

# Youth Nicotine Vaping Cessation

**RCT of Varenicline Added to Remote Young Adult Lay Counselor  
Delivered Behavioral Cessation Support Vs. Texting Support**



**Massachusetts  
General Hospital**

**Eden Evins, MD, MPH  
Director, MGH Center for  
Addiction Medicine**

**Cox Family Professor of Psychiatry,  
Harvard Medical School**

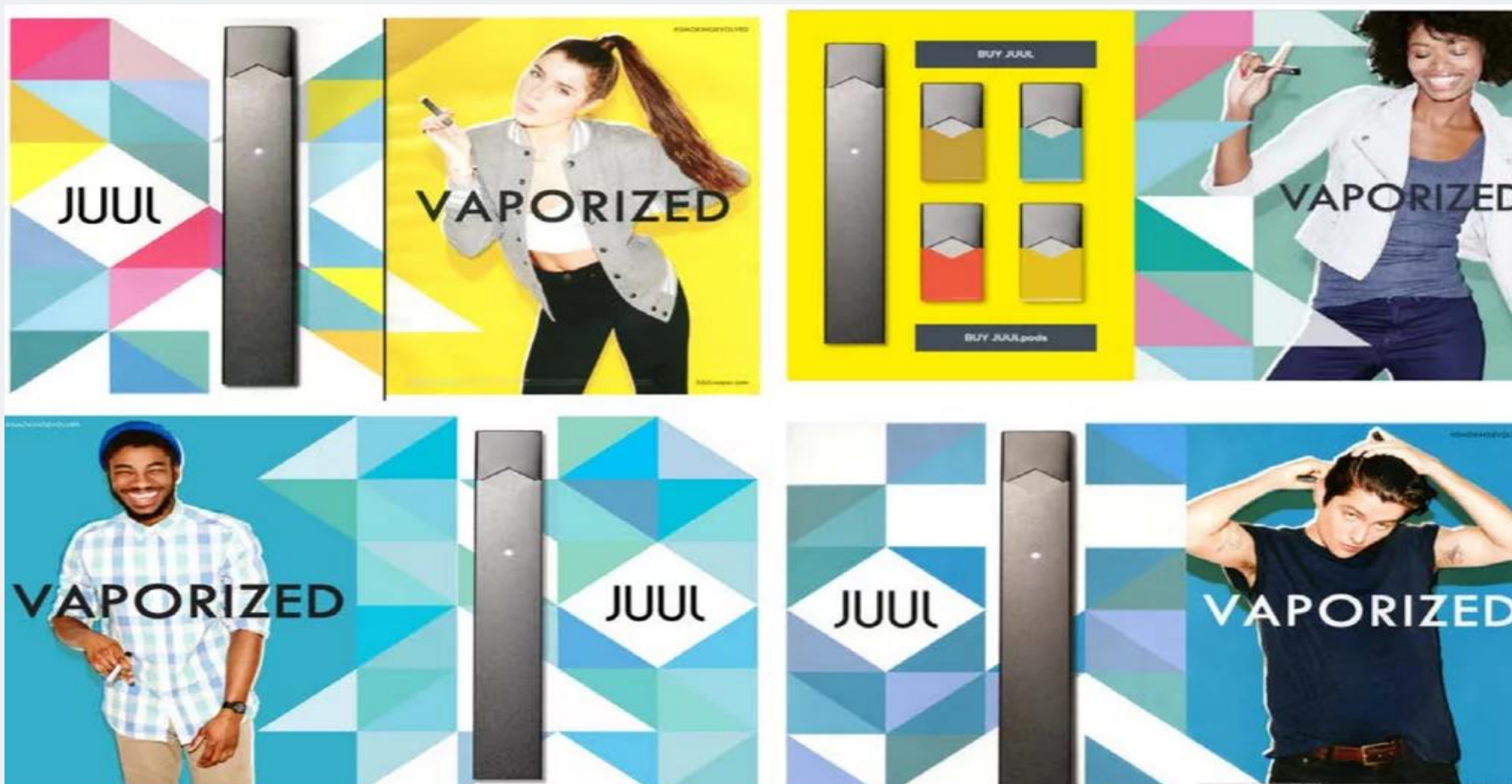
**8/9/2025**

**NIH Collaboratory Grand Rounds**



**Harvard  
Medical School**

Vaping is a less harmful alternative to smoking, but marketed to youth, most of whom have never smoked



