

Tobacco Online Policy Seminar (TOPS)

October 7, 2022

Varenicline Plus Counseling for Smoking Cessation in African Americans

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THE UNIVERSITY OF KANSAS
CANCER CENTER

JAMA | **Original Investigation**

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Effect of Varenicline Added to Counseling on Smoking Cessation Among African American Daily Smokers

The Kick It at Swope IV Randomized Clinical Trial

Lisa Sanderson Cox, PhD; Nicole L. Nollen, PhD; Matthew S. Mayo, PhD; Babalola Faseru, MD, MPH; Allen Greiner, MD; Edward F. Ellerbeck, MD, MPH; Ron Krebill, MPH; Rachel F. Tyndale, PhD; Neal L. Benowitz, MD; Jasjit S. Ahluwalia, MD, MPH

How can
advances in
tobacco treatment
and policy
advance health
equity?

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National Institutes of Health

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Pfizer Global Medical Grants

Providing varenicline and placebo

Conflicts of Interest: None

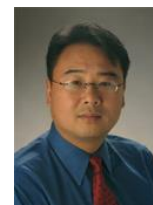
Collaborations

Jasjit S. Ahluwalia, MD, MPH, Brown University

Neal Benowitz, MD, University of California, San Francisco

Rachel Tyndale, PhD, University of Toronto

Kolawole Okuyemi, MD, MPH, University of Utah



Community Engagement:

- Swope Health Services
- Community Advisory Board
- Congressman, Rev. Emanuel Cleaver II

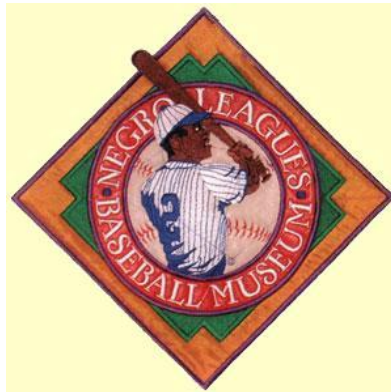
- Black Healthcare Coalition
- Black Chamber of Commerce
- American Jazz Museum
- Negro Leagues Baseball Museum
- The National WWI Museum and Memorial
- Union Station
- YMCA of Kansas City



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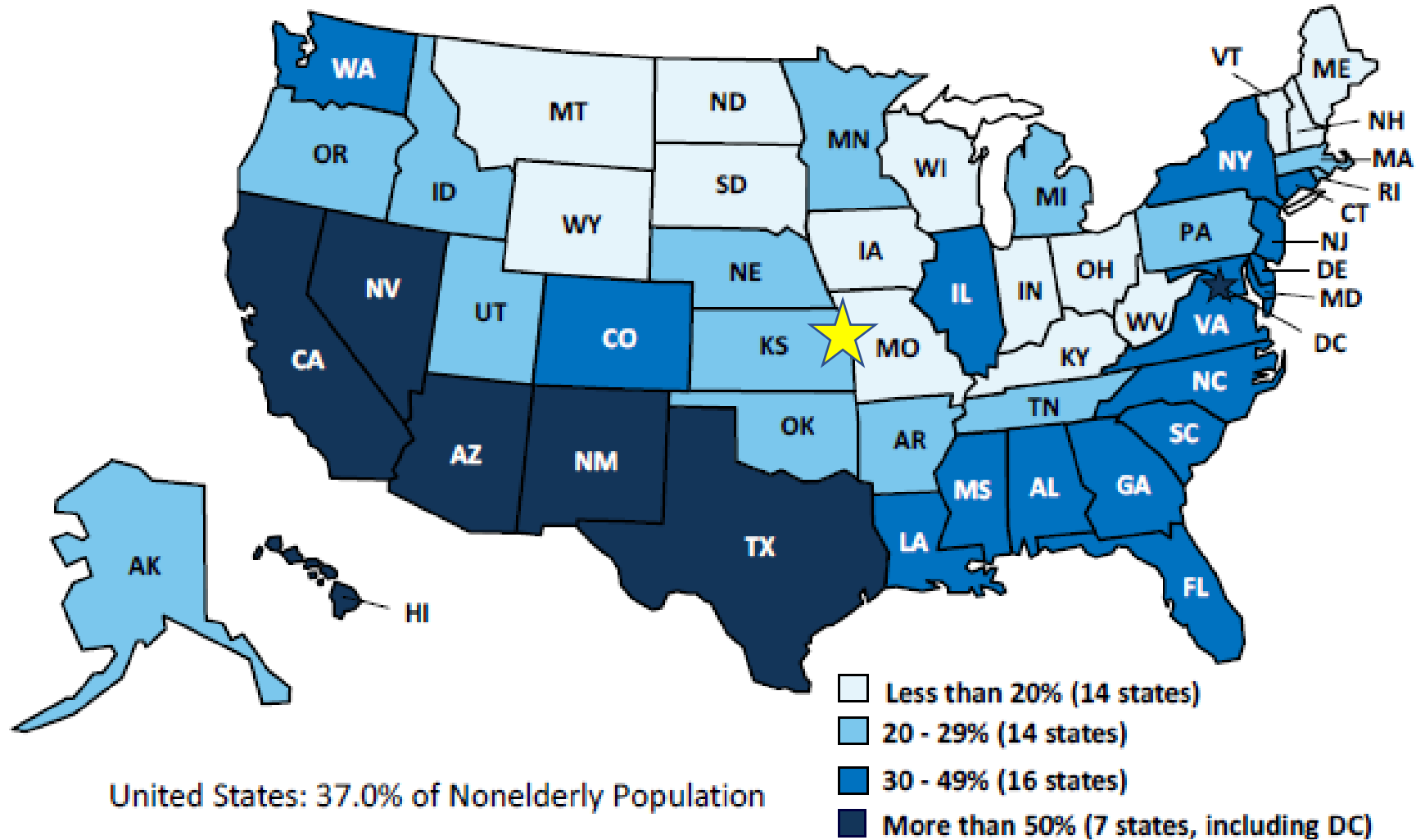


University of Kansas Medical Center – Swope Health Collaborative
Kick It at Swope (KIS) and Quit2Live (Q2L) smoking cessation studies:

