E-cigarettes vs Combination NRT Delivered through State Quitlines on Smoking Outcomes Following a Recent Failed Quit Attempt: A Randomized Trial

Theodore L. Wagener, PhD
Professor & Leonard J. Immke, Jr. and Charlotte L. Immke Chair in Cancer Research

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REACH Study Team

Collaborators

- Katrina Vickerman (RVO Health)
- Alice Hinton (OSU)
- Laura Beebe (OUHSC)
- Michael Businelle (OUHSC)
- Jonathan Hart (OUHSC)
- Matthew Carpenter (MUSC)

Study Staff

- Caryn Chalmers (RVO)
- Ryan Hedrix (RVO)
- Dale Kiss (OSU)
- Susan Match (OSU)
- Neil Molina (OSU)
- Kaila Norton (OSU)
- Brett Phillips (OSU)

NIDA Scientific Officers

- Ann Anderson
- Aidan Hampson
- Kevin Walton

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Quitting Smoking is Difficult

- Cessation is the least likely outcome
- FDA-approved smoking cessation products and counseling can double a smoker's chances of staying quit, but not for all or even most smokers
  - >65% want to quit
  - ~50% try to quit each year
  - <10% stay quit for 1 year
- 1 in 3 smokers will die from smoking-related illness
- 480,000 US deaths/yr; 6 million deaths worldwide/yr

If FDA-approved products and counseling don't work,

what should we do?

CDC, 2015; Lai et al., 2010; Lancaster & Stead, 2005; Stead et al., 2012

Promise of E-cigarettes

- Are likely to be far less harmful than combustible tobacco cigarettes; a *smoker who completely switches to an e-cigarette* is exposed to significantly lower levels of toxicants, resulting in some *reduced short-term adverse health outcomes*.
- Often more appealing and satisfying to smokers than FDA approved nicotine replacement therapies (NRT).
- Smoking cessation with e-cigarettes likely better than NRT
  - E-cigarette: 9-14 out of 100 smokers vs. NRT: 6 out of 100 smokers
    - Walker et al 2019
      - 7% E-cig + Patch (7.6-watt e-cig) > 2% Patch at 6 mo
    - Hajek et al 2019
      - 18% E-cig (14-watt e-cig) > 9.9% Combo NRT at 1 yr
    - Myers-Smith et al 2022
      - 19% E-cig (various e-cigs) > 3% NRT (mono/combo) at 6 mo

2018 NASEM Report; Hartmann-Boyce et al., 2022 Cochrane Database of Systematic Reviews

E-cigarette Evolution

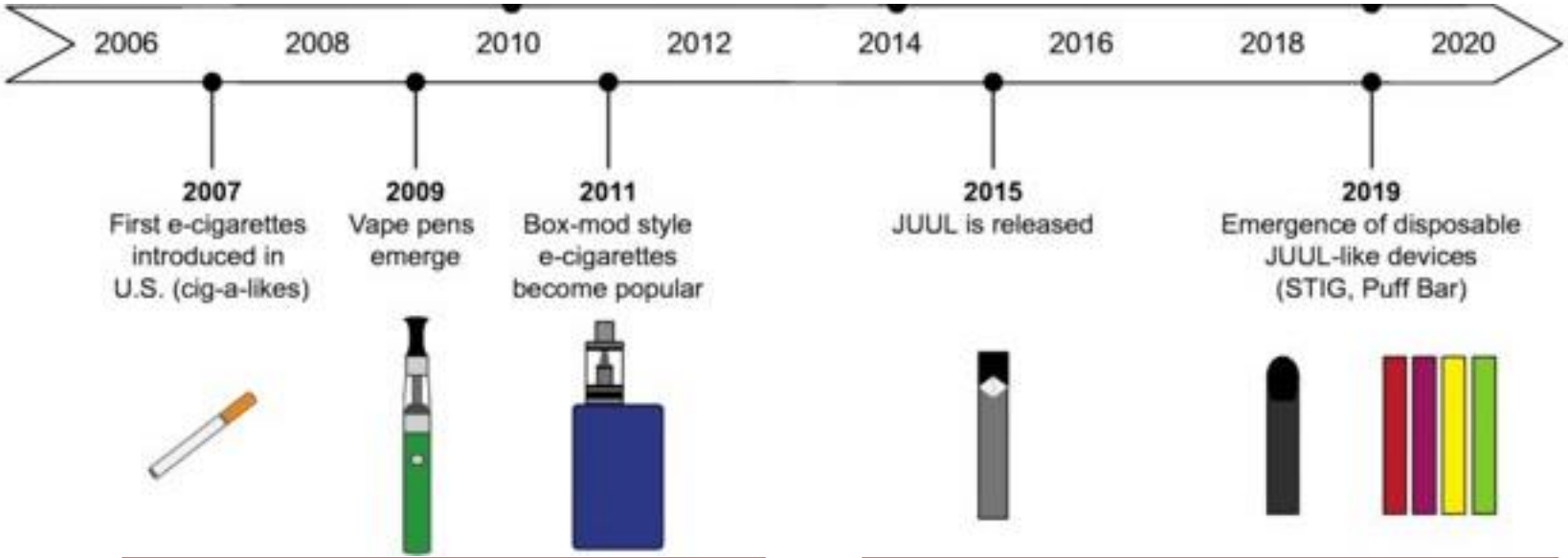
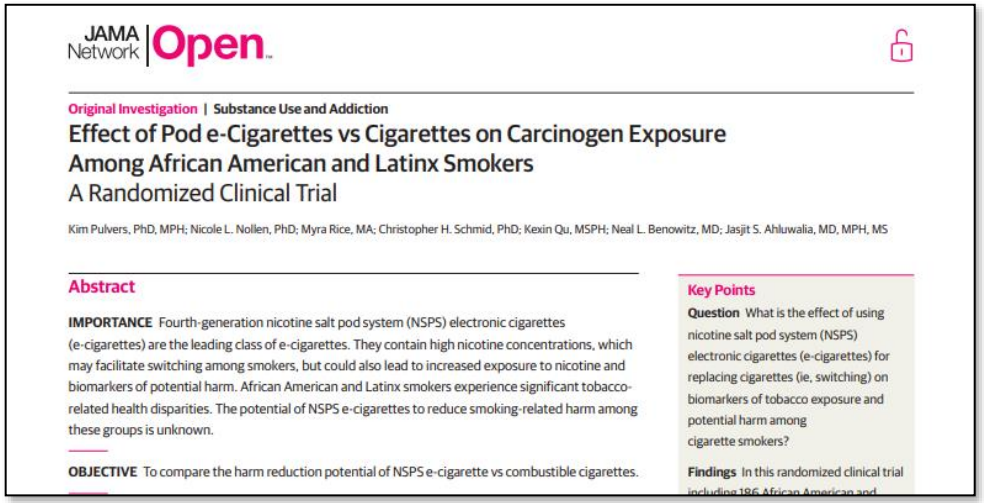