# Vaping Is the Primary Route to Nicotine Addiction in Youth

- Addiction to Nicotine
  - In high school students, 70-75% of past daily vapers remain daily nicotine users, similar to smoked tobacco
  - Persistence suggests addiction not just experimentation
- Associated with Other Substance Use
  - High school students who vape have 25-40 times greater odds of using cannabis or alcohol regularly than non-users
    - Same Odds for daily vapers and daily smokers
    - Vaping is now the most popular route of marijuana use in high schools (16-fold increase in 4 years)





Vaping: Initially promoted to help cigarette smokers, has transformed teen nicotine and cannabis use. Few treatments have been tested.



MASSACHUSETTS  
GENERAL HOSPITAL



Equivalent to  
30 cigarettes

A woman with long brown hair is shown in profile, exhaling a large cloud of white vapor from a blue Elf Bar device she is holding. The background is a solid yellow color.

**ELF BAR**  
MAKE IT ELF, ENJOY YOURSELF.

A row of 15 small, colorful Elf Bar devices in various shades including red, purple, orange, yellow, blue, green, and pink.

**FROM £3.50 - MIX & MATCH**

A circular icon with a battery symbol and a lightning bolt.

550 MAH  
Battery

A circular icon with a bag of money symbol and the letter 'N'.

Nic  
Salts

# TREATMENT TRIAL: PROPOSED PARTICIPANTS ...

- *300 adolescents recruited from community settings*
- *Ages 16-20*
- *Who are addicted to vaped nicotine and wish to reduce or quit nicotine use*
- *Have never smoked tobacco regularly ( $\geq 5$  days per week)*
- *Few other exclusions to maximize generalizability*
  - *Comorbid drug use, drug use disorders, psych dx and tx allowed*

# BASELINE CHARACTERISTICS OF PARTICIPANTS

- 300 adolescents consented, 261 randomized, from community settings
- Age 16-25, mean age 21
  - Few <18 enrolled; some cited parental consent requirement
- Mean nicotine dependence moderate to severe (ECDI = 12-13)
- Combusted tobacco use average 0 days / week, 21 participants (8%) had smoked 100 cigarettes lifetime
- Cannabis use past 30 days in 70% of participants, avg ~1.5 days/wk
- Psych dx in 176 (67%)

# AIM 1 ...FOR THE PROPOSED TWO ARM TRIAL

- *Aim 1: Evaluate efficacy of varenicline, added to behavioral support for cessation of vaped nicotine in adolescent non-smokers with addiction to vaped nicotine.*
- *Hypothesis 1.1: Those assigned to varenicline will have a higher rate of cotinine-verified, continuous nicotine vaping abstinence from study week 9 to end of treatment (weeks 9-12) and end of follow up (weeks 9-24) (primary) than those assigned to placebo.*
- *Hypothesis 1.2: Those assigned to varenicline will have greater reduction in vaped nicotine product exposure as determined by nicotine metabolite concentration at each study visit than those assigned to placebo.*
- *Hypothesis 1.3: Those assigned to varenicline will have earlier onset of abstinence, and longer latency to first lapse, latency to relapse, and duration of abstinence, and greater total number of days of vaping abstinence.*

# AIM 2 ... FOR THE PROPOSED TWO ARM TRIAL

- *Aim 2: Assess safety & tolerability of varenicline in adolescents attempting vaping cessation*
- *Hypothesis 2.1: Nicotine withdrawal symptoms, craving, and negative mood symptoms will be less frequent and severe in the varenicline than the placebo group.*
- *Hypothesis 2.2: Those assigned to varenicline will have no greater incidence or severity of adverse events than those assigned to placebo during treatment and follow-up.*
- *Exploratory Hypothesis: Those assigned to varenicline will have less consumption of alcohol, combusted tobacco, cannabis, and non-medical prescription drugs in the treatment and follow-up period than those on placebo.*



# MODIFICATIONS: BUDGET CONSIDERATIONS: ~50% CUT

## *NECESSITY IS THE MOTHER OF INVENTION -PLATO*

- Non-clinical interventionists
  - Young adult interventionists, CRCs given TTS training and weekly group supervision
  - Short videos to standardize psychoeducation component and allow for sessions to be consistently brief, 20-25 min, but deliver CBT and psychoed content
- Fully remote intervention and assessments
  - Developed zoom based bio-verification of self reported abstinence with saliva cotinine
  - Mailed medication and saliva cotinine test kits
  - Semi-quantitative cotinine bio-verification reduced postage costs, eliminated assay costs

