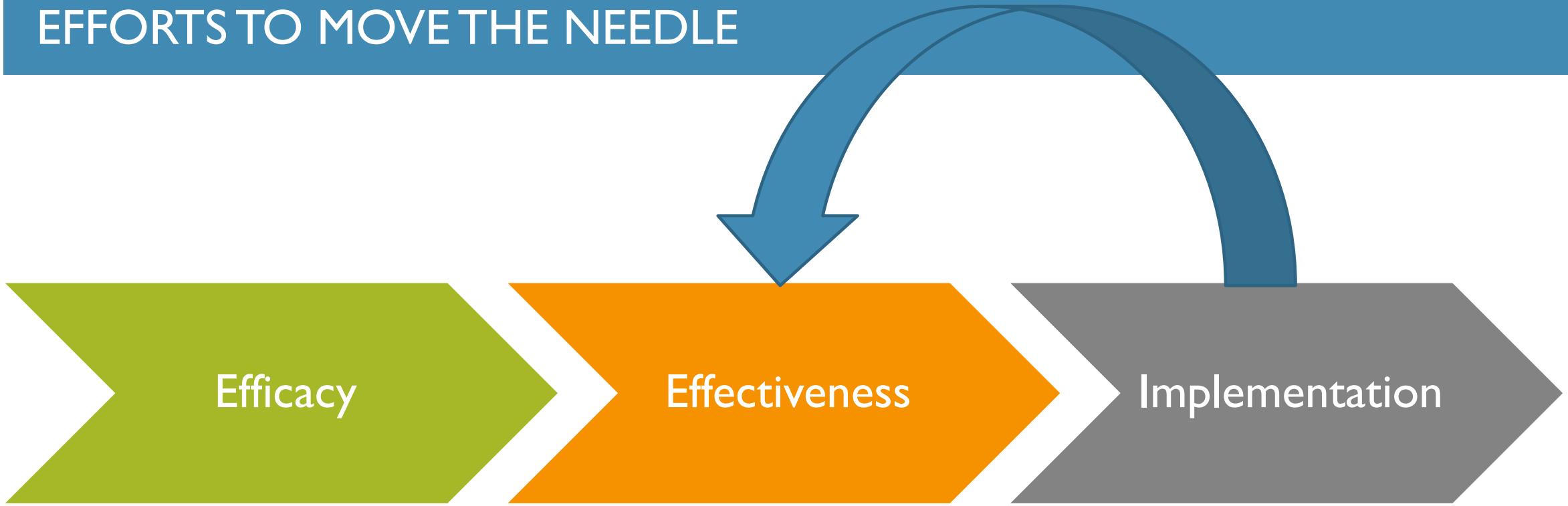
Edelman et al. *JAMA Network Open 2022*

IMPACT OF IMPLEMENTATION FACILITATION ON PREFERRED MODELS OF CARE WITH ON-SITE RESOURCES



Muvvala et al *Journal of Addiction Medicine* 2023

EFFORTS TO MOVE THE NEEDLE



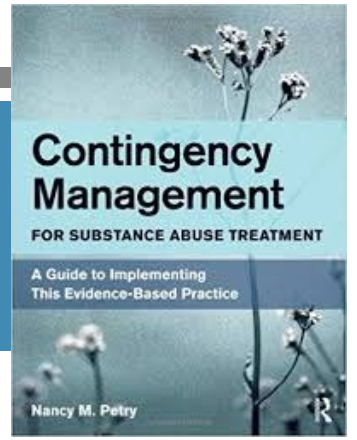
SMARTTT

A Smart Approach to Treating Tobacco Use Disorder in Persons with HIV

A SMART APPROACH TO TREATING TOBACCO USE DISORDER IN PERSONS WITH HIV (SMARTTT) TRIAL

Funding: #R01CA243910-02, Edelman/SL Bernstein

WHAT IS CONTINGENCY MANAGEMENT?



- Use of tangible and timely incentives for achievement of verifiable behaviors
- Goal is to motivate behavior change, especially for behaviors likely to have greater future than present reward to offset discounting of delayed rewards
- Beneficial in decreasing substance use, including tobacco use, and promoting HIV related outcomes
- Builds on our team's experience using contingency management for alcohol and tobacco use in HIV treatment settings

WHY PRIORITIZE NICOTINE REPLACEMENT THERAPY (NRT) OVER VARENICLINE?

- NRT and varenicline are effective in the general population and safe among PWH
- Limited prior studies have compared the efficacy of NRT to varenicline to guide prioritization of one treatment over another
- Focus group data suggest that patients may not prefer taking additional pills
- No studies have yet studied the benefit of switching NRT to varenicline

WHY RELY ON CLINICAL PHARMACISTS?

- Integrated treatment models to address substance use work best
- Interdisciplinary teams are the norm in HIV clinics
- Clinical pharmacist involvement is associated with improved HIV-related outcomes and also increasingly used across health systems and community-based settings to deliver tobacco use interventions

HOW TO CREATE AN ADAPTIVE, SCALABLE INTERVENTION?