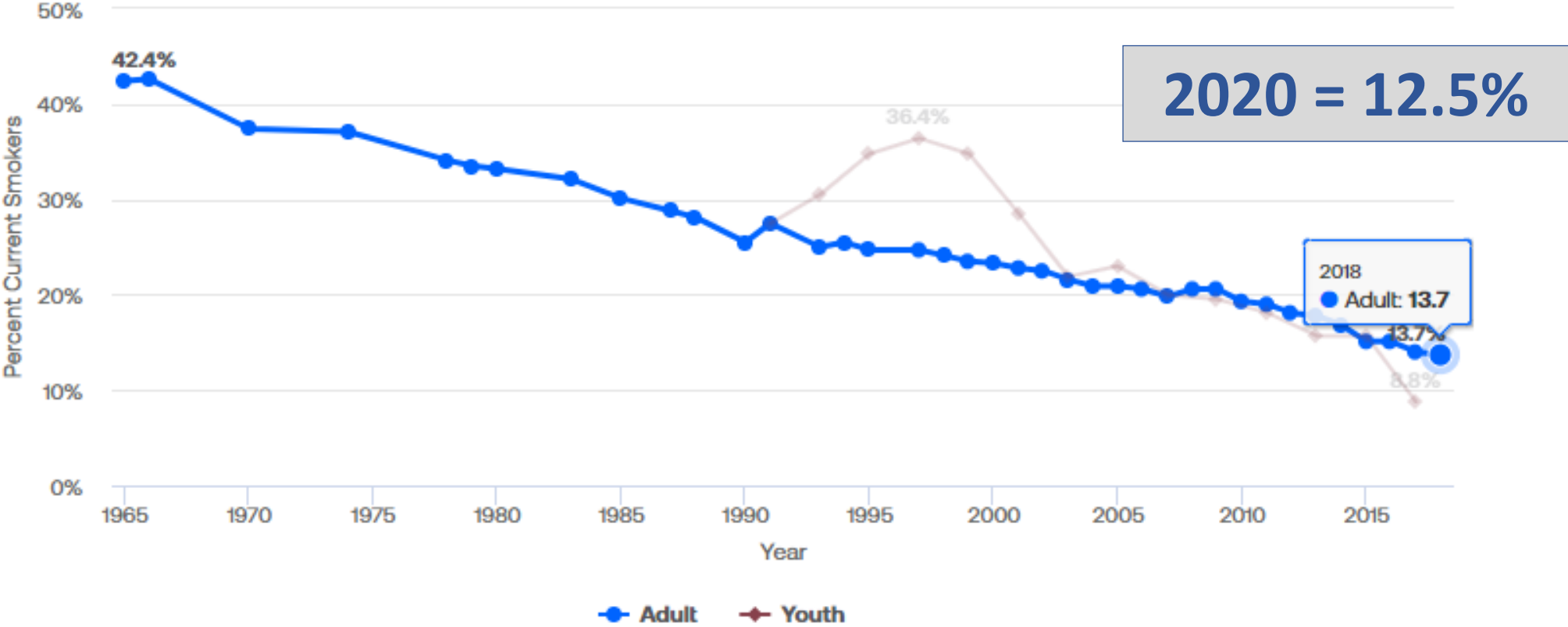
Funding Agency	Grant Title	PI
National Cancer Institute R01 CA77856	Does bupropion help African Americans quit smoking? (KIS-I)	Jasjit S. Ahluwalia
National Cancer Institute R01 CA85930	African Americans smokers in low income housing (Pathways to Health)	Jasjit S. Ahluwalia
National Cancer Institute R01 CA091912	Helping African American light smokers quit (KIS-II)	Jasjit S. Ahluwalia
National Cancer Institute R01 CA091912	Enhancing tobacco use treatment for African American light smokers (KIS-III)	Lisa Sanderson Cox
National Institute on Drug Abuse R01 DA031815	Understanding disparities in quitting in African American and White smokers (Q2L)	Nicole Nollen
National Institute on Drug Abuse R01DA035796	Advancing tobacco use treatment for African American smokers (KIS-IV)	Lisa Sanderson Cox
PCORI AD-1310-08709	Informing tobacco-treatment guidelines for African American non-daily smokers (Q2L ²)	Nicole Nollen
National Institute on Drug Abuse R01 DA046576	Individualizing Pharmacotherapy: A novel optimization strategy to increase smoking cessation in the African American community (Q2L ³)	Nicole Nollen
National Cancer Institute R01 CA259256	Improving smoking abstinence outcomes in the African American community through extended treatment (KIS-V)	Lisa Sanderson Cox
National Institute on Drug Abuse R01 DA055999	The impact of menthol flavoring on switching in adult menthol smokers	Nicole Nollen



Share of Nonelderly Population that is a Person of Color



Tremendous progress at reducing smoking rate but 34 million America adults still smoke



Source: ALA/NHIS/CDC

Cigarette smoking is down, but about
34 MILLION

American adults still smoke

**Cigarette smoking remains high
among certain groups**



Men



Adults 25-64
years old



Lower education



Below
poverty level



Midwest
and South



Uninsured
or Medicaid



Disabled



Serious
psychological
distress



American Indians,
Alaska Natives and
Multiracial



Lesbians, gays,
and bisexuals

Higher rates of tobacco use

- < high-school education (23%)
- live \leq 100% FPL (21%)
- receive Medicaid (25%)
- have serious psychological distress (35%)
- identify as lesbian, gay, or bisexual (20%)
- racial/ethnic minorities (7%-23%)

