Varenicline Plus Counseling for Smoking Cessation in African Americans

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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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- 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

**National Institutes of Health**
- National Institute on Drug Abuse

**Pfizer Global Medical Grants**
- Providing varenicline and placebo

Conflicts of Interest: None
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
<table>
<thead>
<tr>
<th>Funding Agency</th>
<th>Grant Title</th>
<th>PI</th>
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<tr>
<td>National Cancer Institute</td>
<td>Does bupropion help African Americans quit smoking? (KIS-I)</td>
<td>Jasjit S. Ahluwalia</td>
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<tr>
<td>National Cancer Institute</td>
<td>African Americans smokers in low income housing (Pathways to Health)</td>
<td>Jasjit S. Ahluwalia</td>
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<tr>
<td>National Cancer Institute</td>
<td>Helping African American light smokers quit (KIS-II)</td>
<td>Jasjit S. Ahluwalia</td>
</tr>
<tr>
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<td>Enhancing tobacco use treatment for African American light smokers (KIS-III)</td>
<td>Lisa Sanderson Cox</td>
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<td>National Institute on Drug Abuse</td>
<td>Understanding disparities in quitting in African American and White smokers (Q2L)</td>
<td>Nicole Nollen</td>
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<td><strong>Advancing tobacco use treatment for African American smokers (KIS-IV)</strong></td>
<td>Lisa Sanderson Cox</td>
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<td>PCORI</td>
<td>Informing tobacco-treatment guidelines for African American non-daily smokers (Q2L)</td>
<td>Nicole Nollen</td>
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<td>National Institute on Drug Abuse</td>
<td>Individualizing Pharmacotherapy: A novel optimization strategy to increase smoking cessation in the African American community (Q2L³)</td>
<td>Nicole Nollen</td>
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<tr>
<td>National Cancer Institute</td>
<td>Improving smoking abstinence outcomes in the African American community through extended treatment (KIS-V)</td>
<td>Lisa Sanderson Cox</td>
</tr>
<tr>
<td>National Institute on Drug Abuse</td>
<td>The impact of menthol flavoring on switching in adult menthol smokers</td>
<td>Nicole Nollen</td>
</tr>
</tbody>
</table>
Share of Nonelderly Population that is a Person of Color

United States: 37.0% of Nonelderly Population

SOURCE: KCMU/Urban Institute analysis of 2011 and 2012 ASEC Supplements to the CPS.

from: Kaiser Family Foundation www.kff.org
Tremendous progress at reducing smoking rate but
34 million America adults still smoke

Source: ALA/NHIS/CDC

2020 = 12.5%
Cigarette smoking is down, but about 34 MILLION American adults still smoke.

Higher rates of tobacco use among certain groups:
- < high-school education (23%)
- live ≤ 100% FPL (21%)
- receive Medicaid (25%)
- have serious psychological distress (35%)
- identify as lesbian, gay, or bisexual (20%)
- racial/ethnic minorities (7%-23%)
**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

Overall

Psychiatric

Non-Psychiatric

% continuous abstinence weeks 9-24

VAR BUP Patch Placebo

VAR BUP Patch Placebo

Nollen et al., 2021, JAMA Network Open
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 status
  • 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