Image from Hickman & Jaspers (2020)

Pod E-cigarettes - Impact on Smoking

Smoking Abstinence

- 6-week: 28.1% (biochemically verified)
- 6-month: 24.0% (not biochemically verified)



JAMA Network | Open

Original Investigation | Substance Use and Addiction

Effect of Pod e-Cigarettes vs Cigarettes on Carcinogen Exposure Among African American and Latinx Smokers
A Randomized Clinical Trial

Kim Pulvers, PhD, MPH; Nicole L. Nollen, PhD; Myra Rice, MA; Christopher H. Schmid, PhD; Kexin Qu, MSPH; Neal L. Benowitz, MD; Jasjit S. Ahluwalia, MD, MPH, MS

Abstract

IMPORTANCE Fourth-generation nicotine salt pod system (NSPS) electronic cigarettes (e-cigarettes) are the leading class of e-cigarettes. They contain high nicotine concentrations, which may facilitate switching among smokers, but could also lead to increased exposure to nicotine and biomarkers of potential harm. African American and Latinx smokers experience significant tobacco-related health disparities. The potential of NSPS e-cigarettes to reduce smoking-related harm among these groups is unknown.

OBJECTIVE To compare the harm reduction potential of NSPS e-cigarette vs combustible cigarettes.

Key Points

Question What is the effect of using nicotine salt pod system (NSPS) electronic cigarettes (e-cigarettes) for replacing cigarettes (ie, switching) on biomarkers of tobacco exposure and potential harm among cigarette smokers?

Findings In this randomized clinical trial including 186 African American and

Pulvers et al (2020) *JAMA Netw Open*

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Quitlines (QL) on Smoking Cessation

- Are an effective means for treating cigarette dependence, even in populations that have historically been hard to reach
- QL practice is guided by best available evidence
  - Typically, includes counseling and NRT
- To date, QL have not incorporated the use of e-cigarettes as a quit strategy
  - Lack of FDA-approval
  - Few RCTs comparing e-cigarettes vs NRT
  - None examining their efficacy delivered *via* QL

Vickerman et al (2021) *Am J Prev Med*

Brief Question Session 1

Aims & Study Design

Primary Aim

- Among recent QL users who did not successfully quit smoking, we examined the impact of QL counseling + JUUL e-cigarette vs. QL counseling + NRT on:
  - Smoking behavior – CPD, quit attempts, and abstinence
  - Cigarette dependence
  - Withdrawal symptoms
  - Safety

Study Design

- 2-group, randomized (1:1), controlled trial
  - 3 counseling calls, 8 weeks of product (no cost), 3 assessments (baseline, 8, 12 weeks)
  - Daily dairy + iCO
- Outbound recruitment of 372 participants (target) from the Oklahoma Tobacco Helpline and South Carolina Tobacco Quitline

Eligibility Criteria

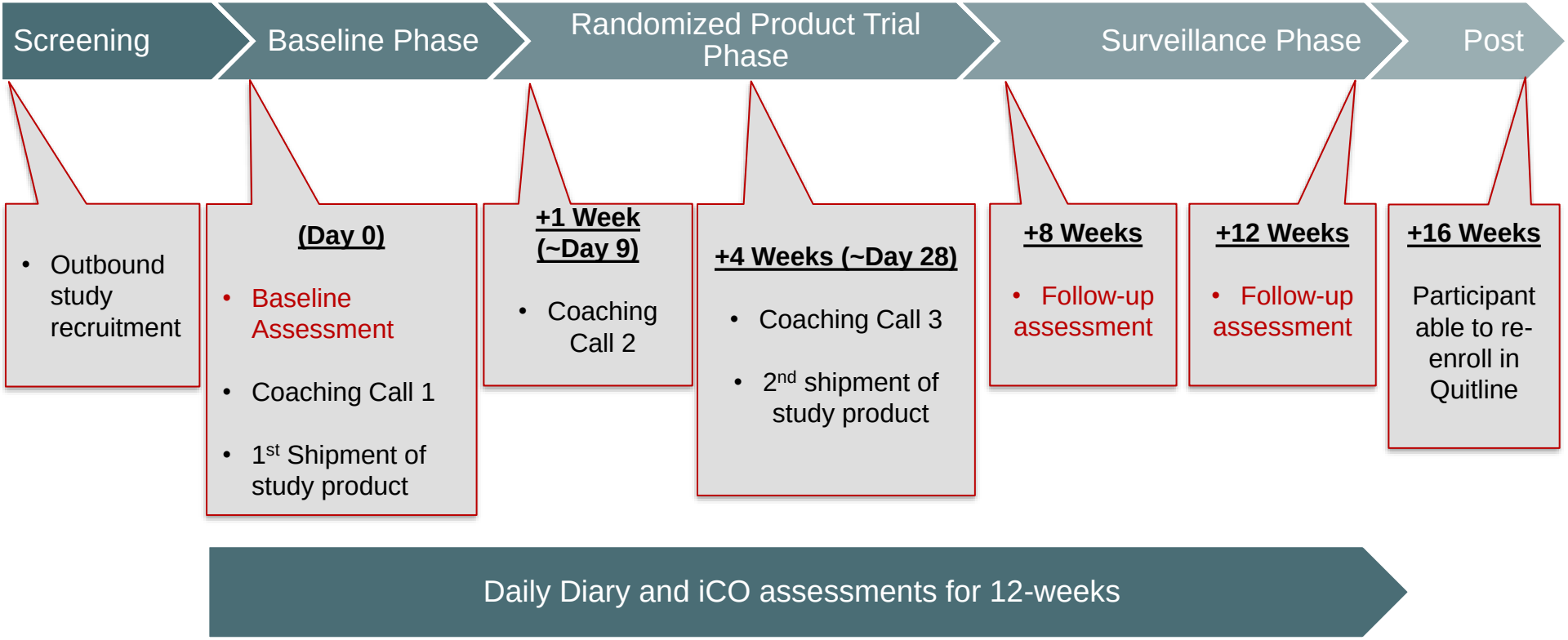
Inclusion Criteria:

