Medication Sampling and Smoking Cessation

Matthew Carpenter, PhD
Hollings Cancer Center
Medical University of South Carolina

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Before We Get Started

Disclosures:

- Consulting honoraria from Pfizer (2018, 2019);
- Consulting honoraria from Frutarom (2020);
- Medication (varenicline) provided from Pfizer;
- Direct pricing / product from GSK (NRT) & Njoy (E-Cigs)

We do not accept support from the tobacco industry,
nor do we accept free product from the e-cigarette industry

Medication Sampling → Empowering Smokers to Quit

Simply providing a short course (2 weeks) of one or more cessation medications, with minimal instructions
without any firm commitment to quit

Concrete, behavioral, immediately actionable, **Cue To Action**

Kick the Tires of Cessation
Test Drive Abstinence
Take a Small Easy Step Before a Hard Step
whatever metaphor you like

NRT Sampling

Cluster Randomized Controlled Trial

- Standard Care (SC): naturalistic, unscripted physician advice per routine
- SC + NRT: 2 week supply of both nicotine patch & lozenge (uniform dosing)

22 primary care clinics across South Carolina

- 12 SC clinics (2 poor performing clinics replaced)
- 10 NRT clinics
- All study procedures (screening, consenting, baseline assessment, treatment delivery) done by clinic staff; No research staff present
- All clinics given 1x 60-90min overview of USPHS Guidelines upon study start
- All providers were encouraged to deliver cessation advice as done typically
  - "baggies" given to all smokers in all clinics with cessation materials; +/- NRT

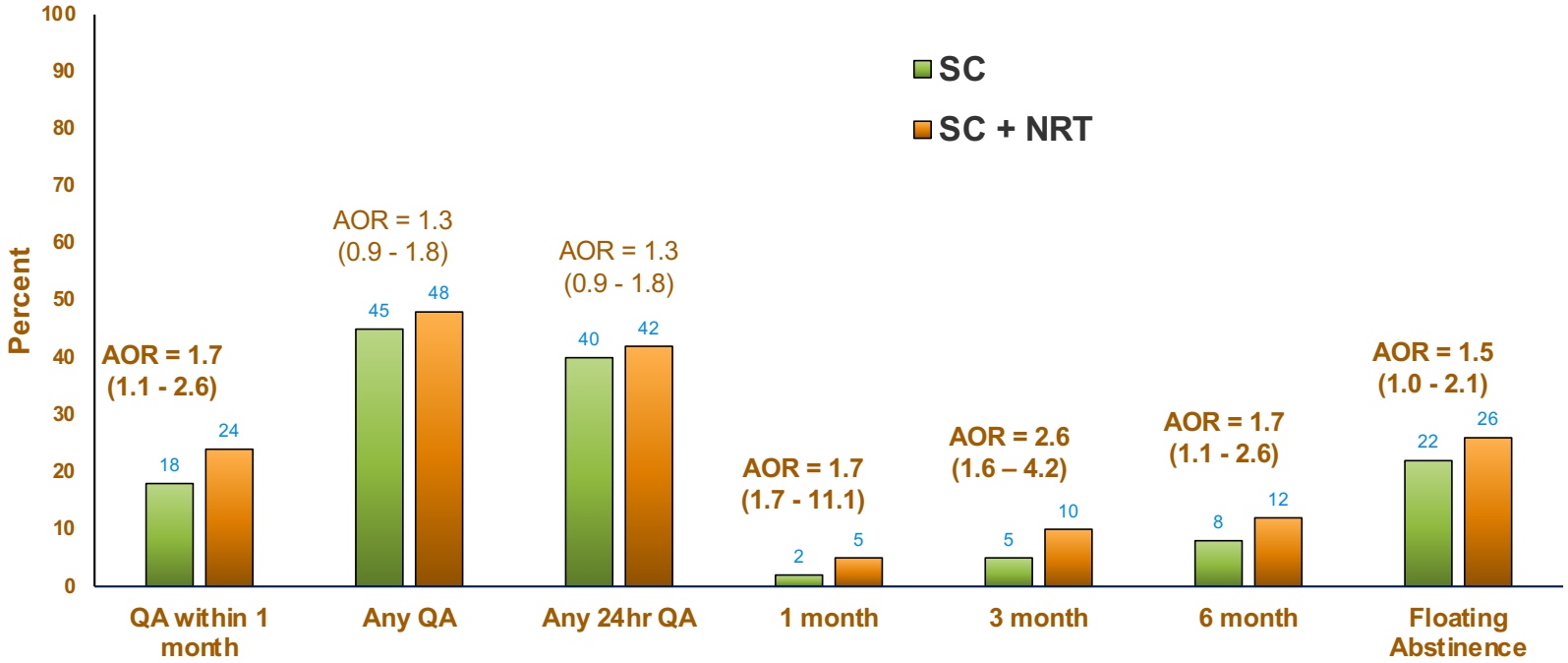
Final N = 1245 adult smokers, seen during routine clinic visit

- Broad inclusion criteria
- MTQ not required, nor willingness to sample cessation medication

Follow-up thru 6 months, managed centrally by research staff via phone

Methods: Dahne et al. 2018. *Contemporary Clinical Trials*; 72:1-7.
Outcomes: Carpenter et al (2020). *Addiction*; 115: 1358-1367.

NRT Sampling



AOR adjusting for: a) site, b) nicotine dependence [Heaviness of Smoking Index], c) gender, and d) race.