# MODIFICATIONS TO ENHANCE ADHERENCE

- Prior well-conducted smoking cessation trials in adolescents suffered from suboptimal adherence, jeopardizing power to detect treatment effects.
  - No tx to date shown effective for TUD Tx in adolescents, perhaps for this reason.
- Consistent, near-aged peer interventionists tasked to develop therapeutic alliance
- Sessions brief: 20-30 min to maximize adherence
- Fully remote intervention and assessments, often via participant phones, allowing flexible scheduling during school day etc.
- **Video documentation of bid study med adherence compensated \$1/video**

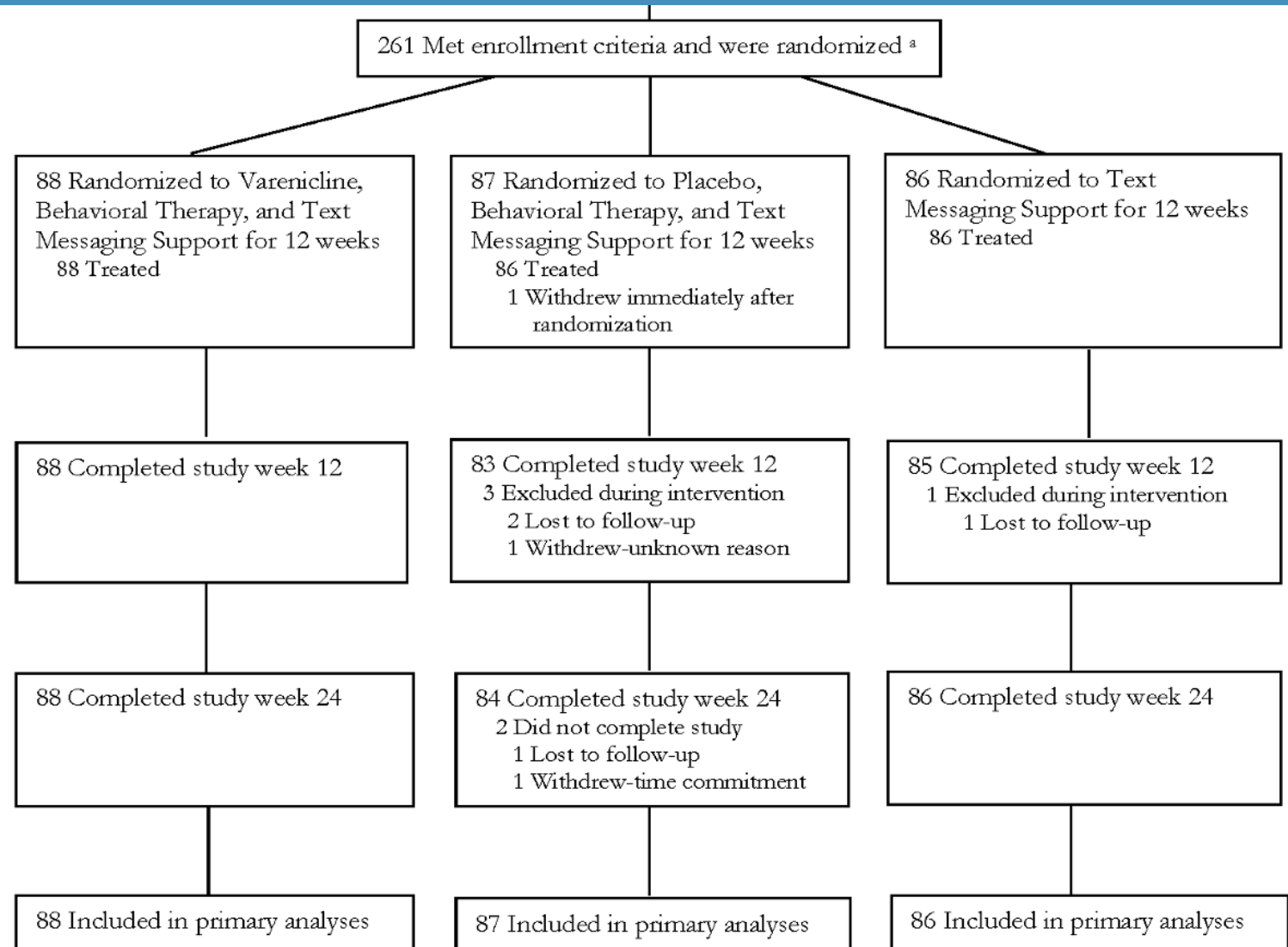
# DETECTING AN EFFECT OF THE BEHAVIORAL INTERVENTION: ADDITION OF A THIRD ARM

- Because adolescent population without years of nicotine use, we considered it possible that the behavioral intervention may work particularly well.
- If behavioral treatment very effective, trial could fail.
  - Failure to detect difference between tx arms.
  - Perhaps we became a bit enamored of the innovations we made to the 'near peer' delivered behavioral intervention with its short animated videos and remote delivery...
  - Texting support app could be considered usual care, free, easily accessed, two trials reporting efficacy
- Before beginning enrollment, added third arm despite budget constraints
  - Random assignment to referral to TIQ texting support for youth vaping cessation and single blind assessments.