- Participation in the Oklahoma Tobacco Helpline or South Carolina Tobacco Helpline within the last 4-7 months
- ≥ 21 years old
- Currently smoke ≥5 cigarettes per day
- At least minimal interest in switching to an alternative product (> 0 "not at all" on a 0-10 scale)
- English speaking/reading/writing

Exclusion Criteria:

- Report NRT use or making a quit attempt within the last 7 days
- Current daily use of an e-cigarette over last month
- Unstable or significant medical or psychiatric conditions (past and stable conditions allowed)
- History of cardiac event or distress within the past 6 months
- Currently pregnant, planning to become pregnant in next 3 months, or breastfeeding.
- Severe physical reaction to using patch medication or adhesive tape or known allergy to propylene glycol or vegetable glycerin

Study Flow



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Study Groups: 3 Coaching Calls + Product

E-cigarette Group

- Phone + paid service for 16 weeks
- iCO device
- Clincard
- Pamphlet
- JUUL device with charger
- 8-week of supply of Menthol 5% or Virginia Tobacco 5% JUUL pods
  - 4-week supply, sent in two shipments

Combination NRT Group

- Phone + paid service for 16 weeks
- iCO device
- Clincard
- Pamphlet
- 8-week supply of Generic nicotine patches and Nicorette lozenges
  - 4-week supply, sent in two shipments

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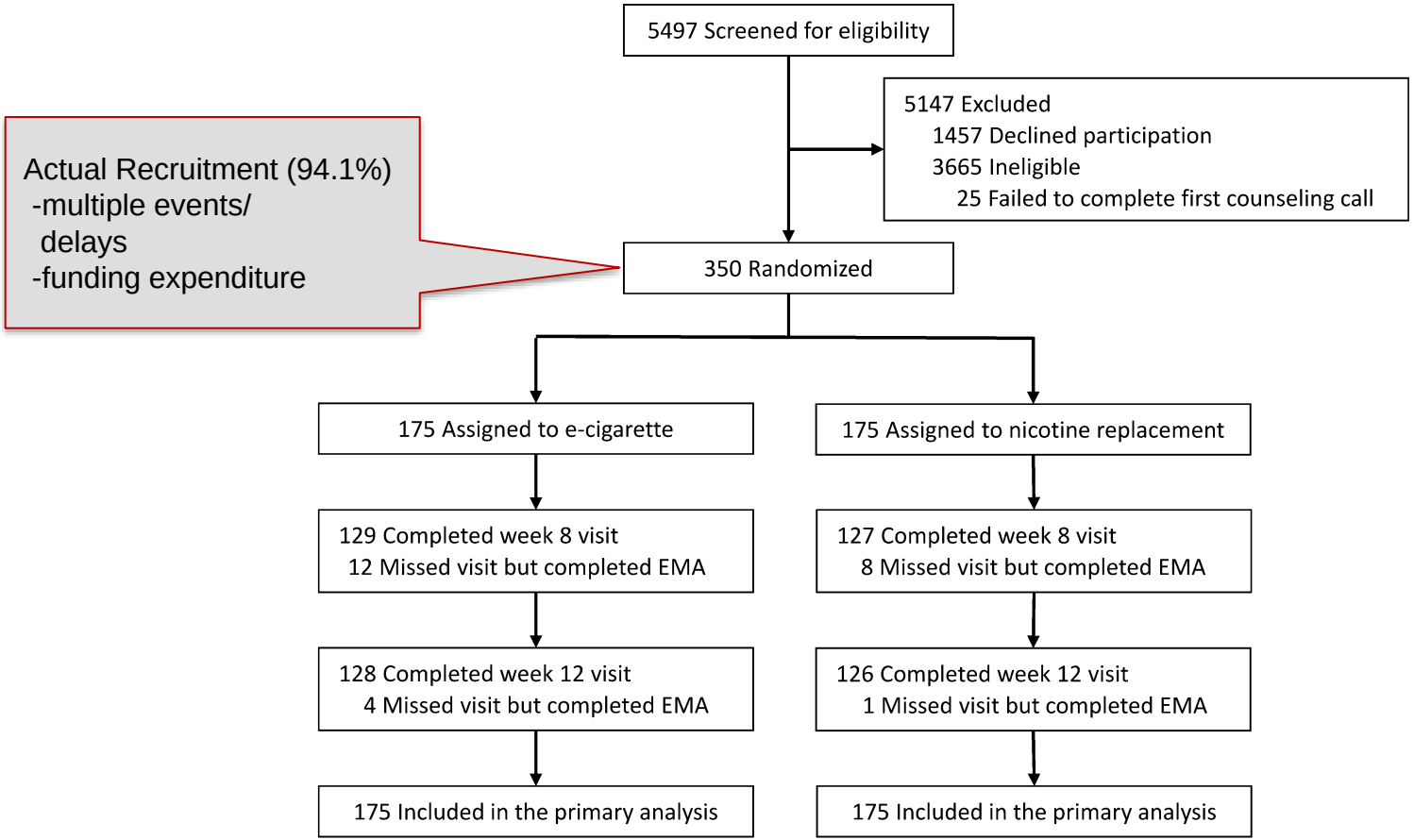
Consort Diagram