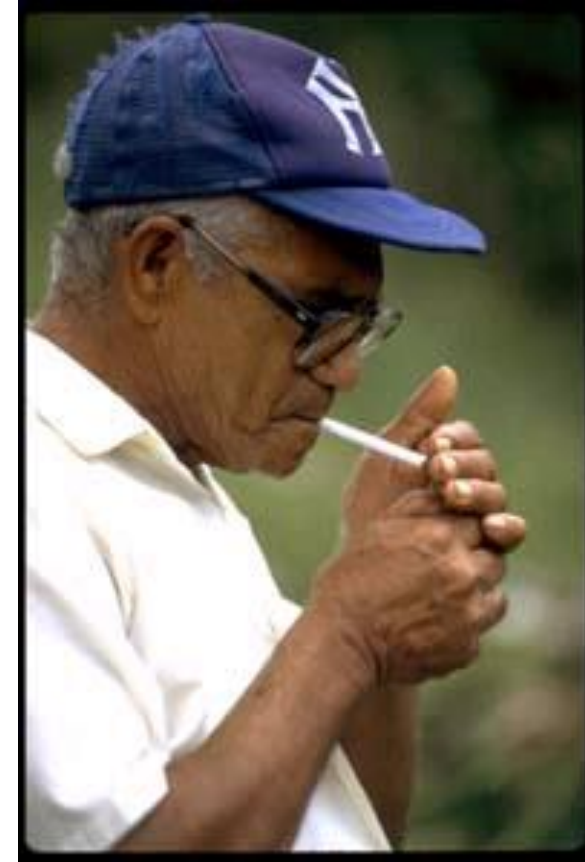
**A Socioecological
Approach to
Addressing
Tobacco-Related
Health Disparities**

Major Conclusions

1. Addressing TRHD is necessary to reduce the disease burden of tobacco use.
2. Some groups have benefited less from efforts to reduce tobacco use.
 - racial and ethnic minorities
 - light smokers
3. Broader implementation of known effective strategies to reduce tobacco use would contribute substantially to reducing TRHD.

African American Smokers

- Prevalence similar to non-Hispanic Whites
- Start smoking later
- Try to quit smoking more often
- High relapse rate
- More likely to smoke menthol cigarettes
- Higher cotinine levels per cigarette
- Smoke fewer cigarettes per day
- **Have highest cancer incidence and morbidity**





Original Investigation | Substance Use and Addiction

Assessment of Racial Differences in Pharmacotherapy Efficacy for Smoking Cessation

Secondary Analysis of the EAGLES Randomized Clinical Trial

Nicole L. Nollen, PhD; Jasjit S. Ahluwalia, MD; Lisa Sanderson Cox, PhD; Kolawole Okuyemi, MD; David Lawrence, PhD; Larry Samuels, PhD; Neal L. Benowitz, MD

Abstract

IMPORTANCE Understanding Black vs White differences in pharmacotherapy efficacy and the underlying reasons is critically important to reducing tobacco-related health disparities.

OBJECTIVE To compare pharmacotherapy efficacy and examine variables to explain Black vs White differences in smoking abstinence.

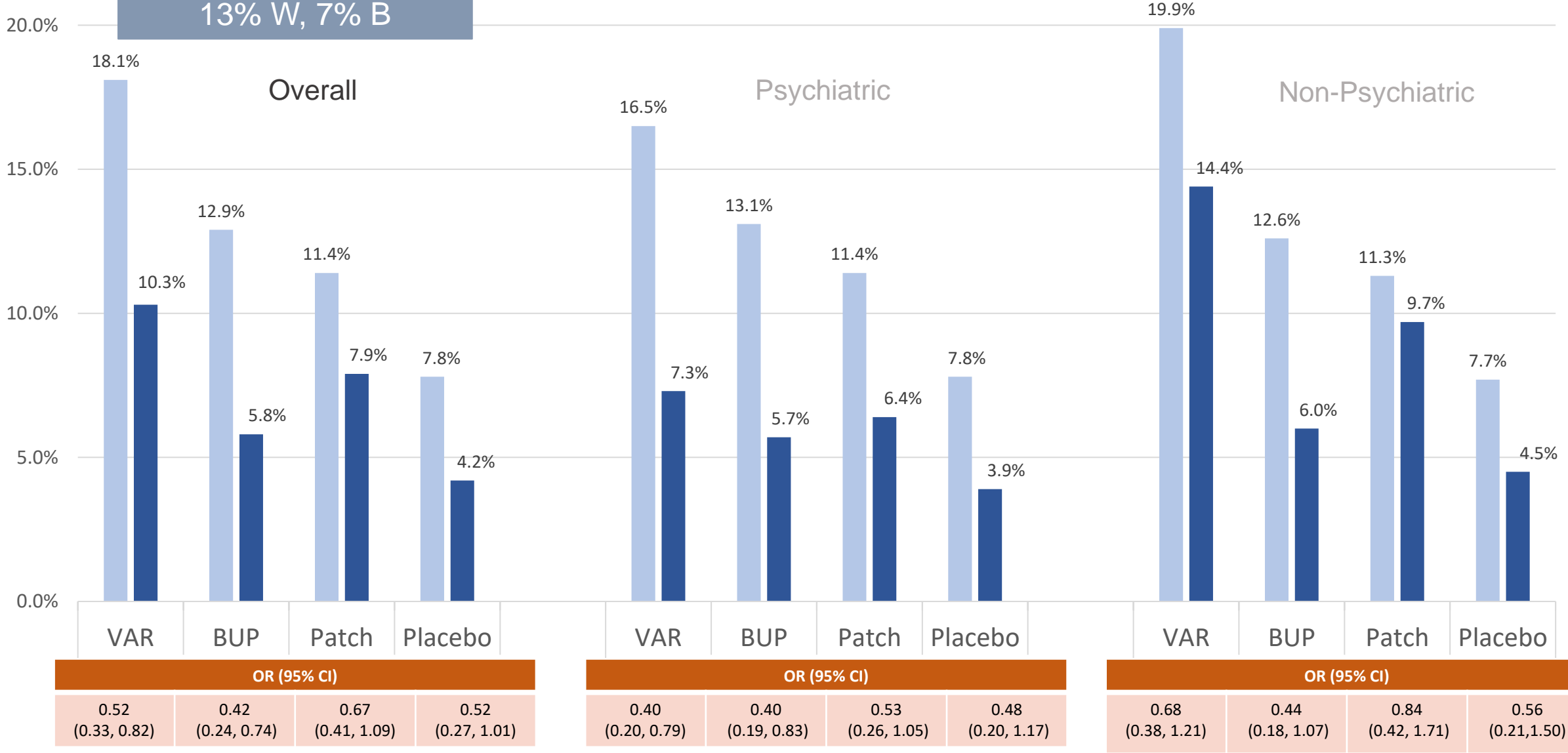
Key Points

Question Does the efficacy of varenicline, bupropion, and nicotine patch differ for US Black and White smokers, and what variables explain the difference?