SMART design

- Sequential, multiple assignment, randomized trial
- Promotes tailoring of intervention based on patient response
- Allows for determination of optimal strategy to reach target outcome as well as intervention components

Implementation-focused evaluation

- Hybrid effectiveness-implementation type I design
- Grounded in PARiHS and RE-AIM frameworks
- Perspectives of clinician and staff pre- and post-trial

STUDY AIMS (REVISED*)

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

Among 320 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 smoking reduction.
- **Aim 2.** To identify the impact of various tobacco treatment regimens 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:

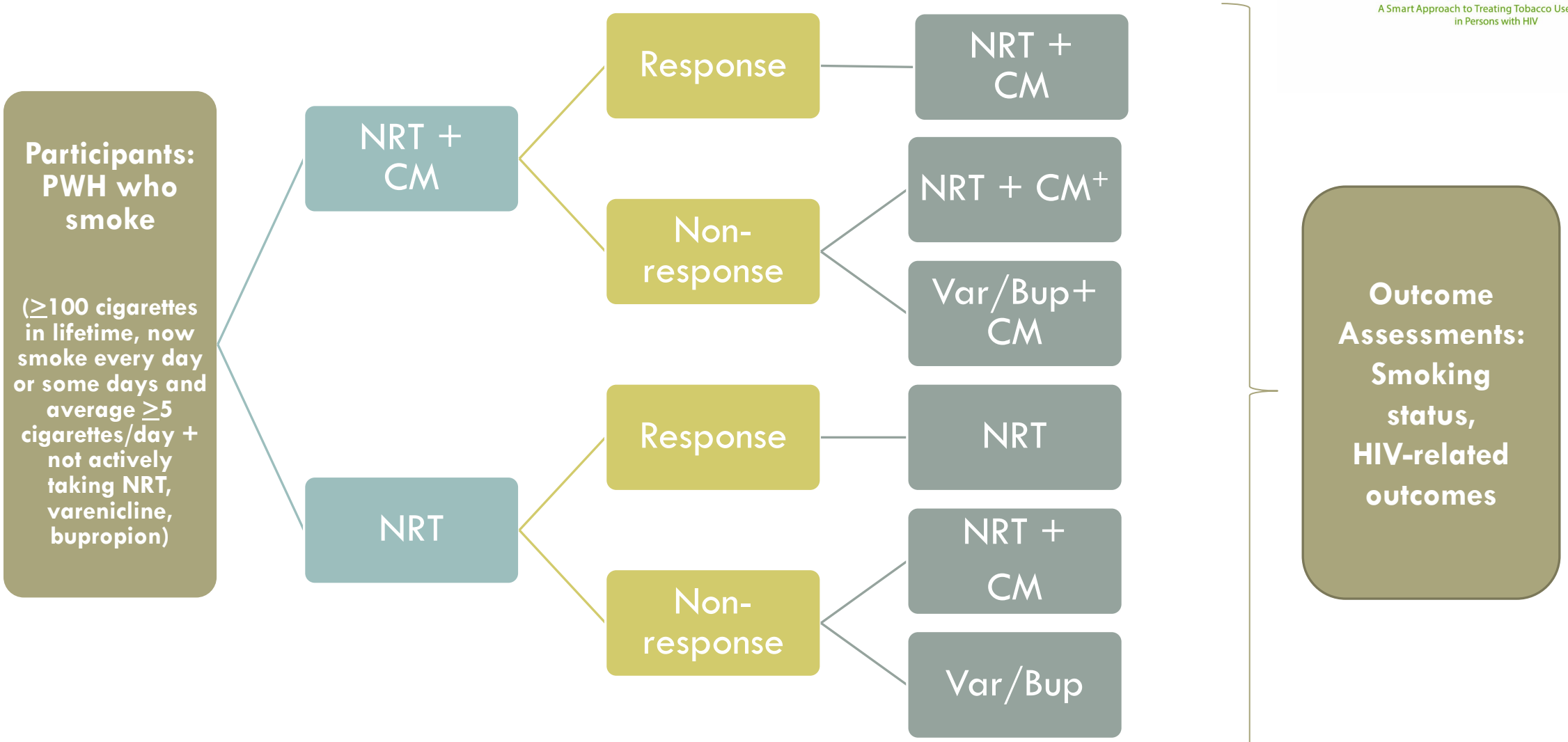
- **Aim 3.** To conduct an implementation-focused evaluation of a clinical pharmacist-delivered intervention involving nicotine replacement therapy, oral tobacco treatment medication, and contingency management