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Brief Question Session 2

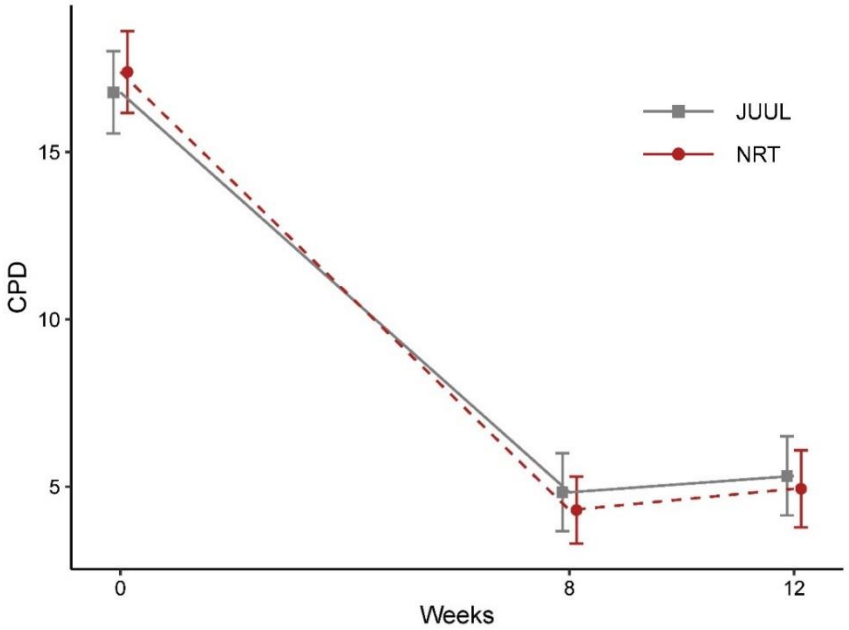
Demographics & Baseline Tobacco Use

	JUUL (n=175)		NRT (n=175)		p-value
Age *mean, SD*	55.3	12.7	54.2	12.5	0.43[d]
Sex *n, %*					0.83[a]
Female	107	61.9	105	60.7	
Hispanic *n, %*					0.99[b]
Yes	2	1.2	2	1.2	
Race *n, %*					0.93[a]
Black or African American	21	12.1	23	13.3	
White or Caucasian	125	72.3	122	70.5	
Other	27	15.6	28	16.2	
Household Yearly Income *n, %*					0.92[a]
<$35k	136	80.0	136	80.5	
Employment *n, %*					0.16[a]
Unemployed/Unable to work/disabled	96	55.8	83	48.3	
Cigarettes per Day *mean, SD*	16.8	8.2	17.4	8.2	0.48[d]
Cigarette Dependence Scale *mean, SD*	19.3	2.8	19.2	3.2	0.73[d]
E-cigarette Use (≥ 'Monthly' but < 'Daily') *n, %*	21	12.2	11	6.4	0.36[a]

Notes: [a] Chi-square; [b] Fisher exact test; [c] Wilcoxon rank sum test; [d] t-test

Changes in Cigarettes Per Day

Figure. Mean cigarettes per day with corresponding 95% confidence intervals.



Within-subjects: JUUL: 8- and 12-weeks vs Baseline, p<.0001
NRT: 8- and 12-weeks vs Baseline, p<.0001

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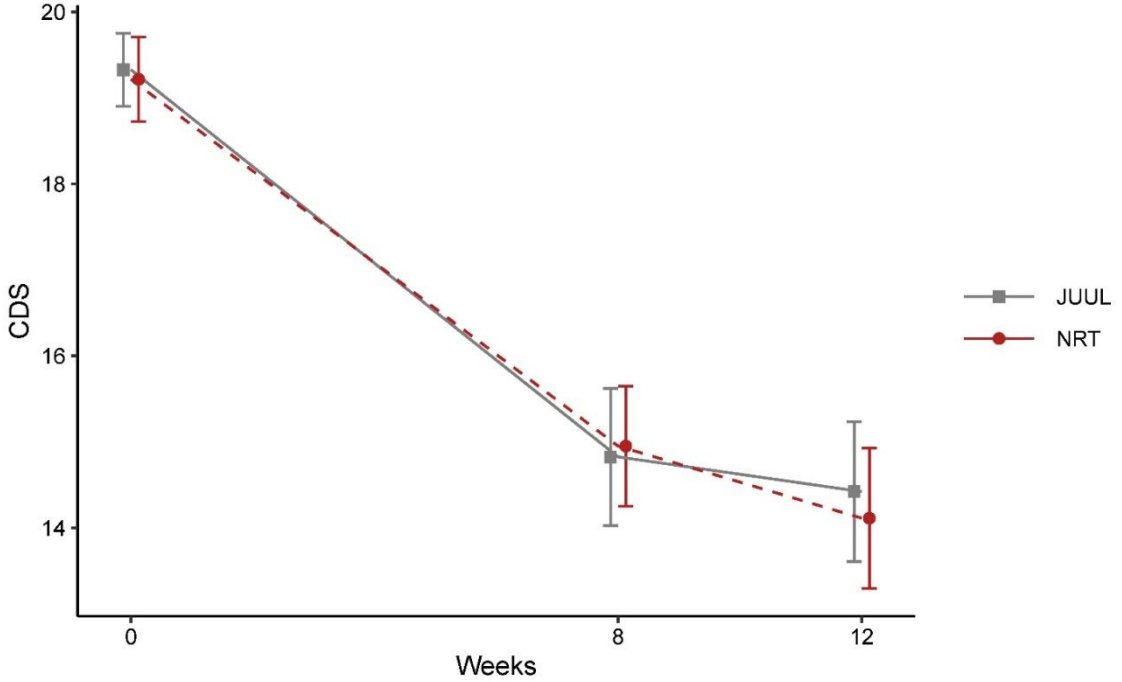
Changes in Cigarette Dependence