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NRT Sampling

Sensitivity Comparisons of Cessation-Related Outcomes by Baseline Motivation to Quit

	Low Motivation to Quit (n=573)				High Motivation to Quit (n=671)			
	SC (n=315)	SC + NRT (n=258)	AOR	p	SC (n=336)	SC + NRT (n=335)	AOR	p
Any QA	109 (35%)	94 (36%)	1.2	0.4	186 (55%)	193 (58%)	1.2	0.3
Any 24hr QA	92 (29%)	78 (30%)	1.2	0.4	166 (49%)	171 (51%)	1.2	0.3
Abstinence, 6 months	15 (5%)	20 (8%)	1.7	0.1	37 (11%)	50 (15%)	1.5	0.1
Floating Abstinence	44 (14%)	47 (18%)	1.6	.06	97 (29%)	105 (31%)	1.3	0.1

To Note:

1. All sub-group treatment comparisons non-significant (dimin. power)
2. Absolute QA & Abstinence rates: HMTQ > LMTQ
3. **All treatment effect sizes: LMTQ ≥ HMTQ**

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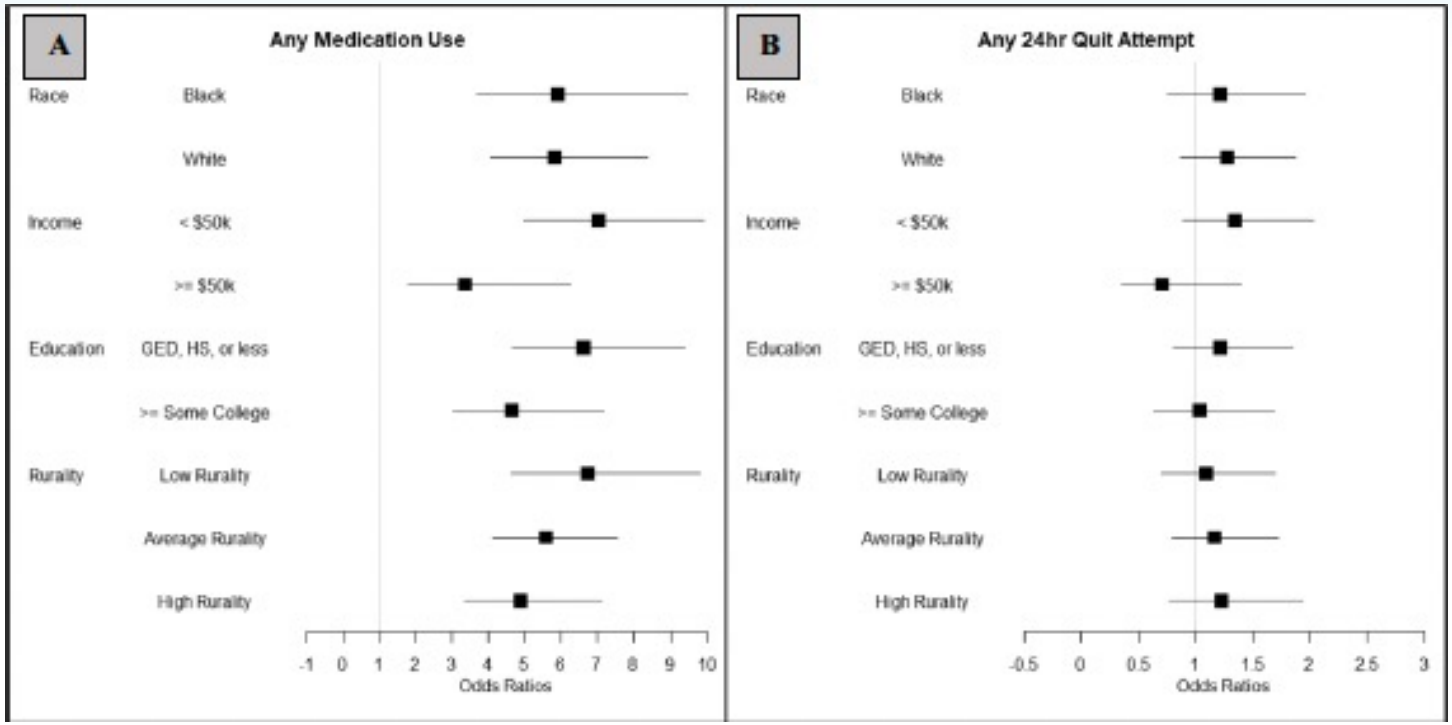
NRT Sampling

Differential Impact across Disparity Groups



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Cost Effectiveness: Chen et al (in review)