11% Global Abstinence
13% W, 7% B

White Black

% continuous abstinence weeks 9-24



Nollen et al., 2021 Assessment of racial differences...EAGLES secondary analysis

Conclusions:

- Black moderate to heavy smokers significantly less likely than Whites to achieve abstinence
 - Varenicline only pharmacotherapy demonstrating efficacy over placebo for Black participants
- Limitations –
 - No evaluation of key factors, e.g., menthol, metabolism, socioeconomic status¹
 - No light smokers

➤ Race is a proxy for social, contextual, and biological differences (Nollen et al., 2019)

- Studies needed to identify why – i.e., what mechanisms

Nollen NL, Mayo MS, Cox LS, et al. Factors that Explain Differences in Abstinence between Black and White Smokers: : A Prospective Intervention Study. *JNCI: Journal of the National Cancer Institute*. 2019. doi:10.1093/jnci/djz001.

KIS-IV



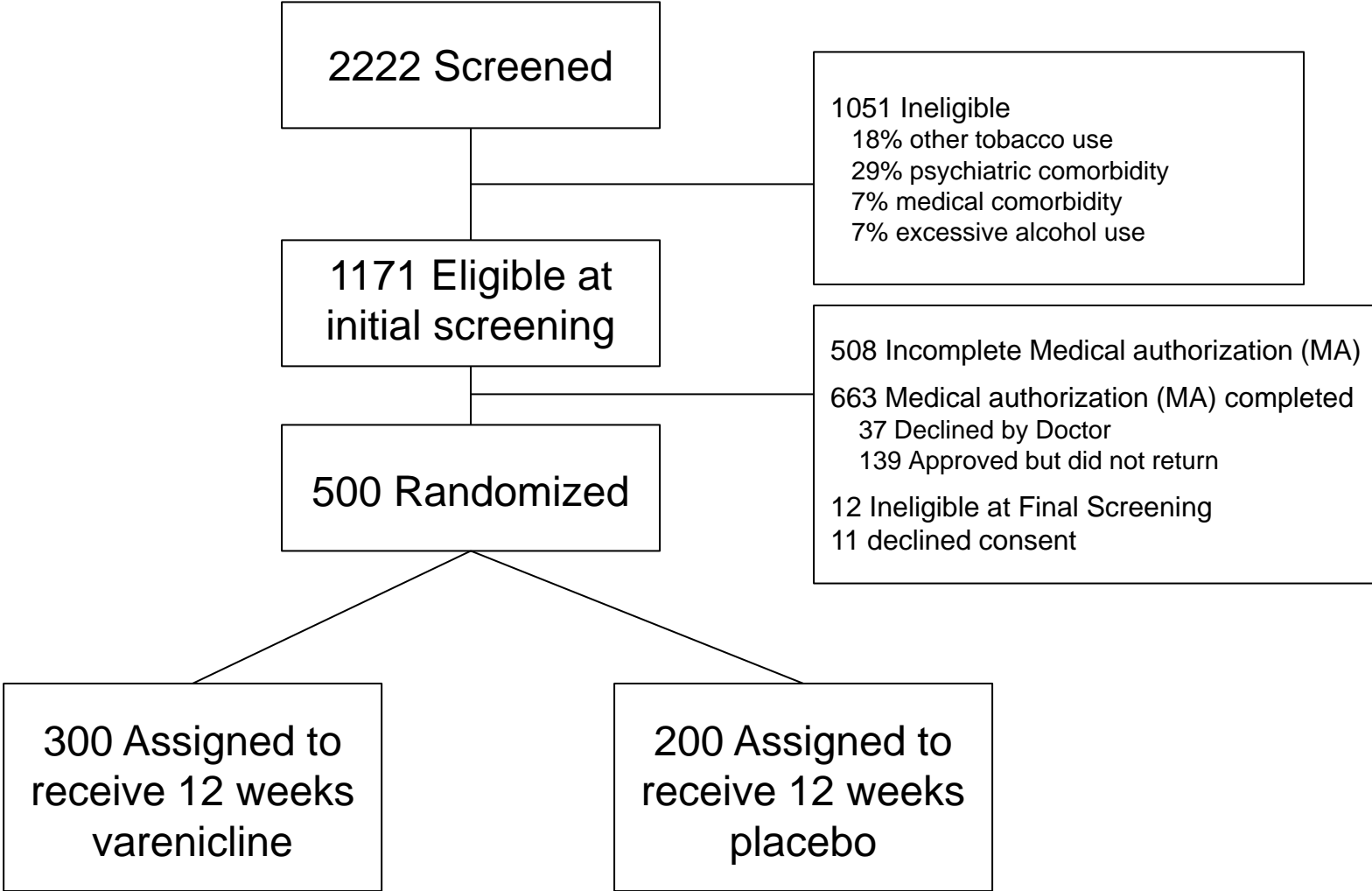
- Primary Aim:
 - To evaluate the efficacy of varenicline versus placebo for tobacco use treatment. Main outcome was cotinine-confirmed 7-day abstinence at Month 6.
- Design:
 - Randomized placebo-controlled trial of 12 weeks varenicline among 500 African American daily smokers (300 to varenicline, 200 to placebo) including light, moderate, and heavy daily smokers.
 - 3:2 randomization stratified by sex and cigarettes per day (1-10cpd or >10cpd)
 - Culturally relevant, individually tailored, cognitive behavioral counseling and health education for all participants.