# OUTCOME MEASURES ...

- Abstinence from vaped nicotine.
  - Cotinine-verified self-report of abstinence
  - 1° abstinence outcome: continuous nicotine vaping abstinence from weeks 9-12: self-report of 7-days vaping abstinence at weeks 9, 10, 11, and 12 by weekly TLFB interview aided by daily survey self-report, and saliva cotinine <30 ng/ml.
- Severity of addiction to nicotine, withdrawal sx., craving: ECDI, MNWS, QVC
- Use of addictive substances other than nicotine: TLFB
- Psychiatric symptoms: MASQ, NAEI

# RETENTION





# TREATMENT UPTAKE

- 254 (97%) participants completed the 24-week trial
- Study drug adherence assessed with pill counts indicated ~70% of pills were taken
- Video evidence of medication adherence: 52% of possible varenicline doses and 42% of possible placebo doses.
- Behavioral counseling attendance was 84% in the varenicline group and 66% in the placebo group
  - ≥80% of counseling sessions attended by 78% of those assigned to varenicline and 60% (52/87) of those assigned to placebo

# Varenicline for Youth Nicotine Vaping Cessation

## A Randomized Clinical Trial

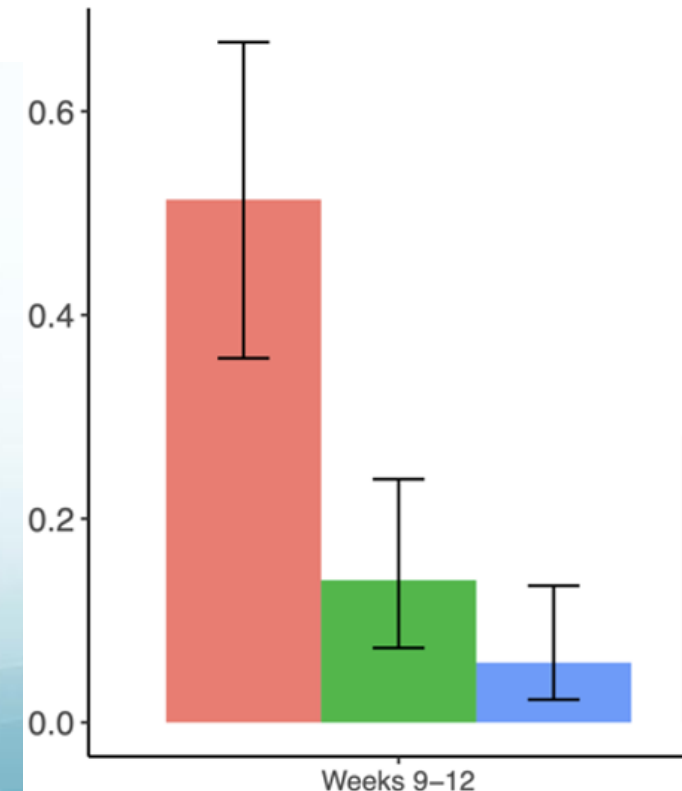
A. Eden Evins, MD; Corinne Cather, PhD; Harrison T. Reeder, PhD; Bryn Evohr, BS; Kevin Potter, PhD; Gladys N. Pachas, MD; Kevin M. Gray, MD; Sharon Levy, MD; Nancy A. Rigotti, MD; Vanessa Iroegbulem, BA; Jason Dufour, BS; Kelly Casottana, BS; Meghan A. Costello, PhD; Jodi M. Gilman, PhD; Randi M. Schuster, PhD