• 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

<table>
<thead>
<tr>
<th>Inclusion Criteria</th>
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<tbody>
<tr>
<td>• Self-identified African American</td>
<td>• Renal impairment</td>
</tr>
<tr>
<td>• ≥ 18 years of age</td>
<td>• Evidence or history of clinically significant allergic reactions to varenicline</td>
</tr>
<tr>
<td>• <strong>Smokes &gt;1cpd</strong></td>
<td>• A cardiovascular event in the past month</td>
</tr>
<tr>
<td>• Smoke on ≥25 days of the past 30 days</td>
<td>• History of alcohol or drug dependence in the past year</td>
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<tr>
<td>• Functioning telephone</td>
<td>• Major depressive disorder in the last year requiring treatment</td>
</tr>
<tr>
<td>• <strong>Interested in quitting smoking</strong></td>
<td>• History of panic disorder, psychosis, bipolar disorder, or eating disorders</td>
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<tr>
<td>• Interested in taking varenicline for 12 weeks</td>
<td>• Use of tobacco products other than cigarettes in past 30 days</td>
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<tr>
<td>• Willing to complete all study visits</td>
<td>• Use of smoking cessation pharmacotherapy in the month prior to enrollment, including varenicline</td>
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<td>• <strong>Medication approval from physician</strong></td>
<td>• Pregnant, contemplating getting pregnant, or breastfeeding</td>
</tr>
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<td></td>
<td>• Plans to move from KC during the treatment and follow-up phase</td>
</tr>
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<td></td>
<td>• Another household member enrolled in the study</td>
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</table>
Community and clinic-based recruitment.

KIS-IV CONSORT Diagram

2222 Screened

1171 Eligible at initial screening

500 Randomized

300 Assigned to receive 12 weeks varenicline

200 Assigned to receive 12 weeks placebo

1051 Ineligible
- 18% other tobacco use
- 29% psychiatric comorbidity
- 7% medical comorbidity
- 7% excessive alcohol use

508 Incomplete Medical authorization (MA)

663 Medical authorization (MA) completed
- 37 Declined by Doctor
- 139 Approved but did not return
- 12 Ineligible at Final Screening
- 11 declined consent
Medication given at Weeks 0, 4, 8.  
Retention: (%) completed scheduled visit within window.
• Average age = 52 years
• 52% female
• $27,600 total gross income
• 86% ≥ 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 |
<table>
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<tr>
<td>Quit at Week 4</td>
<td>16.00 %</td>
<td>5.00 %</td>
<td>3.62</td>
<td>0.0002</td>
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<tr>
<td></td>
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<td></td>
<td>(1.79-7.34)</td>
<td></td>
</tr>
<tr>
<td>Quit at Week 12</td>
<td>18.67 %</td>
<td>7.00 %</td>
<td>3.04</td>
<td>0.0002</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>(1.65-5.64)</td>
<td></td>
</tr>
<tr>
<td>Quit at Week 16</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Quit at Week 26</td>
<td></td>
<td></td>
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Cotinine verified (< 15ng/ml). Those lost to follow-up were treated as smokers.
### KIS-IV Cotinine-verified 7-day Abstinence

<table>
<thead>
<tr>
<th></th>
<th>Varenicline n=300</th>
<th>Placebo n=200</th>
<th>Odds (95% CI)</th>
<th>P value</th>
</tr>
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<tr>
<td>Quit at Week 4</td>
<td>16.00 %</td>
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<td>7.00 %</td>
<td>3.04 (1.65-5.64)</td>
<td>0.0002</td>
</tr>
<tr>
<td>Quit at Week 16</td>
<td>18.00 %</td>
<td>6.50 %</td>
<td>3.16 (1.67-5.96)</td>
<td>0.0002</td>
</tr>
<tr>
<td>Quit at Week 26</td>
<td>15.67 %</td>
<td>6.50 %</td>
<td>2.67 (1.40-5.08)</td>
<td>0.0020</td>
</tr>
</tbody>
</table>

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)

- Wk 4: 22%
- Wk 12: 21%
- Wk 16: 20%
- Wk 26: 19%

Moderate to Heavy Smokers (>10 cpd)