KIS-IV Eligibility Criteria

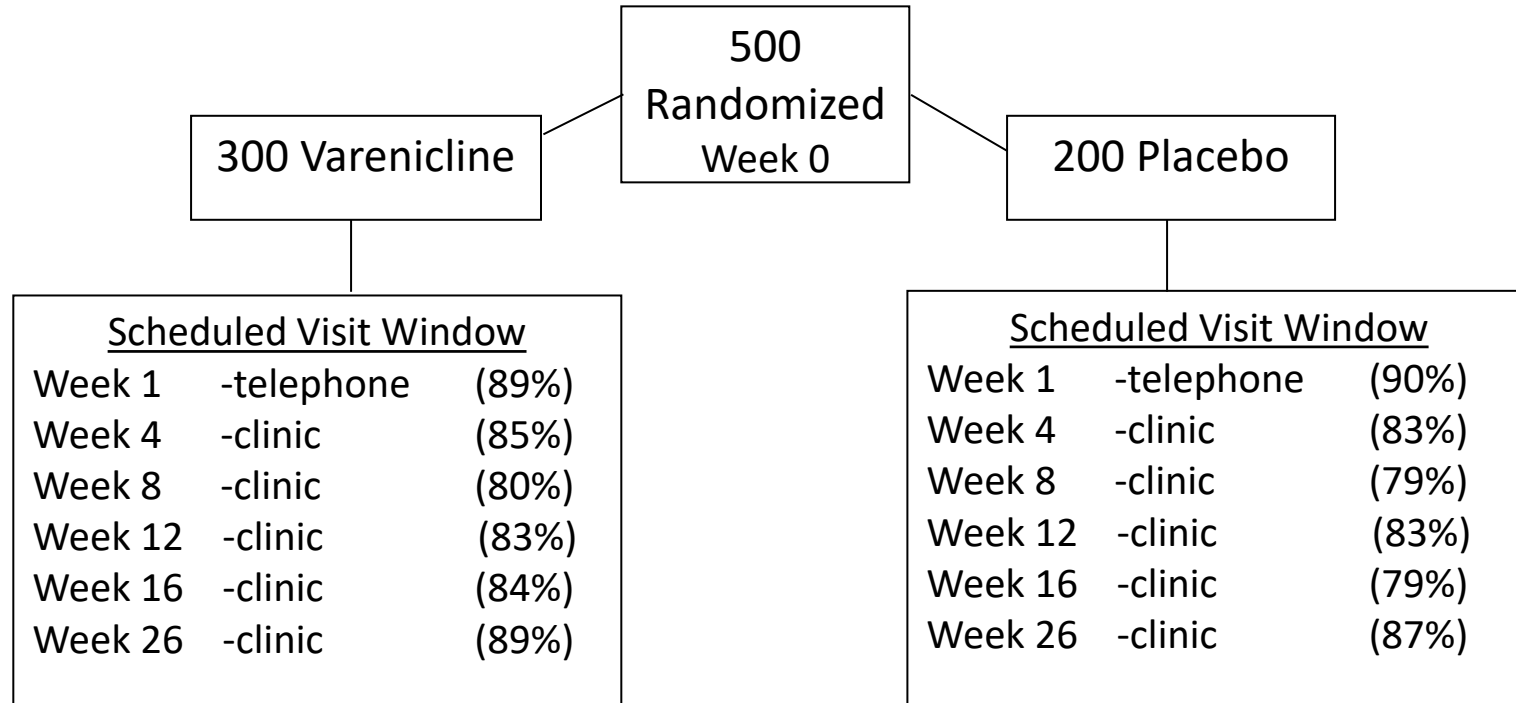
Inclusion Criteria	Exclusion Criteria
<ul style="list-style-type: none">• Self-identified African American• ≥ 18 years of age• Smokes ≥ 1cpd• Smoke on ≥ 25 days of the past 30 days• Functioning telephone• Interested in quitting smoking• Interested in taking varenicline for 12 weeks• Willing to complete all study visits• Medication approval from physician	<ul style="list-style-type: none">• Renal impairment• Evidence or history of clinically significant allergic reactions to varenicline• A cardiovascular event in the past month• History of alcohol or drug dependence in the past year• Major depressive disorder in the last year requiring treatment• History of panic disorder, psychosis, bipolar disorder, or eating disorders• Use of tobacco products other than cigarettes in past 30 days• Use of smoking cessation pharmacotherapy in the month prior to enrollment, including varenicline• Pregnant, contemplating getting pregnant, or breastfeeding• Plans to move from KC during the treatment and follow-up phase• Another household member enrolled in the study

KIS-IV CONSORT Diagram

Community and clinic-based recruitment.



KIS-IV Flowchart



Medication given at Weeks 0, 4, 8.

Retention: (%) completed scheduled visit within window.

KIS-IV Participants n=500

- Average age = 52 years
- 52% female
- \$27,600 total gross income
- 86% \geq high school education
- 27% married or living with partner
- 65% covered by health insurance

KIS-IV Participants n=500

- Cigarettes per day, mean (SD) = 12.6 (6.6)
- 52% light smokers (1-10 cpd)

- 79% smoked within 30 min. of waking
- 86% smoked menthol cigarettes
- 26% lived in smoke-free home

- 80% attempted to quit in past year
- Number of quit attempts in past year = 1.9
- 48% past use of pharmacotherapy to quit
- 22% past use of varenicline to quit

KIS-IV Cotinine-verified 7-day Abstinence

	Varenicline n=300	Placebo n=200	Odds (95% CI)	P value
Quit at Week 4	16.00 %	5.00 %	3.62 (1.79-7.34)	0.0002
Quit at Week 12	18.67 %	7.00 %	3.04 (1.65-5.64)	0.0002
Quit at Week 16				
Quit at Week 26				

Cotinine verified (< 15ng/ml).

Those lost to follow-up were treated as smokers.