NRT Sampling

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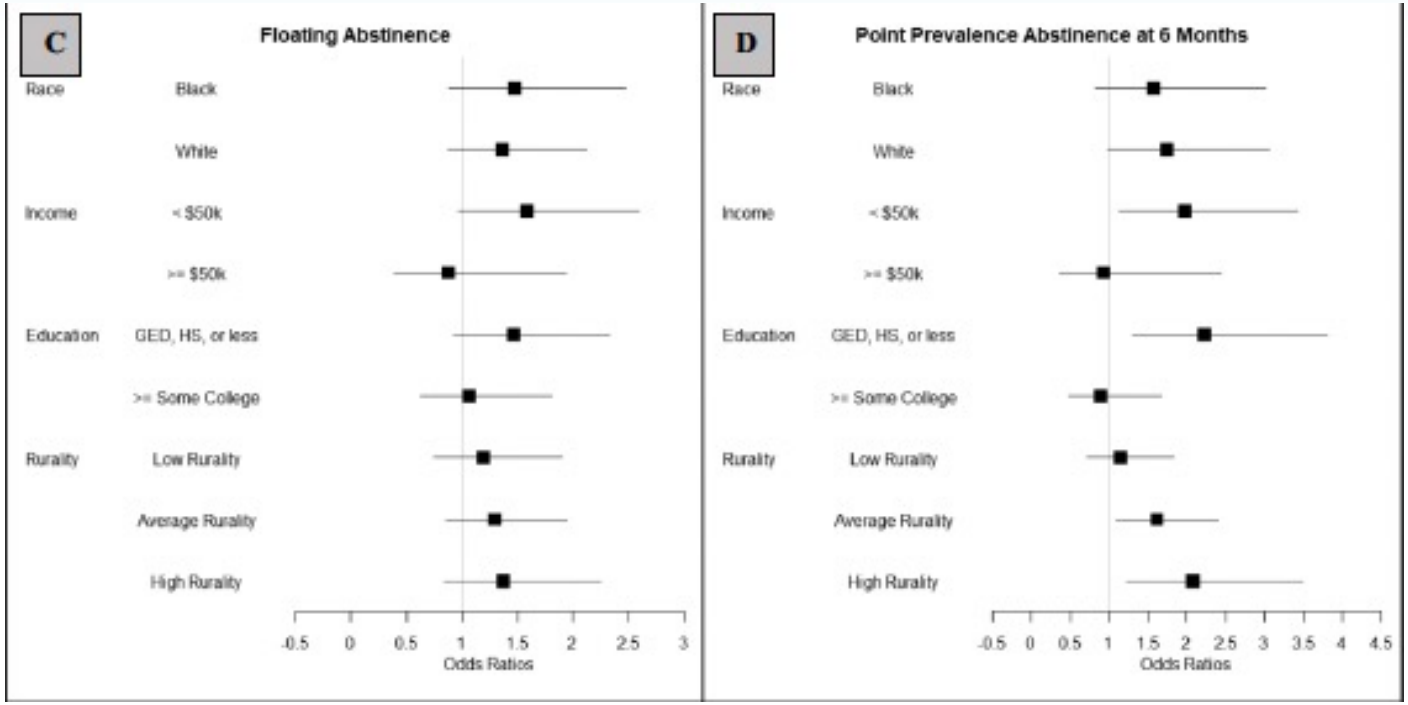

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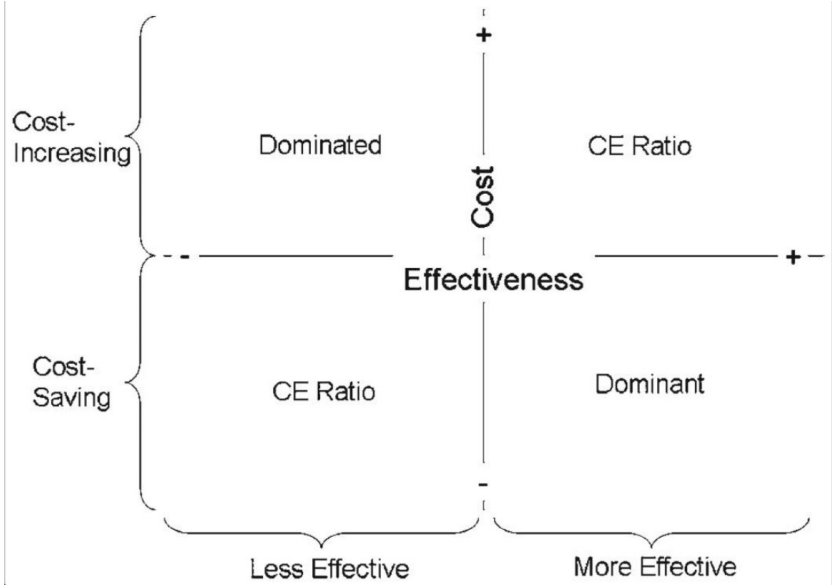
NRT Sampling

Cost Effectiveness: Quick Crash Course

Cost of Treatment Relative to Control



Efficacy of Treatment Relative to Control

When a new intervention is both clinically inferior and cost increasing, it is referred to as a **"dominated"** strategy. Few novel technologies will fall here.

When a new strategy adds both benefits and costs (**upper right-hand quadrant**) or reduces both (**lower left-hand quadrant**), a **Cost Effective** ratio must be calculated to **judge benefits relative to costs.**

When a new intervention is both clinically superior and cost saving, it is referred to as an economically **"dominant"** strategy. Few novel technologies will fall here.

See: Cohen & Reynolds MR. (2008). *Am J Cardiology*; 52:2119-2126.

NRT Sampling

Cost Effectiveness

	Our Study: One and Done		
	NRT Sampling	Standard Care	Difference
Cost			
Cost of NRT Sampling	$75	$0	$75
Discounted cost of subsequent health care	$299,061	$301,200	-$2,139
Total discounted cost	$299,136	$301,200	-$2,064
Outcomes			
Discounted Life Years	16.815	16.795	0.020
Discounted Quality Adjusted Life Years	13.065	13.046	0.019
Incremental Cost-Effectiveness Ratio (ICER)			
$/LY	N/A. NRT sampling is dominant		
$/QALY	N/A. NRT sampling is dominant		

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NRT Sampling

Cost Effectiveness

	Our Study: One and Done			Hypothetical: 50% of smokers reissued NRT samples each quarter, for 6 months			Hypothetical: 50% of smokers reissued NRT samples each quarter, for 12 months		
	NRT Sampling	Standard Care	Difference	NRT Sampling	Standard Care	Difference	NRT Sampling	Standard Care	Difference
Cost									
Cost of NRT Sampling	$75	$0	$75	$172	$0	$172	$232	$0	$232
Discounted cost of subsequent health care	$299,061	$301,200	-$2,139	$299,156	$302,431	-$3,275	$298,458	$302,431	-$3,973
Total discounted cost	$299,136	$301,200	-$2,064	$299,328	$302,431	-$3,103	$298,690	$302,431	-$3,741
Outcomes									
Discounted Life Years	16.815	16.795	0.020	16.879	16.851	0.028	16.885	16.851	0.034
Discounted Quality Adjusted Life Years	13.065	13.046	0.019	13.114	13.084	0.029	13.120	13.084	0.036
Incremental Cost-Effectiveness Ratio (ICER)									
$/LY	N/A. NRT sampling is dominant			N/A. NRT sampling is dominant			N/A. NRT sampling is dominant		
$/QALY	N/A. NRT sampling is dominant			N/A. NRT sampling is dominant			N/A. NRT sampling is dominant		