**97% study completion rate using remote methods for intervention delivery and data collection**

**53%** of those offered Varenicline + Counseling quit vaping and were abstinent for  $\geq 1$  month at the end of treatment

**14%** 4-week abstinence on Placebo + Counseling

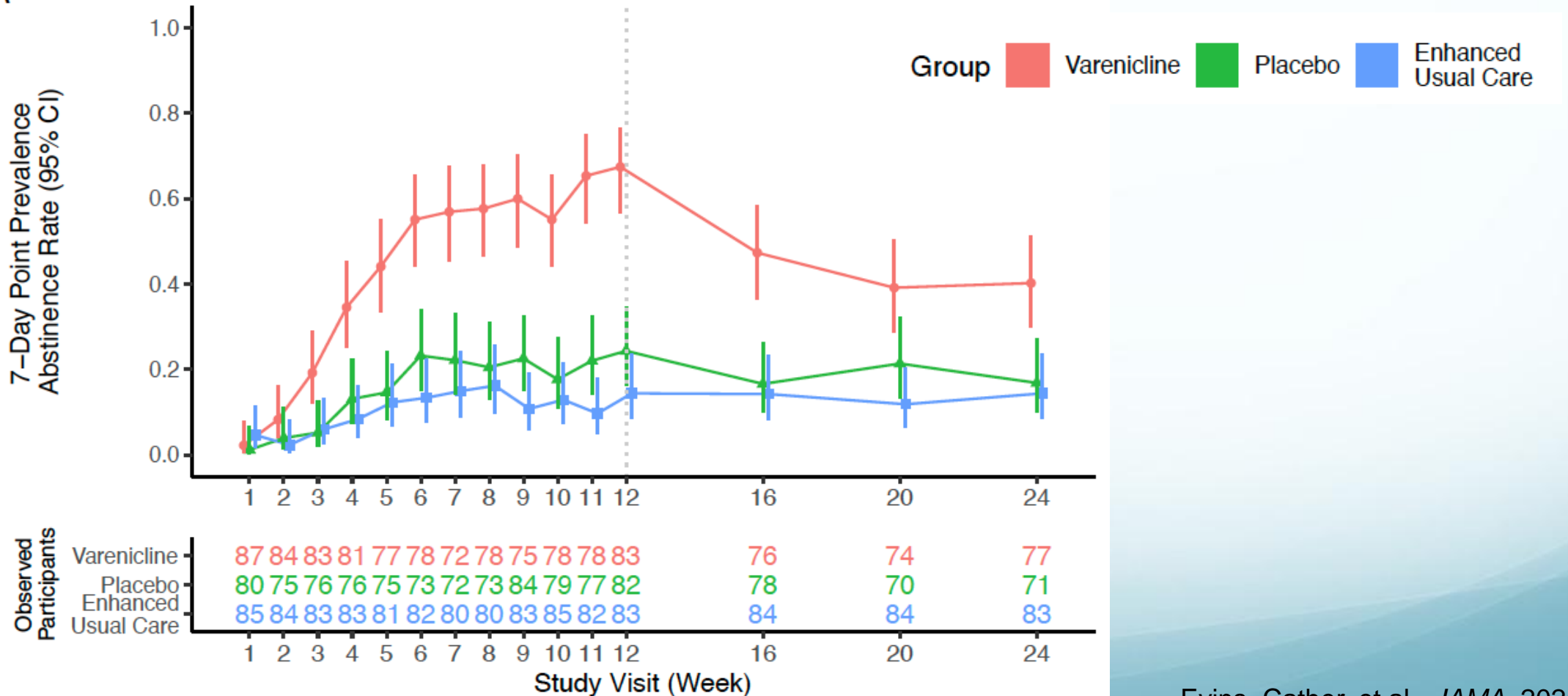
**6%** abstinence with TIQ Texting Support referral only