Edelman et al. *CCT* 2021; Funding: #R01CA243910-02, Edelman/SL Bernstein

Protocol Overview

NRT= nicotine replacement therapy, CM=contingency management, bup=bupropion

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

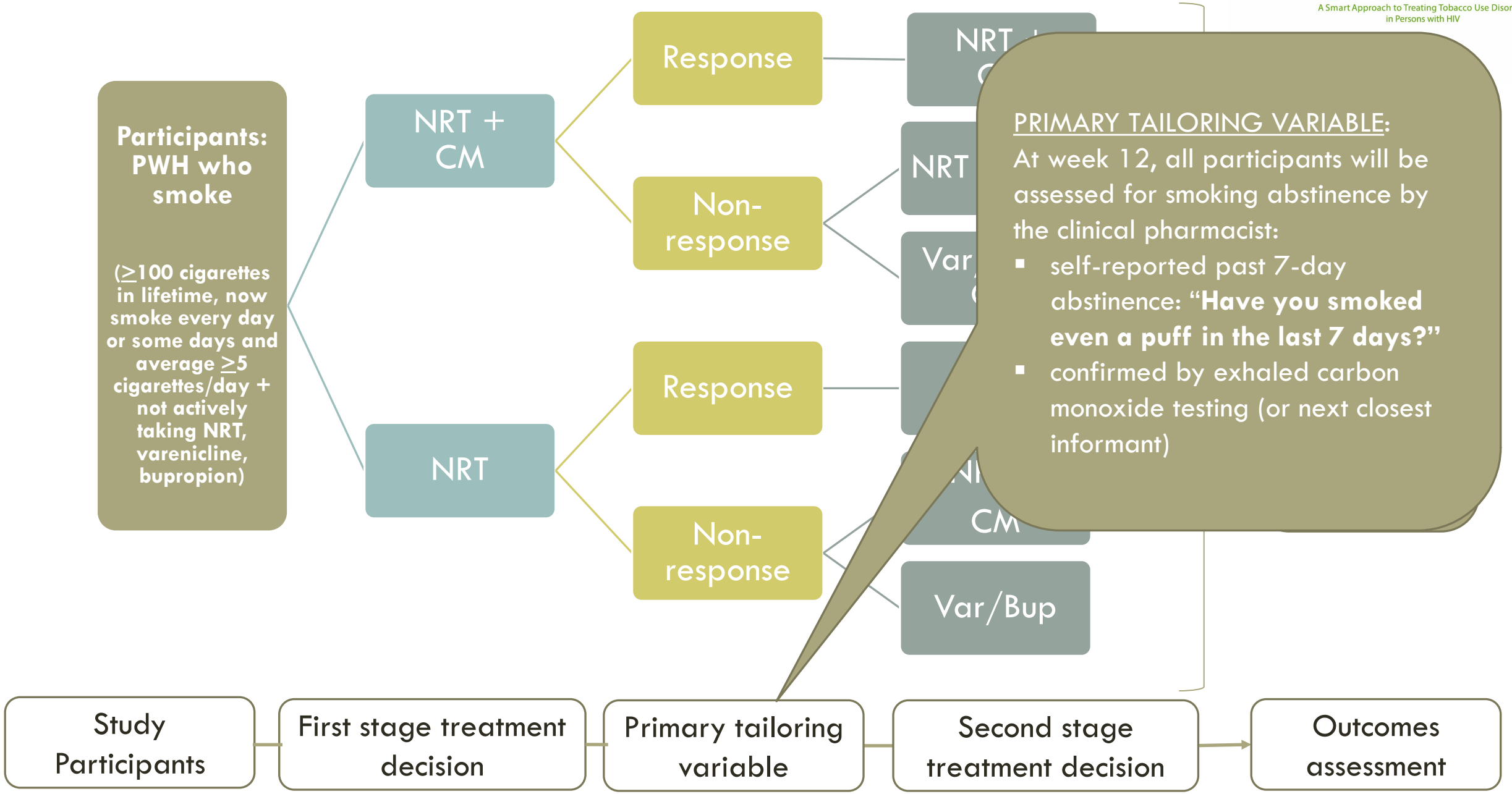


Study Participants → First stage treatment decision → Primary tailoring variable → Second stage treatment decision → Outcomes assessment

Protocol Overview

NRT= nicotine replacement therapy, CM=contingency management, bup=bupropion

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



INTERVENTION COMPONENTS: CLINICAL PHARMACIST-DELIVERED

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

Dual nicotine replacement therapy

Contingency management

Oral tobacco treatment medications

CONTINGENCY MANAGEMENT

- Fishbowl prizes
- Draws earned gift cards
- Resets if self-reported tobacco use, unable to confirm abstinence, unexcused absence
- 5 potential visits over each 12- week stage of treatment
- Balancing regular clinic schedules vs. contingency management principles

OUTLINE

What's the problem?

- Epidemiology
- Gaps in treatment services

Integrating addiction and HIV treatment

- STEP Trials
- WHAT-IF?
- SMARTTT

Current and future directions

- Mateo…
- Moving beyond HIV clinical settings

SUMMARY AND NEXT STEPS

- Implementation science principles are useful for guiding efforts to improve adoption of what works
- Ongoing need to cycle between efficacy, effectiveness, and implementation designs
- New efforts can be directly informed by mixed methods to inform tailoring of the intervention strategy to stakeholder and contextual needs
- With success of HIV and addiction treatment, there is growing need to enhance primary and secondary prevention of medical comorbidities

QUESTIONS, COMMENTS, DISCUSSION!

EJENNIFER.EDELMAN@YALE.EDU