Figure. Mean CDS-5 with corresponding 95% confidence intervals.



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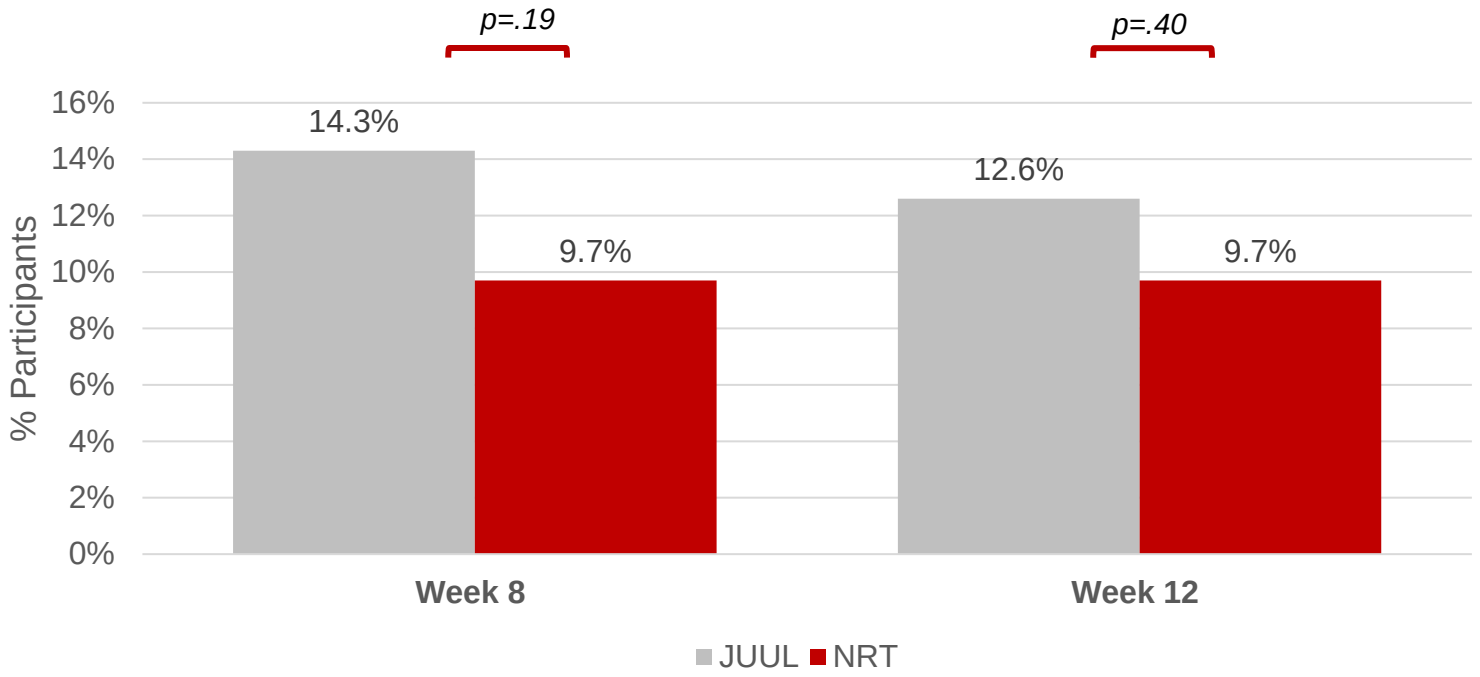
7 Day PPA