KIS-IV Cotinine-verified 7-day Abstinence

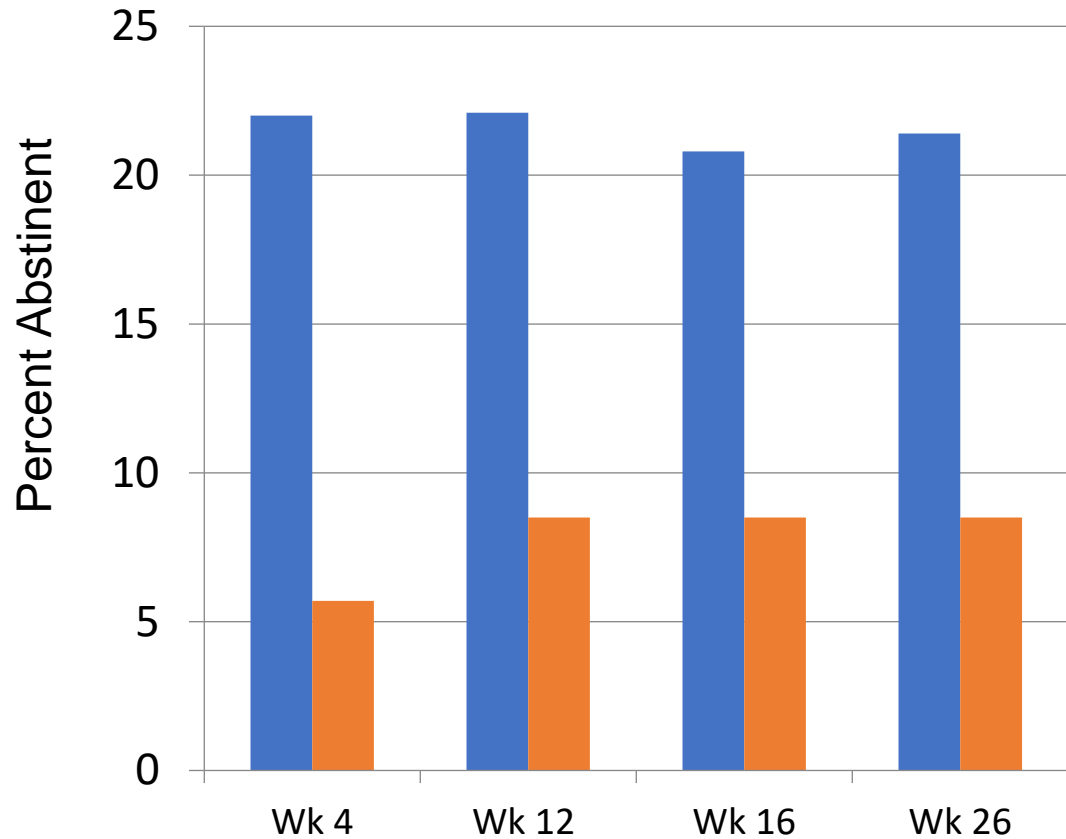
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Quit at Week 12	18.67 %	7.00 %	3.04 (1.65-5.64)	0.0002
Quit at Week 16	18.00 %	6.50 %	3.16 (1.67-5.96)	0.0002
Quit at Week 26	15.67 %	6.50 %	2.67 (1.40-5.08)	0.0020

Cotinine verified (< 15ng/ml).

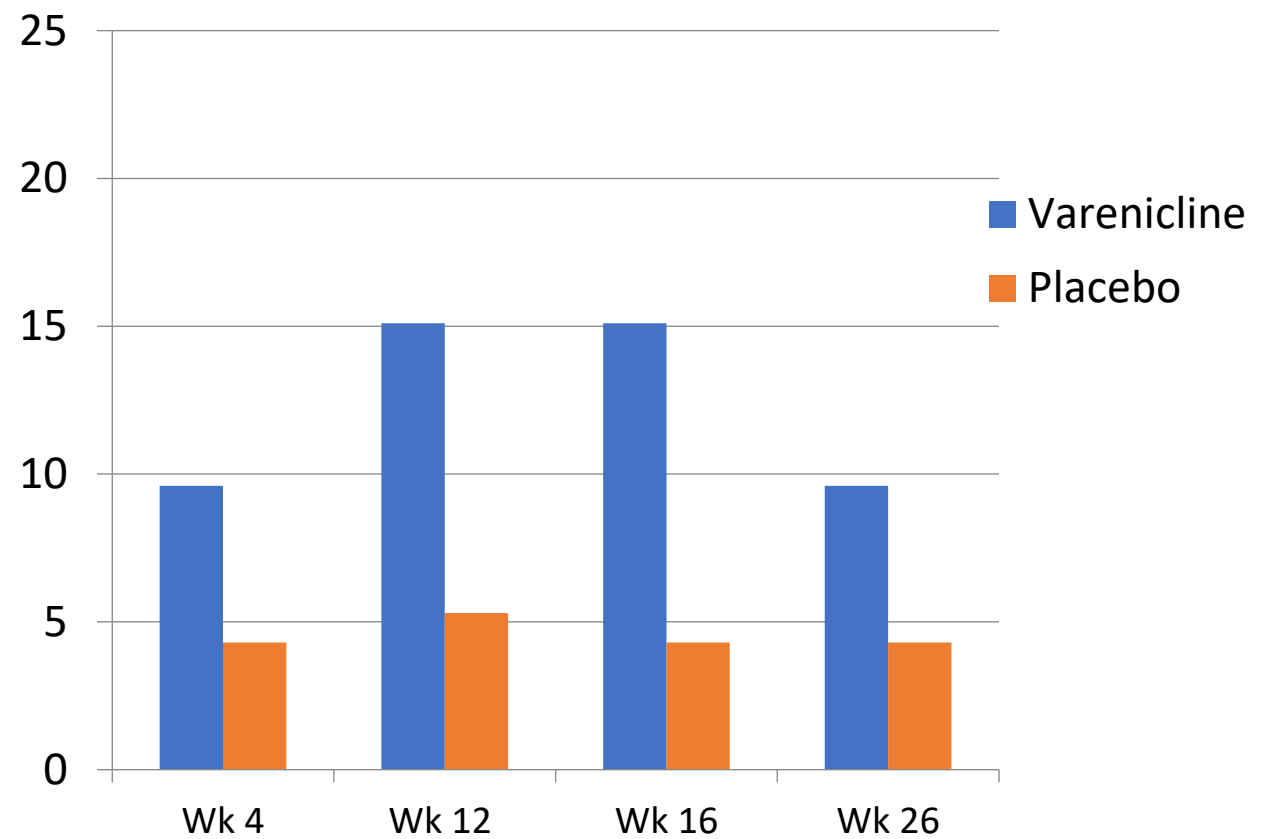
Those lost to follow-up were treated as smokers.