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NRT Sampling

Cost Effectiveness

Variable	Values	Total Cost (NRT Sampling)	Total Cost (Standard Care)	Diff Cost	QALYs (NRT Sampling)	QALYs (Standard Care)	Diff QALYs	Cost Effectiveness Dominant Group
NRT sampling effectiveness (% quit, low)	8%	$301,275	$301,200	$75	13.045	13.045	0.000	Standard Care
NRT sampling effectiveness (% quit, high)	16%	$296,997	$301,200	-$4,203	13.085	13.045	0.040	NRT sampling
Age	35	$282,536	$284,269	-$1,733	18.462	18.445	0.017	NRT sampling
Age	55	$284,131	$286,120	-$1,989	11.280	11.260	0.020	NRT sampling
Age	75	$216,737	$218,556	-$1,819	5.896	5.885	0.011	NRT sampling NRT sampling
Percent male (low)	50%	$293,311	$295,344	-$2,033	12.958	12.939	0.019	NRT sampling
Percent male (high)	80%	$277,135	$279,084	-$1,949	12.659	12.642	0.017	NRT sampling
NRT sampling cost (50% of base case)	$37.50	$299,099	$301,200	-$2,101	13.065	13.045	0.020	NRT sampling
NRT sampling cost (150% of base case)	$112.50	$299,174	$301,200	-$2,026	13.065	13.045	0.020	NRT sampling

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Cost Effectiveness: Chen et al (in review)

Medication Sampling → Empowering Smokers to Quit

Can smokers sample varenicline?

Sure!	Absolutely Not!
• It's our best single agent option for cessation • Possibility of OTC switch • Lots of studies have shown VRN for unmotivated smokers, flexible dosing, pre-quit, etc • EAGLES trial → safe • **Worth testing!**	• Rx medication; need oversight by clinician • Complicated titration • Ad libitum use may be inactive use? • Enduring concerns of safety • **Worth testing?**

Recently completed RCT of varenicline sampling

Purpose: Pilot remote clinical trial of varenicline sampling vs. not, focusing on feasibility, uptake, and outcomes from varenicline sampling

Carpenter et al (2021). *NTR*; 23: 983-991.

A Pilot Clinical Trial of Remote Varenicline Sampling: DESIGN

- Adult smokers (n=99) recruited across South Carolina within remote clinical trial design
- Purposeful recruitment of smokers both wanting and not wanting to quit (stratified randomization)
- Smokers receiving varenicline sampling received 1x supply of 56 tablets (0.5mg), with suggestive but not required instructions on use/titration

  "You are not required to take varenicline as part of this study. It is completely up to you if and how you take this medication."

  "Each pill provided to you is 0.5mg. If you choose to try varenicline, start with taking one pill daily for 3 days. After the third day, take two pills each day, one in the morning and one in the evening. Several studies show that this 1mg daily dose helps smokers quit, and results in fewer side effects. After a week of starting varenicline, you may want to increase to a stronger dose. If so, you can take up to two pills in the morning and two more pills in the evening (total of four pills/2mg daily)."

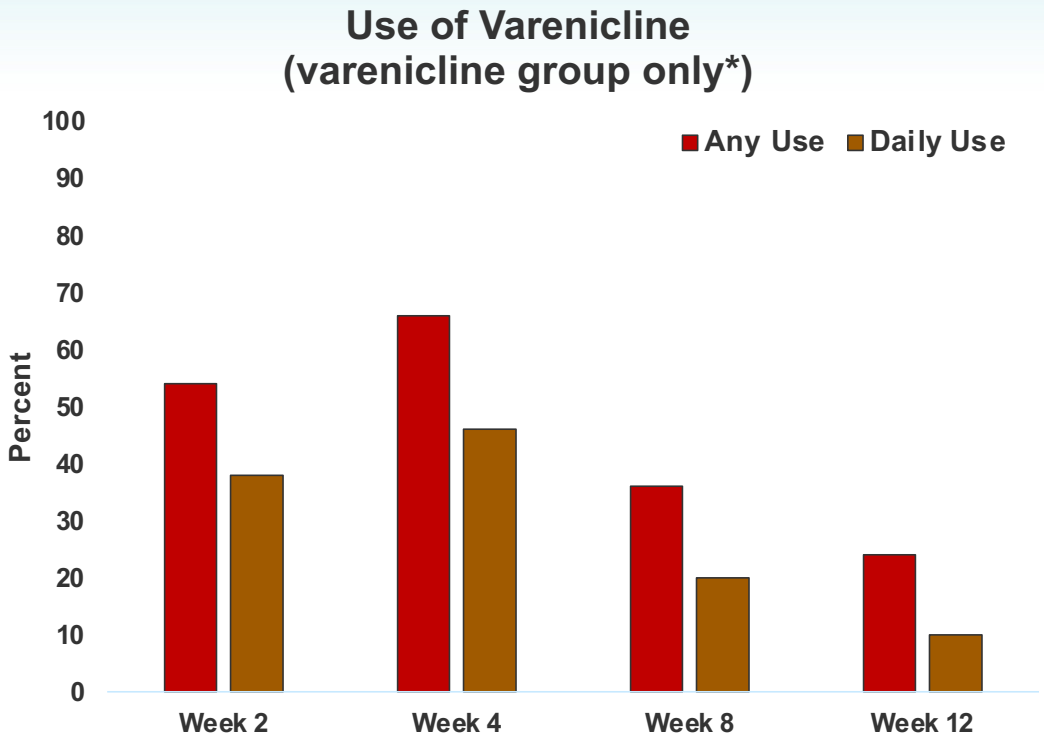
  "If you want more varenicline: We hope this starter kit helps you. After using it, we hope that you continue to use it, for as long as necessary. Talk to your doctor about getting more."