Notes: abstinence = no reported smoking and iCO≤8ppm;
missing data = smoking

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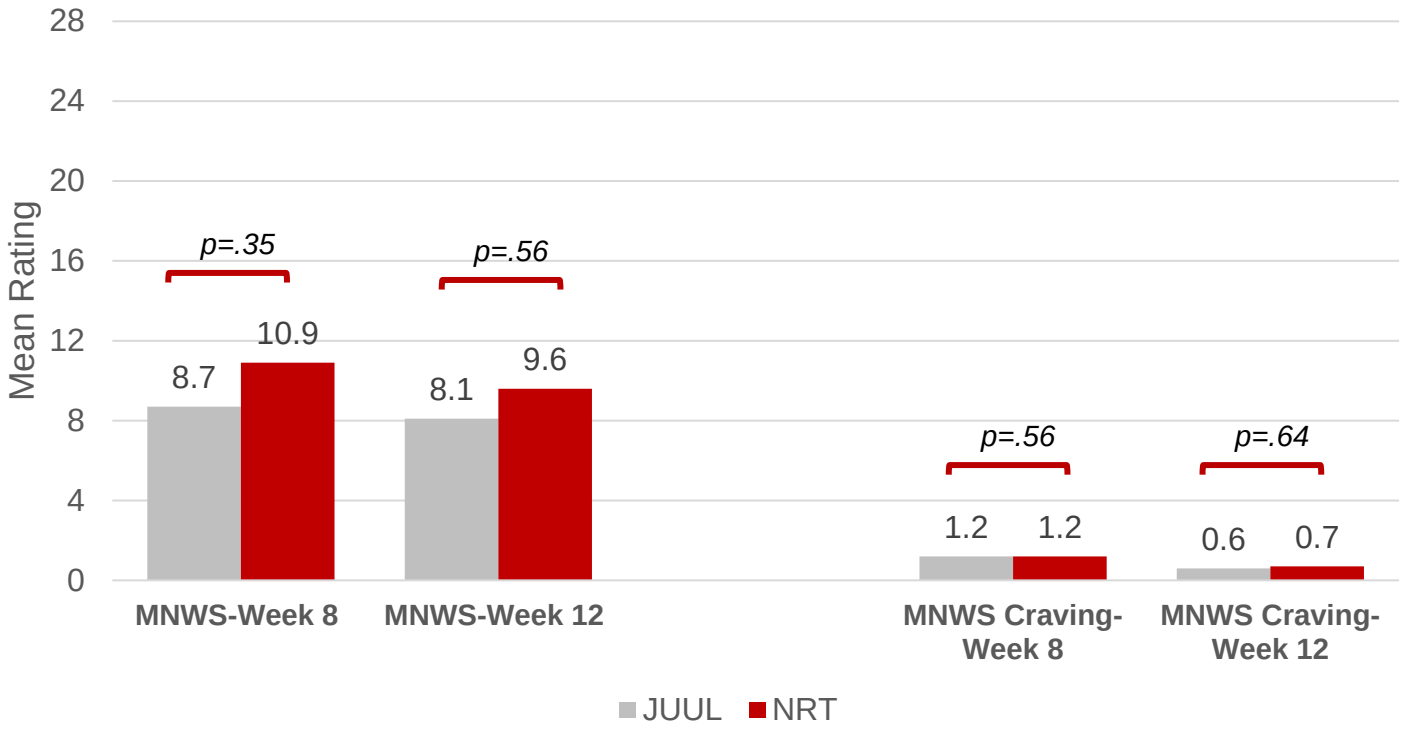
Nicotine Withdrawal Symptoms: Abstainers

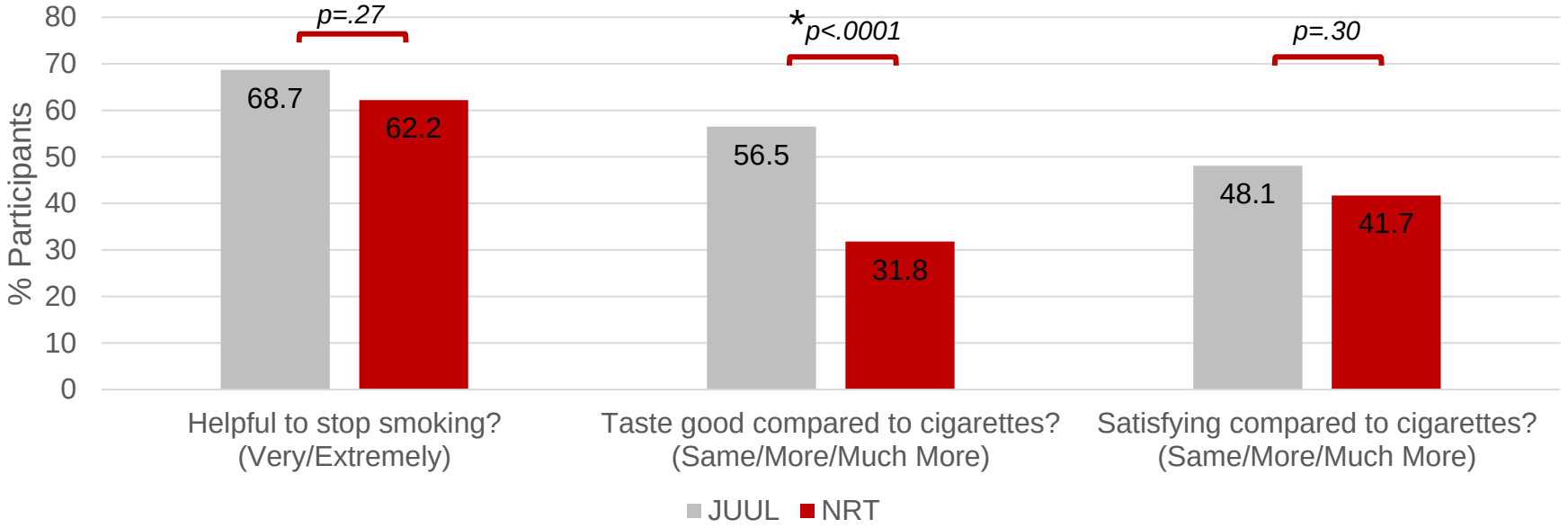


Intervention Adherence

	NRT (n=175)		Juul (n=175)		
	n	*%*	*n*	*%*	*p-value*
No. counseling calls completed					0.6204
1	31	17.7	30	17.1	
2	42	24.0	35	20.0	
3	102	58.3	110	62.9	
Use of assigned product [1]					
8 Weeks	99	56.6	112	64.0	0.1556
12 Weeks	71	40.6	89	50.9	***0.0534***

[1] Participants who did not attend the visit were assumed to not be using the study product

Study Product Evaluation at 8 weeks



- *43% of participants who stopped using JUUL reported wanting **more flavor options**.*