KIS-IV Cotinine-verified 7-day Abstinence

Light Smokers (1-10 cpd)



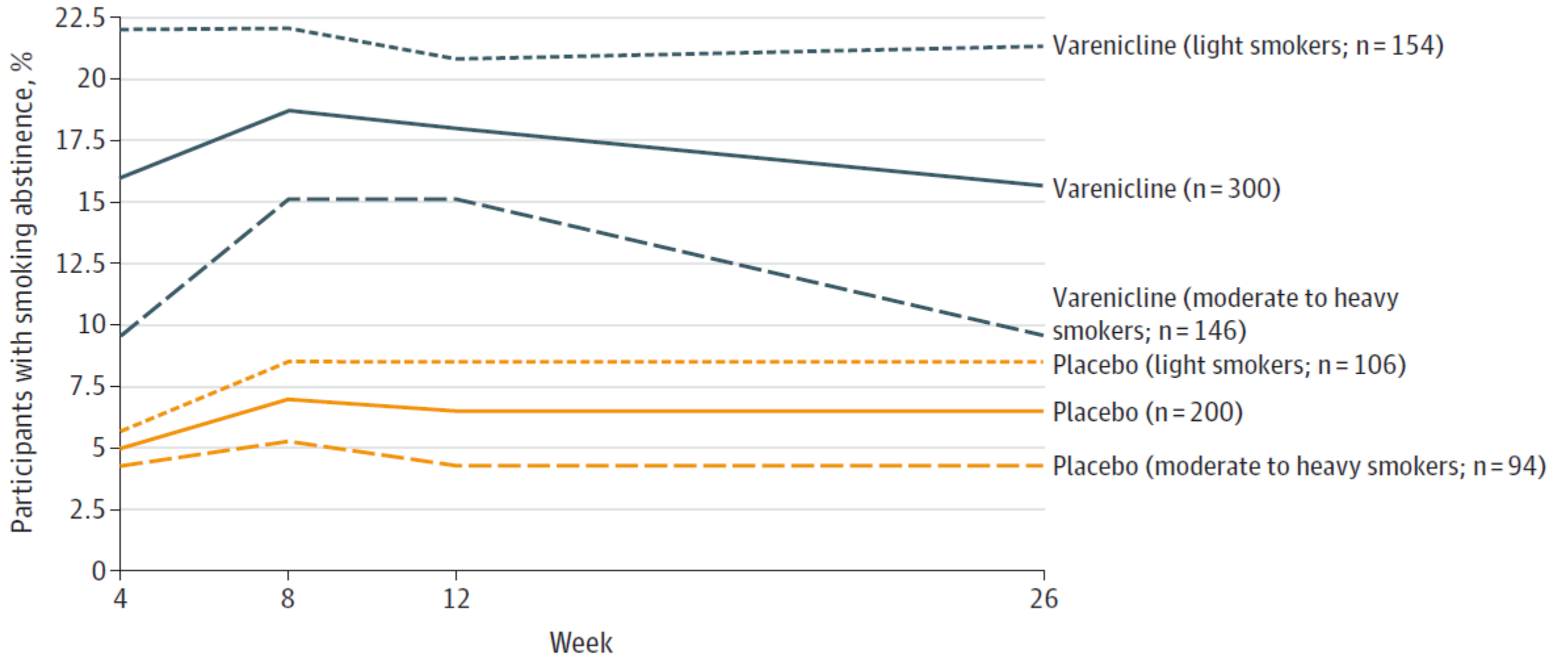
Moderate to Heavy Smokers (>10 cpd)



No significant treatment x cpd interaction.

Cotinine verified (< 15ng/ml). Those lost to follow-up were treated as smokers.

Prevalence of biochemically verified 7-day point prevalence smoking abstinence



KIS-IV Varenicline Side Effects

Prevalence of cumulative adverse events by symptom and globally by treatment, No. (%)

	By Symptom, Weeks 1-16		
	Placebo n=196	Varenicline n=293	(p)
Change in hostility or aggression	79 (40.3)	99 (33.8)	.14
Fatigue or loss of energy	112 (57.1)	163 (55.6)	.74
Nausea	90 (45.9)	163 (55.6)	.03
Trouble sleeping	117 (59.7)	190 (64.8)	.25
Headaches	95 (48.5)	157 (53.6)	.27
Abnormal dreams	93 (47.4)	146 (49.8)	.60
Gas or flatulence	130 (66.3)	191 (65.2)	.79
Constipation	78 (39.8)	120 (41.0)	.80
Dizziness	62 (31.6)	95 (32.4)	.85
Dry mouth	129 (65.8)	183 (62.5)	.45
Irritability	111 (56.6)	167 (57.0)	.94
	Global, Weeks 1-16		
Any	178 (90.8)	276 (94.2)	.15
SAE	2 (1.0)	0 (0.0)	**

**Sparse events No (p) provided.

What accounts for treatment effect?

- No difference between treatment groups in
 - session attendance / retention
 - self-reported medication adherence
 - change in psychological reward from smoking (mCEQ)
 - change in withdrawal symptoms (MNWS)
 - change in craving (QSU-Brief)

KIS-IV Summary

- Varenicline was effective in promoting short (EOT Week 12) and long-term (Month 6) abstinence in African American daily smokers.
 - Varenicline treatment outcomes replicate Quit2Live (Nollen et al, 2019, JNCI)
- Varenicline was effective in promoting abstinence in light smokers and in moderate-heavy smokers.
- Varenicline was safe and well-tolerated
 - Reported side effects were similar between active and placebo groups.
 - Nausea was only symptom reported more frequently in active group.
 - Counseling for medication management
- The need to enhance treatment for African Americans remains.
 - KIS-V will examine extended (24 weeks) varenicline treatment.

Kick It at Swope – Quit2Live

Over 20 years of tobacco treatment research in the African American community -
> 3,200 participants



- African Americans benefit from pharmacotherapy within tobacco treatment
- African American smokers are highly engaged in treatment and successful at quitting across therapies. Across studies:
 - > 80% return for study visits
 - Good compliance to medication (w/exception of gum)
 - 13%-24% still quit at month 6
 - Chance of quitting 50%-200% higher with medication relative to placebo
- Non-nicotine medications (VAR, BUP) may be preferable
 - Adherence is central to success
- Varenicline for treatment of light smokers
 - Non-daily smokers may benefit from pharmacotherapy support
- Continued efforts needed to enhance efficacy of existing medications
 - Extended treatment, changing pharmacotherapy, repeated intervention

Discussion

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How can advances in tobacco treatment and policy advance health equity?