# Varenicline for Youth Nicotine Vaping Cessation

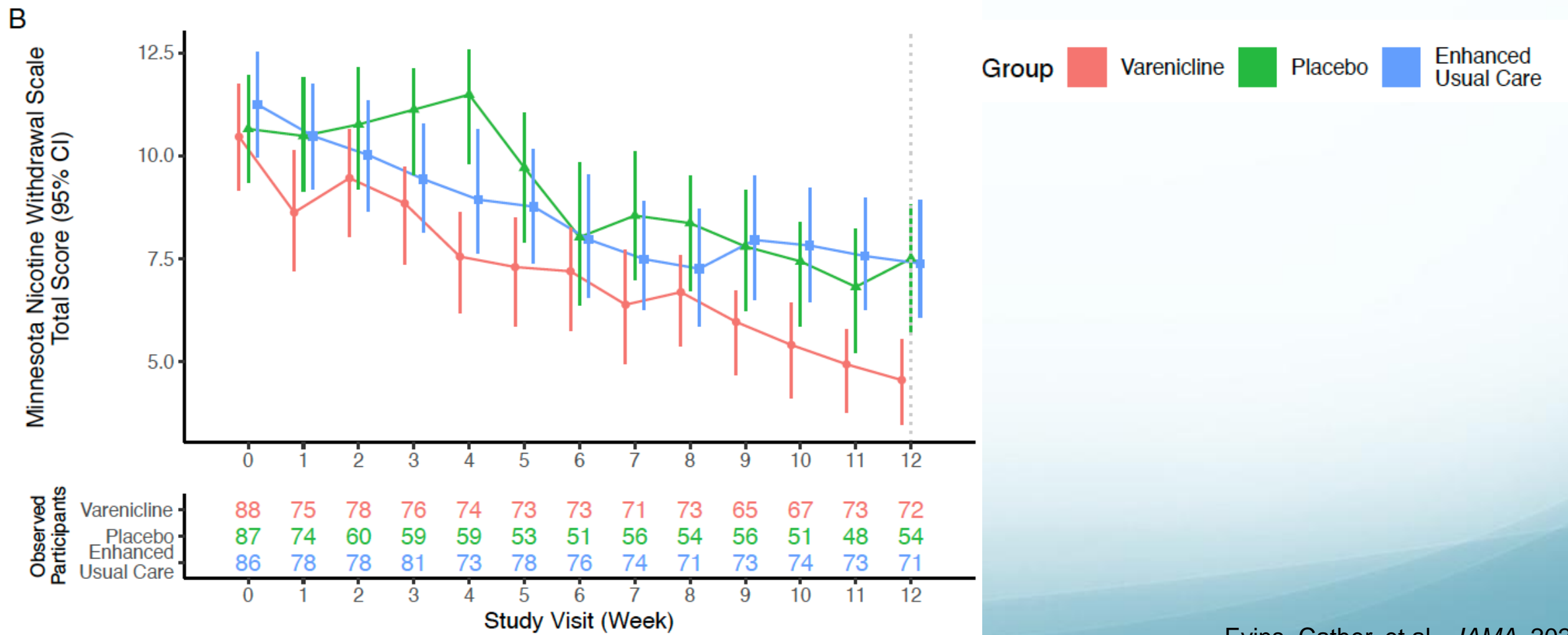
## A Randomized Clinical Trial

A



# Varenicline for Youth Nicotine Vaping Cessation

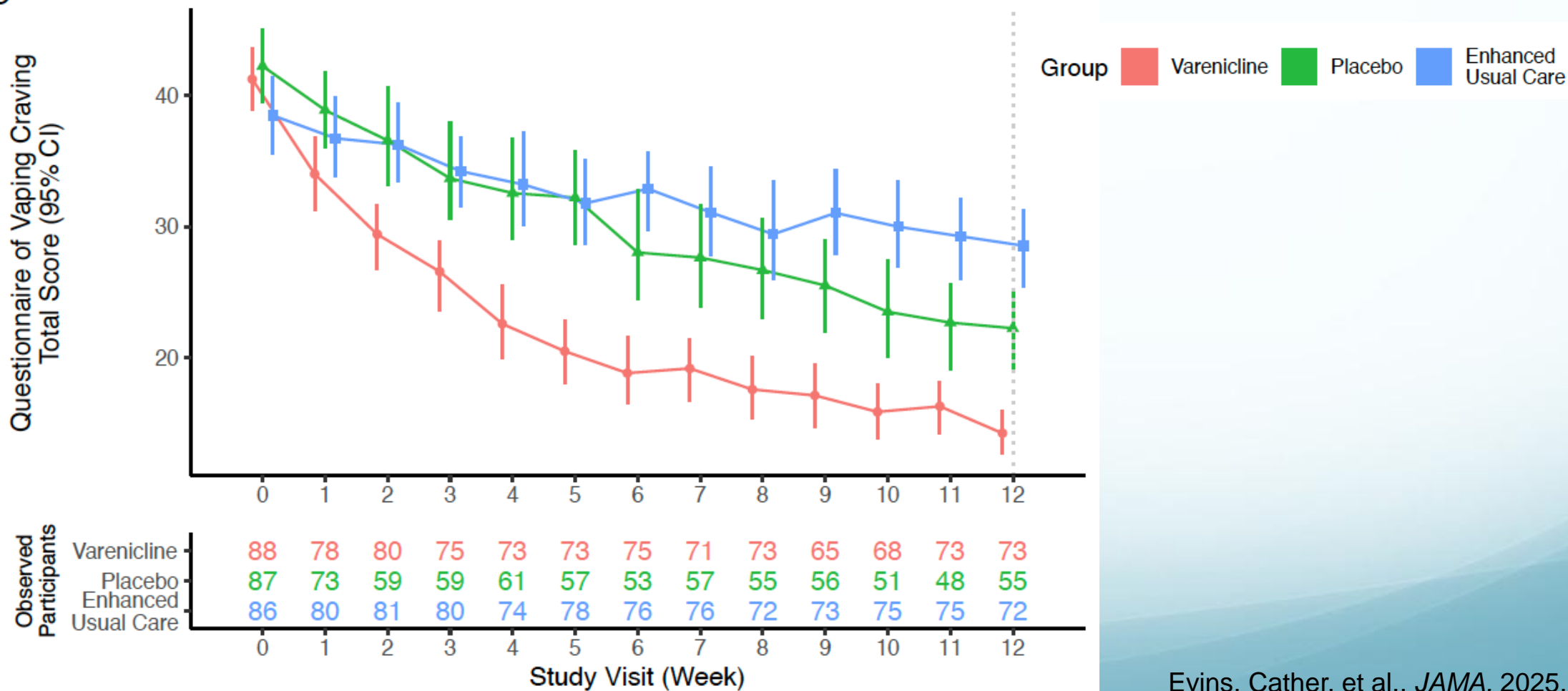
## A Randomized Clinical Trial



# Varenicline for Youth Nicotine Vaping Cessation

## A Randomized Clinical Trial

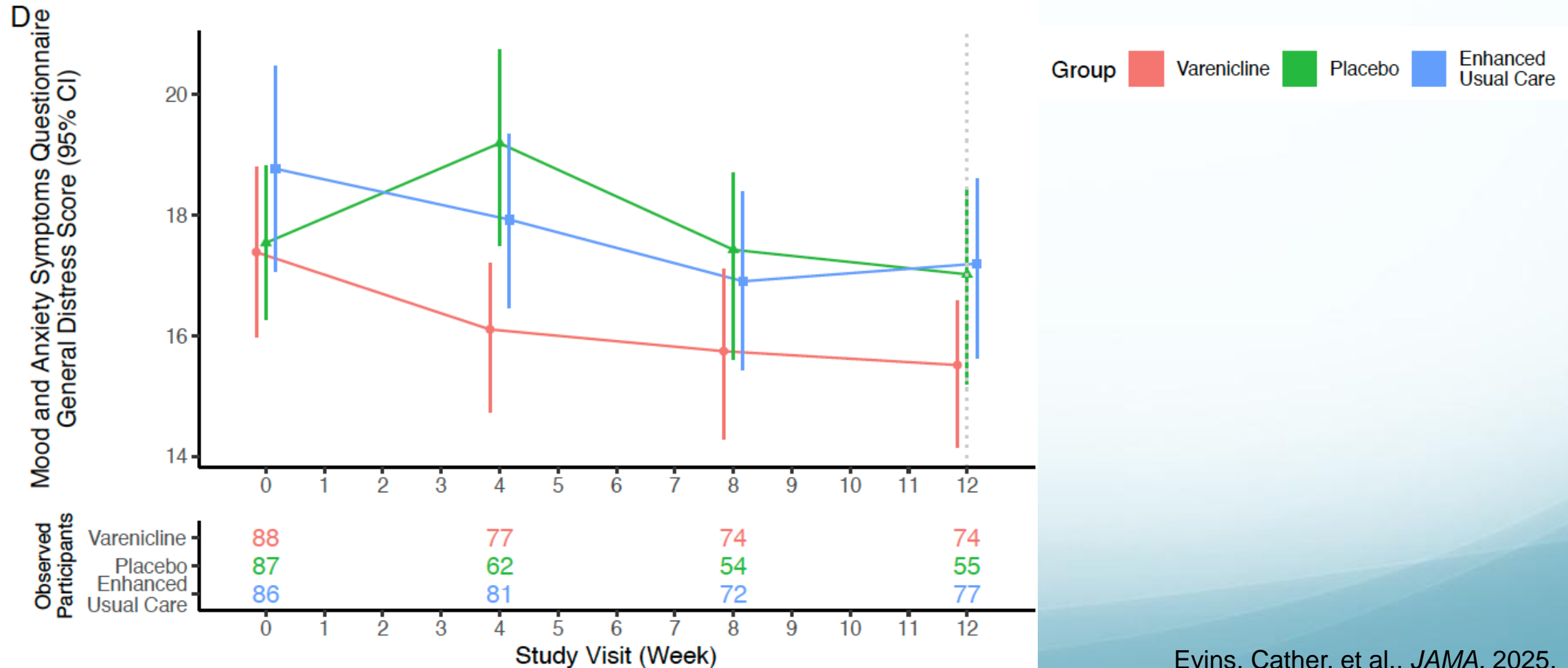
C





# Varenicline for Youth Nicotine Vaping Cessation

## A Randomized Clinical Trial



# Varenicline for Youth Nicotine Vaping Cessation

## A Randomized Clinical Trial

Table 3. Summary of Adverse Events

Outcome	No. (%)		
	Varenicline (n = 88)	Placebo (n = 86) <sup>a</sup>	Enhanced usual care (n = 86)
Any treatment-emergent adverse event	76 (86)	68 (79)	68 (79)
Any NAEI-elicited adverse event <sup>b</sup>	71 (81)	61 (71)	78 (91)