- Wk 4: 10%
- Wk 12: 8%
- Wk 16: 8%
- Wk 26: 7%

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

Cox et al., JAMA, 2022
## KIS-IV Varenicline Side Effects

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

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Placebo</th>
<th>Varenicline</th>
<th>(p)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>By Symptom, Weeks 1-16</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Change in hostility or aggression</td>
<td>79 (40.3)</td>
<td>99 (33.8)</td>
<td>.14</td>
</tr>
<tr>
<td>Fatigue or loss of energy</td>
<td>112 (57.1)</td>
<td>163 (55.6)</td>
<td>.74</td>
</tr>
<tr>
<td>Nausea</td>
<td>90 (45.9)</td>
<td>163 (55.6)</td>
<td>.03</td>
</tr>
<tr>
<td>Trouble sleeping</td>
<td>117 (59.7)</td>
<td>190 (64.8)</td>
<td>.25</td>
</tr>
<tr>
<td>Headaches</td>
<td>95 (48.5)</td>
<td>157 (53.6)</td>
<td>.27</td>
</tr>
<tr>
<td>Abnormal dreams</td>
<td>93 (47.4)</td>
<td>146 (49.8)</td>
<td>.60</td>
</tr>
<tr>
<td>Gas or flatulence</td>
<td>130 (66.3)</td>
<td>191 (65.2)</td>
<td>.79</td>
</tr>
<tr>
<td>Constipation</td>
<td>78 (39.8)</td>
<td>120 (41.0)</td>
<td>.80</td>
</tr>
<tr>
<td>Dizziness</td>
<td>62 (31.6)</td>
<td>95 (32.4)</td>
<td>.85</td>
</tr>
<tr>
<td>Dry mouth</td>
<td>129 (65.8)</td>
<td>183 (62.5)</td>
<td>.45</td>
</tr>
<tr>
<td>Irritability</td>
<td>111 (56.6)</td>
<td>167 (57.0)</td>
<td>.94</td>
</tr>
</tbody>
</table>

**Global, Weeks 1-16**

<table>
<thead>
<tr>
<th></th>
<th>Placebo</th>
<th>Varenicline</th>
<th>(p)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any</td>
<td>178 (90.8)</td>
<td>276 (94.2)</td>
<td>.15</td>
</tr>
<tr>
<td>SAE</td>
<td>2 (1.0)</td>
<td>0 (0.0)</td>
<td>**</td>
</tr>
</tbody>
</table>

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

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
How can advances in tobacco treatment and policy advance health equity?
Discussion
SRNT - University

srnt-u.org

• Smoking Cessation Research Certificate Program
• Themed collections
• Methodology courses
• Webinars and podcasts
• Tools and resources
<table>
<thead>
<tr>
<th>Treatment</th>
<th>Varenicline</th>
<th>Placebo</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>A) Number of participants randomized</td>
<td>300</td>
<td>200</td>
<td></td>
</tr>
<tr>
<td>B) Number of participants who completed Week 26 visit (B/A)</td>
<td>267 (89.0%)</td>
<td>174 (87.0%)</td>
<td>NA</td>
</tr>
<tr>
<td>C) Self-reported completers only abstinence at Week 26 (C/B)</td>
<td>114 (42.7%)</td>
<td>64 (36.8%)</td>
<td>NA</td>
</tr>
<tr>
<td>D) Verification samples obtained at Week 26 (D/C)</td>
<td>109 (95.6%)</td>
<td>62 (96.9%)</td>
<td>NA</td>
</tr>
<tr>
<td>E) Verified abstinence for completers only (E/B)</td>
<td>47 (17.6%)</td>
<td>13 (7.5%)</td>
<td>0.002</td>
</tr>
<tr>
<td>F) Verified abstinence using Russel Standard* (F/A)</td>
<td>47 (15.7%)</td>
<td>13 (6.5%)</td>
<td>0.002</td>
</tr>
<tr>
<td>G) Verified abstinence using Last Observation Carried Forward</td>
<td>71 (23.7%)</td>
<td>19 (9.5%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>H) Verified abstinence using Multiple Imputation**</td>
<td>69.2 (23.1%)</td>
<td>27.8 (13.9%)</td>
<td>0.02</td>
</tr>
</tbody>
</table>

*Participants with missing data imputed as smoking

**Average of 100 imputations assuming monotonic logistic regression with treatment and smoking level
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