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Adverse Events at 8 weeks

	NRT (n=128) n (%)	JUUL (n=131) n (%)	OR (95% CI)
Sore or dry mouth and throat	26 (20.3)	33 (25.2)	1.32 (0.74, 2.37)
Headache	17 (13.3)	13 (9.9)	0.72 (0.33, 1.55)
Gingivitis/gum bleeding	1 (0.8)	2 (1.5)	1.97 (0.18, 21.99)
Mouth or tongue sores/inflammation	10 (7.8)	7 (5.3)	0.67 (0.25, 1.81)
Black tongue	0 (0.0)	0 (0.0)	--
Nose bleeding	4 (3.1)	0 (0.0)	--
Cough	13 (10.2)	43 (32.8)	**4.32 (2.19, 8.53)***
Dizziness	18 (14.1)	5 (3.8)	**0.24 (0.09, 0.67)***
Sleepiness	9 (7.0)	3 (2.3)	0.31 (0.08, 1.17)
Sleeplessness	25 (19.5)	11 (8.4)	**0.37 (0.18, 0.80)***
Heart Palpitations	6 (4.7)	4 (3.1)	0.64 (0.18, 2.32)
Breathing Difficulties	4 (3.1)	10 (7.6)	2.56 (0.78, 8.39)
Allergies	13 (10.2)	0 (0.0)	--
Chest Pain	4 (3.1)	7 (5.3)	1.75 (0.50, 6.13)
Other	9 (7.0)	5 (3.8)	0.52 (0.17, 1.61)

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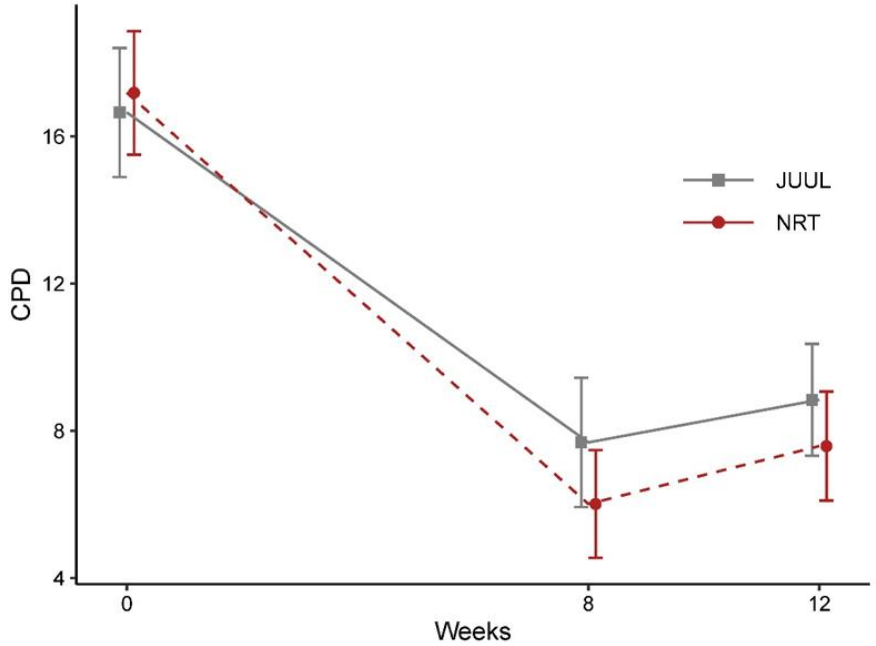
Adverse Events at 12 weeks

	NRT (n=125) N (%)	Juul (n=130) N (%)	OR (95% CI)
Sore or dry mouth and throat	24 (19.2)	24 (18.5)	0.95 (0.51, 1.79)
Headache	13 (10.4)	7 (5.4)	0.49 (0.19, 1.27)
Gingivitis/gum bleeding	3 (2.4)	2 (1.5)	0.64 (0.10, 3.87)
Mouth or tongue sores/inflammation	7 (5.6)	2 (1.5)	0.26 (0.05, 1.29)
Black tongue	1 (0.8)	0 (0.0)	--
Nose bleeding	0 (0.0)	2 (1.5)	--
Cough	**9 (7.2)**	**26 (20.0)**	**3.22 (1.44, 7.19)***
Dizziness	9 (7.2)	6 (4.6)	0.62 (0.22, 1.81)
Sleepiness	4 (3.2)	2 (1.5)	0.47 (0.09, 2.63)
Sleeplessness	**15 (12.0)**	**6 (4.6)**	**0.35 (0.13, 0.95)***
Heart Palpitations	1 (0.8)	4 (3.1)	3.94 (0.43, 35.72)
Breathing Difficulties	2 (1.6)	9 (6.9)	4.57 (0.97, 21.61)
Allergies	8 (6.4)	2 (1.5)	0.23 (0.05, 1.10)
Chest Pain	2 (1.6)	1 (0.8)	0.48 (0.04, 5.32)
Other	4 (3.2)	3 (2.3)	0.71 (0.16, 3.26)

Changes in Cigarettes Per Day: Non-abstainers

Figure. Subset of participants smoking ≥ 1 CPD at week 12 with corresponding 95% CI.



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NRT: 8- and 12-weeks vs Baseline, p<.0001