Any serious adverse event <sup>c</sup>	1 (1)	3 (3)	1 (1)
Study medication discontinuation	2 (2)	1 (1)	NA
Reduced study medication dose due to adverse event	4 (5)	1 (1)	NA
Initiated regular combusted tobacco use during the trial <sup>d</sup>	3 (5)	2 (4)	0
Initiated regular combusted tobacco use among those with e-cigarette abstinence at week 24	0	0	0

# Varenicline for Youth Nicotine Vaping Cessation

## A Randomized Clinical Trial

Adverse events reported by ≥5% in any group <sup>e</sup>			
Nausea and vomiting symptoms	51 (58)	23 (27)	5 (6)
Cold symptoms	41 (47)	29 (34)	35 (41)
Vivid dreams	34 (39)	14 (16)	0
Insomnia	27 (31)	16 (19)	7 (8)
Bloating	25 (28)	22 (26)	2 (2)
Anxiety disorders and symptoms	22 (25)	28 (33)	30 (35)
Mood disorders and disturbances	22 (25)	27 (31)	21 (24)

**Nausea, vivid dreams, insomnia more common in the varenicline group**





National Institute  
on Drug Abuse

NIDA: 1 R01 DA052583,  
3R01DA052583-03S1,  
3R01DA052583-03S2







## SMOKE IN STYLE

With blu Electronic Cigarettes

Freedom never goes out of fashion. Control when and where you want to smoke with blu electronic cigarettes. blu produces no smoke and no ash, only vapor, making it the ultimate accessory and the smarter alternative to regular cigarettes. Step out in style with blu.

SCAN FOR A CHANCE TO WIN A STARTER KIT

**'Like' us on Facebook**  
facebook.com/blucigs

blucigs.com

Available at these fine retailers:

\* Introducing the World's First Smart Pack (Online Only)



## PURE TASTE AND SATISFYING THROAT HIT

Specialized heating system with 0%, 2% or 5% Salt Nic, ELFBAR presents the purest flavor in every vape.