  Thus, we viewed the sampling experience as lasting 2-4 weeks depending on participant choice

- No direct intervention from clinician, though clinician oversight was throughout
- Outcomes assessed through 12 weeks of follow-up: uptake, safety, behavioral outcomes

Carpenter et al (2021). *NTR*; 23: 983-991.

A Pilot Clinical Trial of Remote Varenicline Sampling: Varenicline Usage



- Of varenicline users, most fell into a titration pattern of steady users**, both at Week 2 (54%) and Week 4 (66%)
- Rates of independent use (i.e., getting their own varenicline after sampling:
  Week 12, among entire group: 14%
  Week 12, among users of VRN: 58%
- At no time did anyone exceed the recommended maximum dosage (2 mg /day).

Carpenter et al (2021). *NTR*; 23: 983-991.

*only 1 person in control group used varenicline, on their own accord
**steady users: e.g. 0.5 mg for a few days, then 1 mg and up to 2 mg for all 7 days

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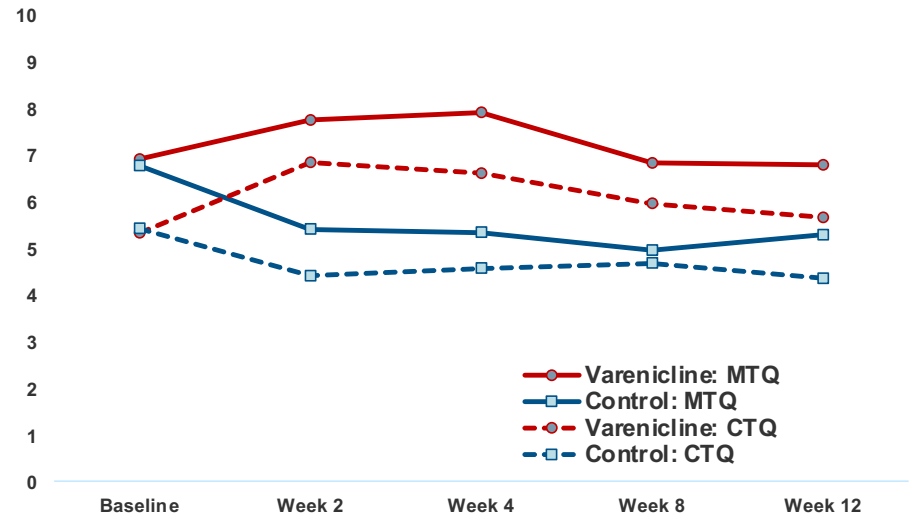
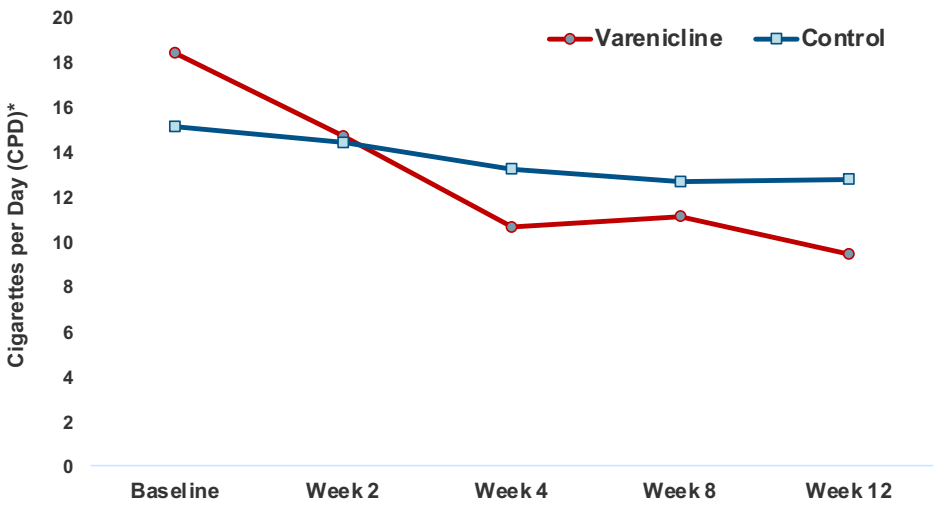
A Pilot Clinical Trial of Remote Varenicline Sampling: Outcomes

Changes in Motivation (MTQ) and Confidence to Quit (CTQ)



Changes in Cigarettes Per Day (*7 day average)



Participants in varenicline group significantly more likely to achieve **50% reduction in CPD**:
Week 4: 36% vs. 12%; AOR = 4.12 (95% CI: 1.39 – 12.17)
Week 12: 42% vs. 12%; AOR = 4.50 (95% CI: 1.56 – 13.01)