Cigarette smoking remains high among certain groups



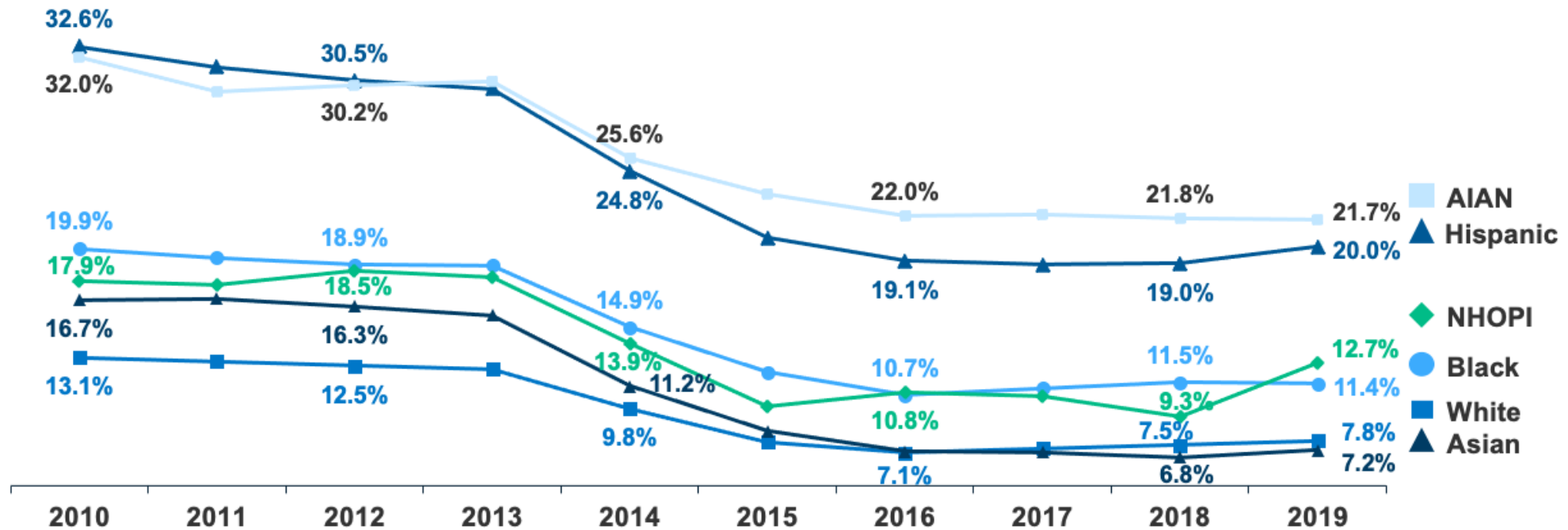
Strategies essential to continue reducing cigarette smoking overall



Access and cost

Access and cost

Uninsured Rates for the Nonelderly Population by Race and Ethnicity, 2010-2019



NOTE: Includes individuals ages 0 to 64. AIAN refers to American Indians and Alaska Natives, NHOPI refers to Native Hawaiians and Other Pacific Islanders. Persons of Hispanic origin may be of any race but are categorized as Hispanic for this analysis; other groups are non-Hispanic

SOURCE: KFF analysis of the 2010-2019 American Community Survey.



Access and cost

- nicotine replacement patch

- \$56-\$81 for 4 weeks (\$2.45/day)

- generic bupropion

- \$58-\$92 for 4 weeks (\$2.68/day)

- generic varenicline

- \$398-\$494 for 4 weeks (\$15.93/day)

= \$1,194 - \$1,482 for 12 weeks of treatment

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advances in
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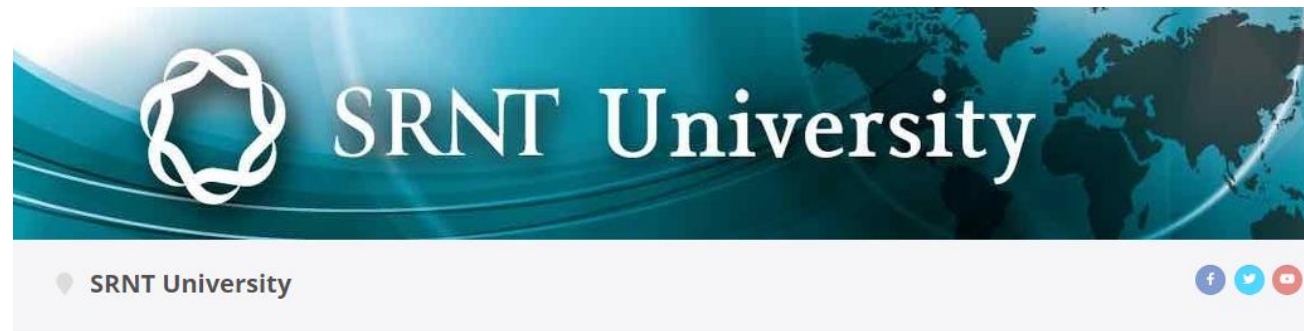
Discussion

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- Themed collections
- Methodology courses
- Webinars and podcasts
- Tools and resources



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Heated Tobacco Products
Themed Collection

Library Section: Heated Tobacco Products



Library Section: E-cigarette Collection



eTable 2. Week 26 self-report and verified 7-day point prevalence smoking abstinence

	Treatment		P value
	Varenicline	Placebo	
A) Number of participants randomized	300	200	
B) Number of participants who completed Week 26 visit (B/A)	267 (89.0%)	174 (87.0%)	NA
C) Self-reported completers only abstinence at Week 26 (C/B)	114 (42.7%)	64 (36.8%)	NA
D) Verification samples obtained at Week 26 (D/C)	109 (95.6%)	62 (96.9%)	NA
E) Verified abstinence for completers only (E/B)	47 (17.6%)	13 (7.5%)	0.002
F) Verified abstinence using Russel Standard* (F/A)	47 (15.7%)	13 (6.5%)	0.002
G) Verified abstinence using Last Observation Carried Forward	71 (23.7%)	19 (9.5%)	<0.001
H) Verified abstinence using Multiple Imputation**	69.2 (23.1%)	27.8 (13.9%)	0.02
*Participants with missing data imputed as smoking			
**Average of 100 imputations assuming monotonic logistic regression with treatment and smoking level			



JAMA | **Original Investigation**

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R01 DA035796: Advancing Tobacco Use Treatment for African American Smokers

Cox, Nollen, Mayo et al. *JAMA*. 2022;327(22):2201–2209.