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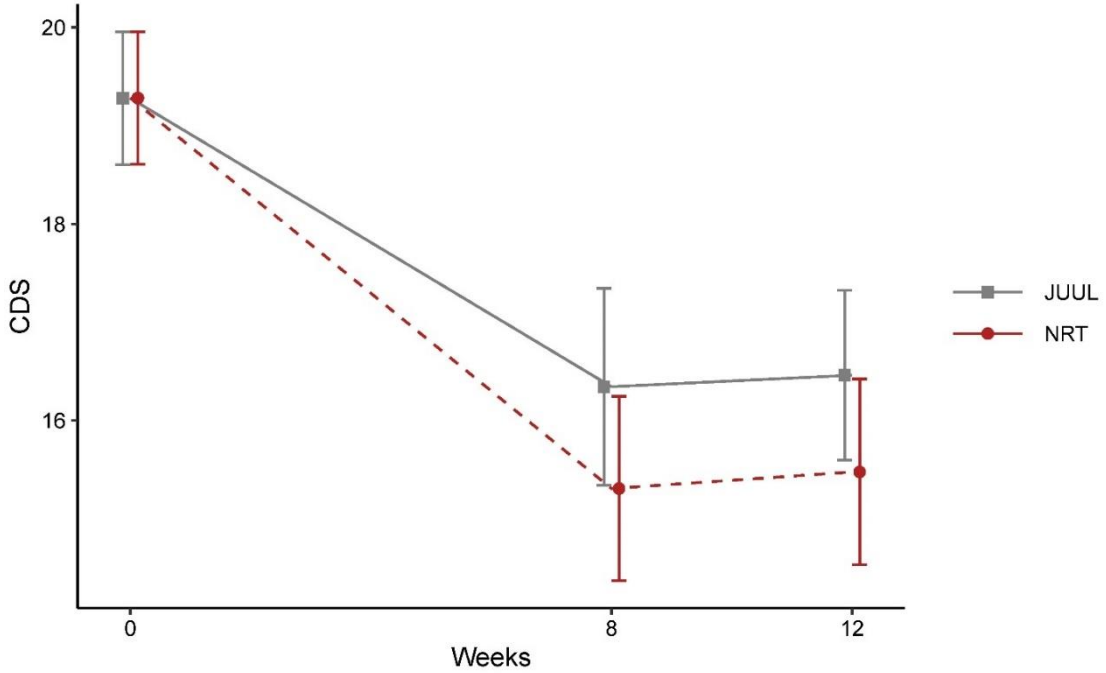
Changes in Cigarette Dependence: Non-abstainers

Figure. Mean CDS-5 with corresponding 95% CI.



Within-subjects: JUUL: 8- and 12-weeks vs Baseline, p<.0001
NRT: 8- and 12-weeks vs Baseline, p<.0001

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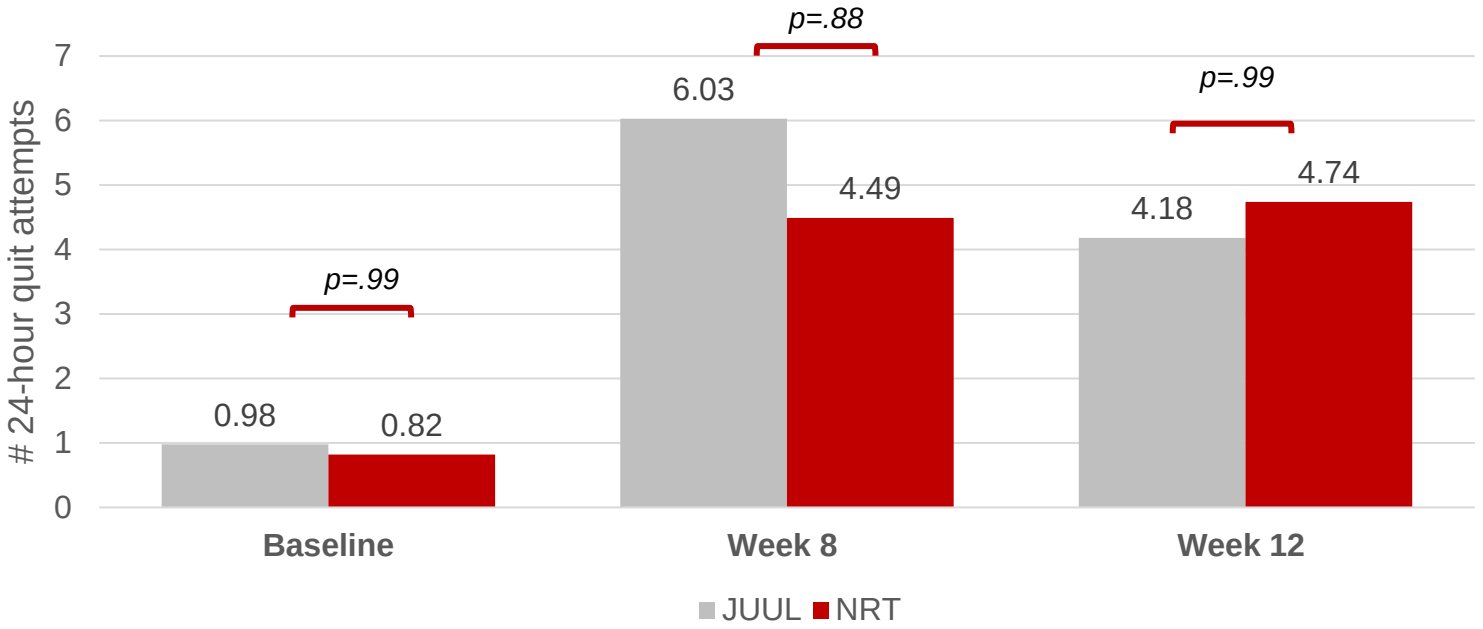
24-hour Quit Attempts (past 30 days): Non-abstainers



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NRT: 8- and 12-weeks vs Baseline, p<.0001

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Conclusions & Next Steps

- Like previous studies comparing e-cigs to NRT both were effective:
  - increasing smoking abstinence
  - reducing cigarettes smoked per day
  - reducing cigarette dependence
- No significant difference found between e-cigs and NRT though e-cigs *may* be slightly more effective, especially earlier in the intervention
- E-cigs and NRT had a similar side effect profile
- Importantly, these effects were seen in the context of reengagement with a state tobacco QL after an unsuccessful QL quit attempt
- E-cigs generally received more positive ratings of appeal – notably participants were often requesting other e-cig flavors
- Next steps: Non-tobacco flavors are preferred by smokers wanting to switch – will they further increase abstinence?

Thank You!