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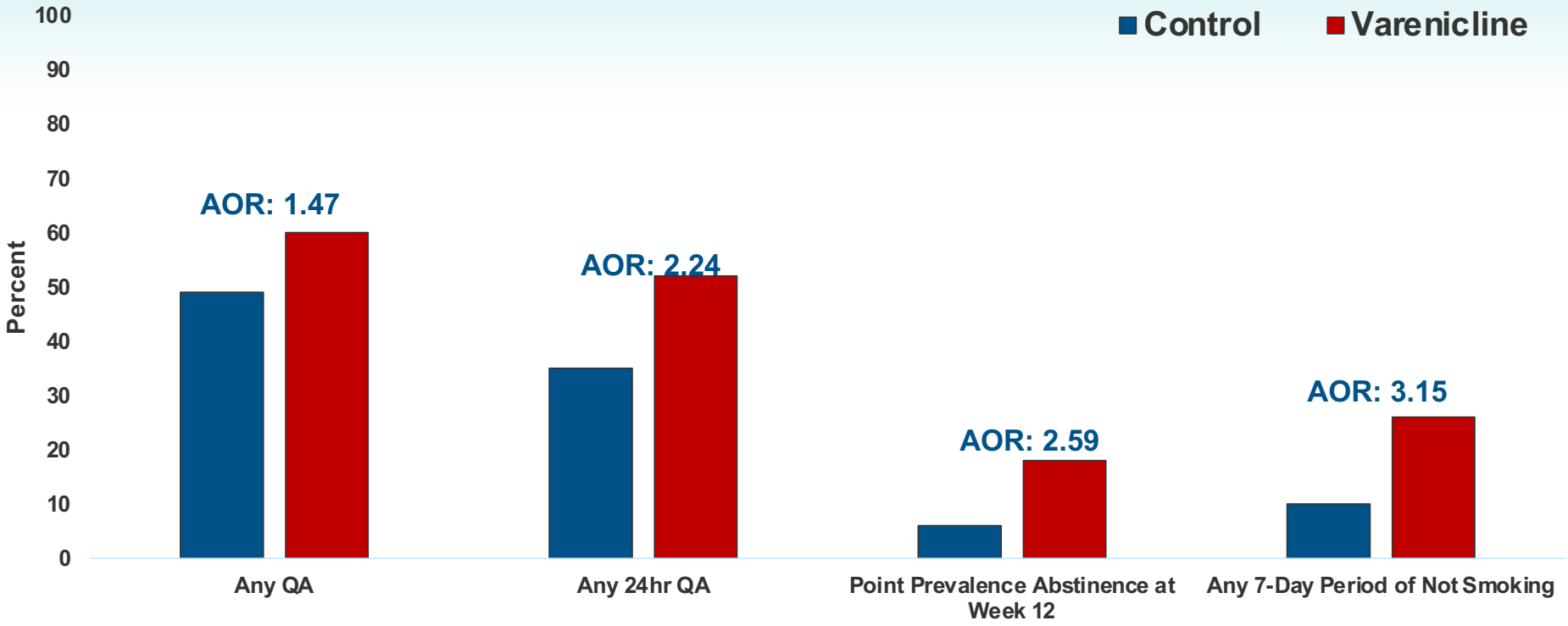
A Pilot Clinical Trial of Remote Varenicline Sampling: Cessation Outcomes



- Abstinence defined as self-reported, 7-day non-smoking (not even a puff), either at Week 12 or 'Floating' (ever in study)
- Adjusted Odds Ratio (AOR): adjusted for gender and nicotine dependence (HSI)
- **All comparisons statistically non-significant**

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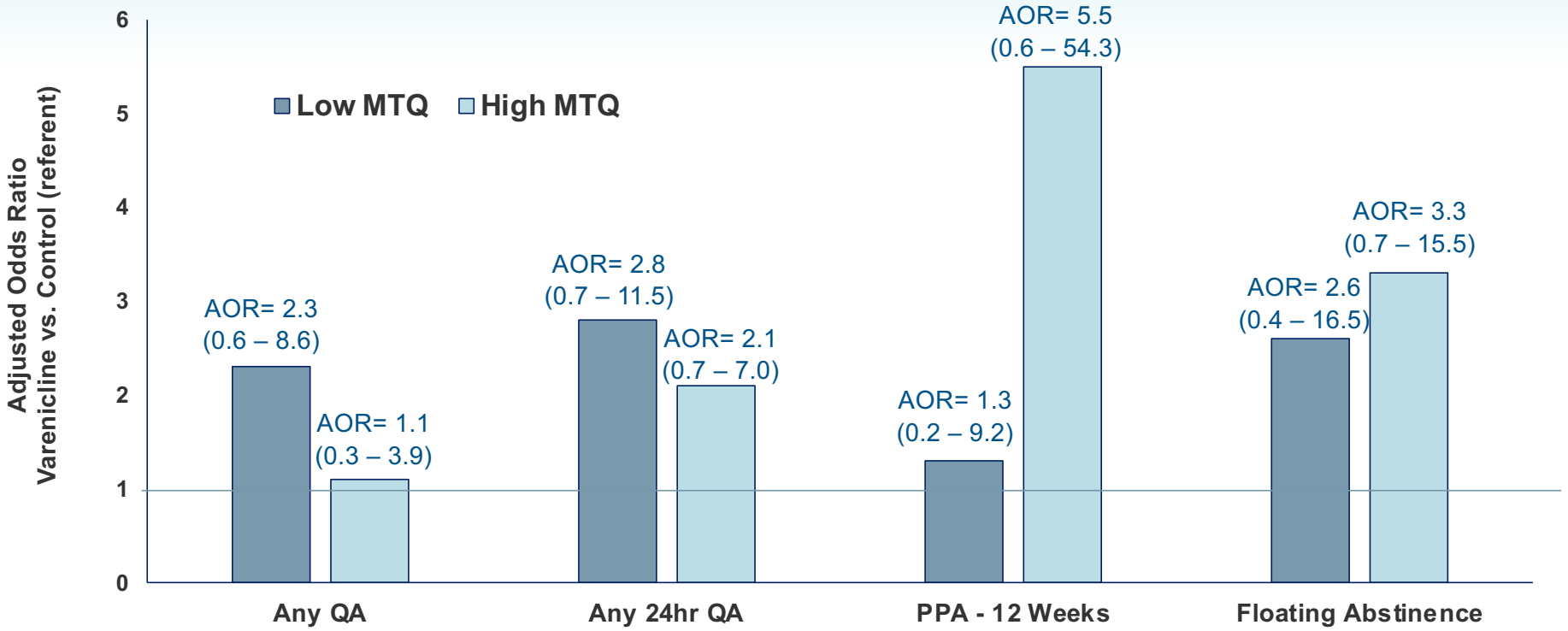
A Pilot Clinical Trial of Remote Varenicline Sampling: Cessation Outcomes

Sensitivity Comparisons of Cessation-Related Outcomes by Baseline Motivation to Quit



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A Pilot Clinical Trial of Remote Varenicline Sampling: Conclusions

Varenicline sampling, in a remote context, with minimal/suggestive guidance on use, emphasizing a user-driven experience, is. . .

- Feasible: uptake was strong
- Safe: incidence and clinical severity of these adverse events were in line with prior trials, with no serious adverse events
- Likely beneficial: all cessation-related (and reductions in smoking) were numerically if not statistically in favor of sampling
- Worth testing in a larger trial (R01CA246729; PI: M. Carpenter)

And may have implications . . .

- Clinical: scalable, practical application into any number of clinical settings (primary care, community mental health, others)
- Regulatory: supportive of alternative delivery modalities for varenicline

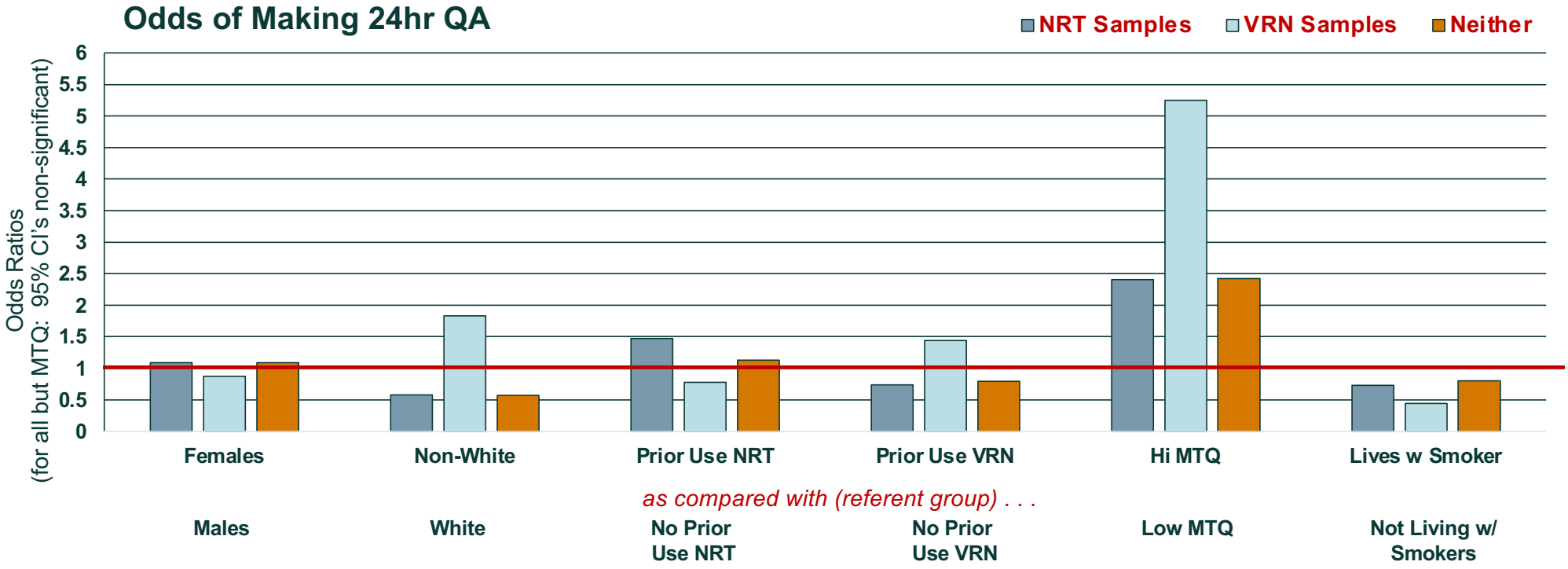
Go Big or Go Home: RCT of VRN vs. NRT vs. No Sampling (N=640): R01 CA46729.

STARS
Smoking Treatment And Remote Sampling

NRT and Varenicline Sampling: Some Enduring Questions

Are there combinations of sampling and demographics that lead to improved outcomes?

- Our ongoing R01 can address this
- Our prior work (2 separate studies: pooled) provides early suggestions (all underpowered)



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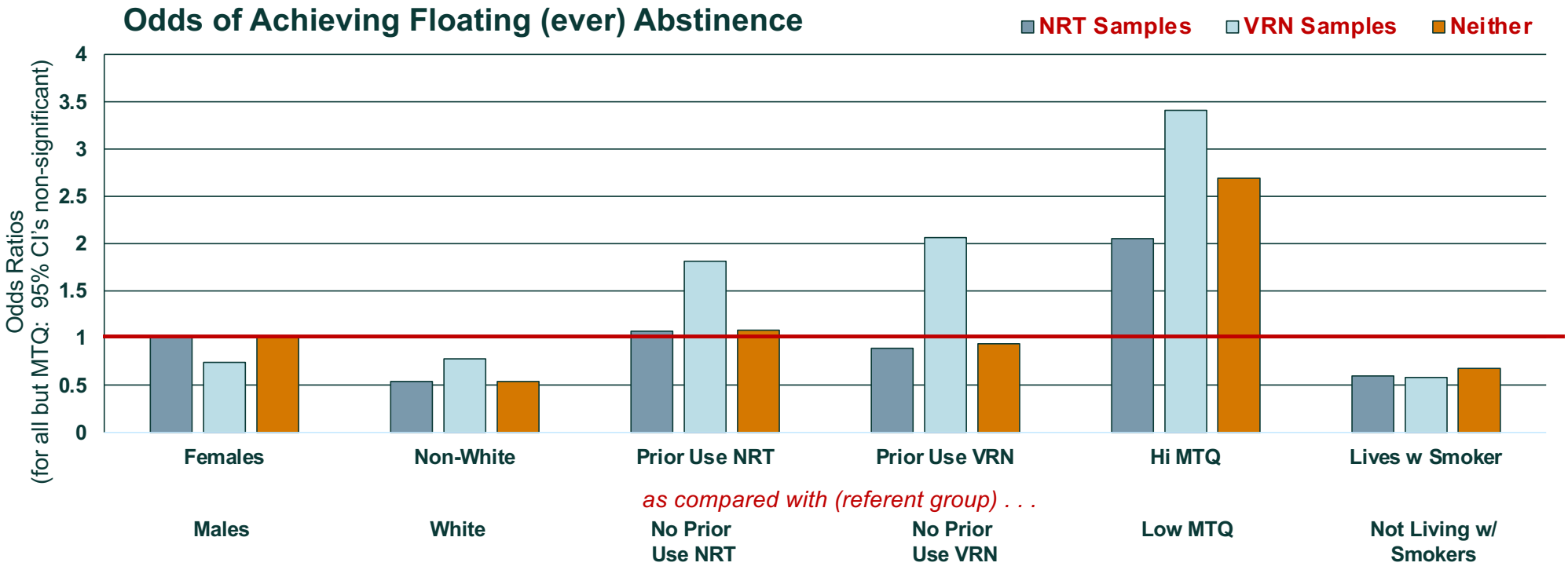

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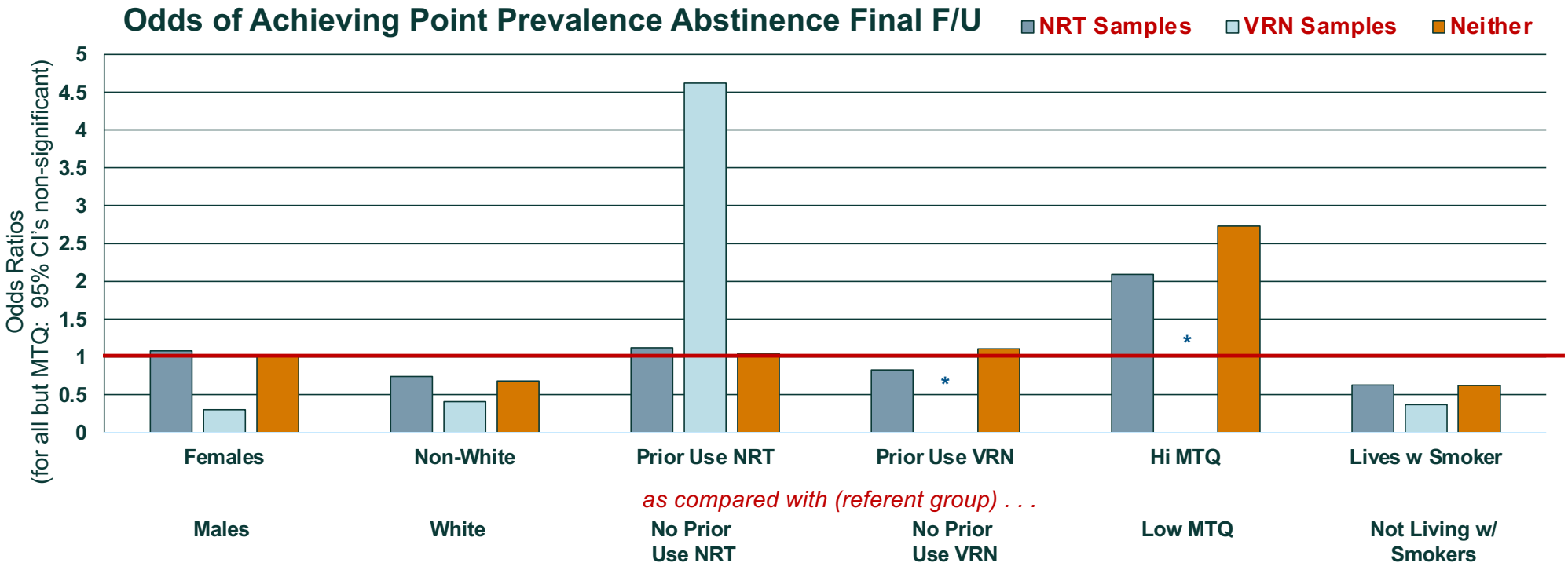

* Not Estimable

Wrapping it all up . . .

Medication sampling:

- Has low quit rates
- Will never replace more the need for more intensive and sustained treatments
- Constrained by lack of biological verification

But also . . .

- Is scalable, pragmatic, and cheap: <$100 and ~1 minute to deliver
- Prompts continued use of the product
- Prompts quit attempts and cessation, and promote reduction
- Is super lay-friendly
- Likely cost effective
- **And is therefore super disseminable**

It takes a Village

Funding
NIDA R01 021619
NIDA 2R01 021619
NCI R01 246729
Hollings Cancer Center

Collaborators
Mike Cummings, PhD, MPH
Rob Davis
Brent Egan, MD
Liz Garrett-Mayer, PhD
Kevin Gray, MD
Mike Saladin, PhD
Amy Wahlquist, MS

Research Staff
Amy Boatright, Lisa Coles, Liz Hawes, Johanna Hidalgo, Caitlyn Hood, Nichols Mabry, Noelle Natale, Hannah Shoemaker

CofC Students
many

Interns → Postdocs → *Faculty Collaborators
Jessica Burris, PhD
*Jennifer Dahne, PhD
*Bryan Heckman, PhD
Bianca Jardin, PhD
Elly Leavens, PhD
Amanda Mathew, PhD
Ellen Meier, PhD
*Tracy Smith, PhD

Thank you.
carpente@musc.edu