The Impact of E-cigarettes on Smoking Cessation:
Results from a Large, Randomized, Nationwide Clinical Trial in the United States
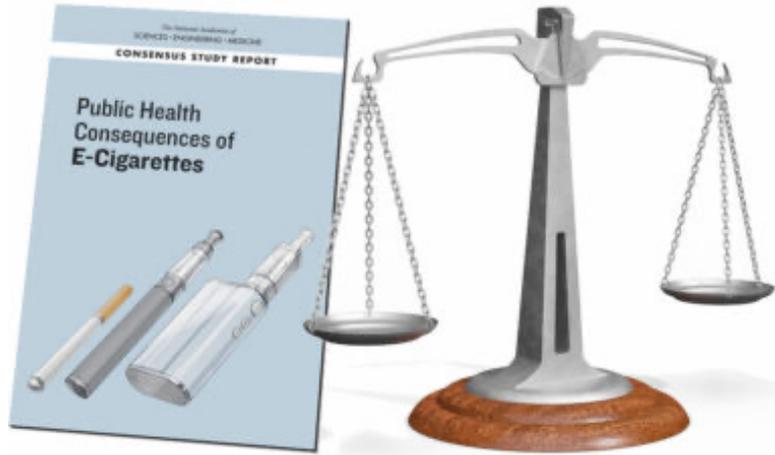
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Hollings Cancer Center
An NCI-Designated Cancer Center

MUSC
Medical University
of South Carolina

A One-Sided Presentation

My Presentation:
Focused on Adult Smoking Cessation
That's Not the Entire Story!

My Presentation:
A clinical presentation (RCT)
But with policy implications

My Presentation:
Includes a few slides with ~Main Outcome Data (denoted). Please do not share.

Funding:
NCI R01 210625

Disclosures from Past 10yrs:
- E-cigarette product purchased from NJoy
- 2018-2019: Consulting for Pfizer
- 2020: Consulting to Frutarom, Inc.
- Multiple NIH Grants as PI

E-cigarettes & Smoking Cessation

➢ Most but not all research(ers) agree: E-cigarettes offer a reduced harm alternative to individual users, as compared to combustible cigarettes
  ➢ Reduced carcinogen exposure, reduced morbidity (mortality?), particularly for those who completely switch.
  ➢ E-cigarettes may not be safe. But they are safer.
➢ E-cigarettes suppress nicotine withdrawal and craving in ways that NRT cannot.
➢ The best, most direct evidence (RCTs) generally suggest that e-cigarettes can help smokers quit and may be superior to NRT.[1-2]
➢ Much of the debate is based on distorted interpretations of science[3]

But most (if not all?) of these RCTs are instructional, purposeful, guided intervention studies of e-cigarettes for cessation/reduction

1. Hartmann-Boyce et al (2022) Cochrane Database of Systematic
2. Butler et al (2022). Prev Med 165:107182.
3. Mendelsohn et al. (in press). Addiction.

CONNECT Trial

Clinical Outcomes for a Nationwide, Naturalistic, E-Cigarette Trial

With acknowledgements to my collaborators:
Tracy Smith, Mike Cummings, Jen Dahne, Kevin Gray, Graham Warren (MUSC)
Amy Wahlquist (East Tennessee State Univ)
Ted Wagener (Ohio St)
Maciej Goniewicz (Roswell Park Cancer Institute)

With acknowledgements to my research staff:
Amy Boatright
Lisa Coles
Liz Hawes
Johanna Hidalgo
Karolina Kazlauskaite
Tatiana Myers
Gabby Mullins

And Interns/Postdocs: **Elly Leavens & Margaret Fahey**

Always get a study logo

Background

General Rationale:

- The best evidence to date (RCTs) generally suggest that e-cigarettes could help smokers quit
- Most of this evidence comes from outside the US, and most of this evidence is based on prescribed/instructional use, for a limited range of smokers (e.g., "use this e-cigarettes to quit/reduce")
- Very few large scale RCTs, even fewer in US, and even fewer with naturalistic intent
- Building on our prior pilot study (Carpenter et at CEBP 2017). . . .

Our intent:

Within randomized design (minimizing selection bias), across a range of all comers (both motivated and unmotivated to quit smoking), we offer smokers the opportunity to use ecigs as they wish, for whatever purpose they wish

General Methods

- Randomized, (2:1) provision of e-cig (NJoy Tank; 3ml pre-filled tanked, 15mg/ml of nicotine) or not, for self-determined use, with follow-up thru 6 months
- E-cig group sent up to 30 days (split over 2 shipments) with choice (up to 2) among 5 flavors: tobacco, menthol, blue/blackberry, apple melon, iced fruit
  - ~"*Use (or not use) as you wish, to reduce, quit, or during smoking restrictions. It's completel up to you*"
  - To be clear: providing ecigs for free is not naturalistic. We're focused on naturalistic outcomes when cost is not a barrier
- Daily diaries for first 30 days; Phone-based follow-up periodically for deeper assessment
- Product supplied to us, at cost, by NJoy. No financial or other support from e-cig industry
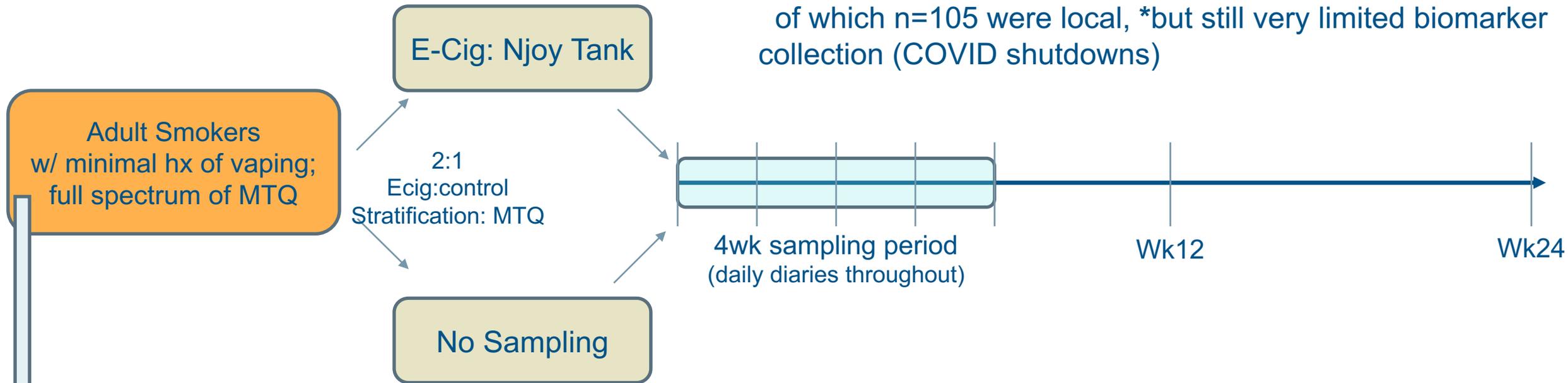- 11 Cities recruited

Outcomes (some of which presented today):
- Uptake, and patterns of it: trajectories, frequency/quantity of use, adoption (independent purchase
- Attitudinal & subjective responses: liking, reward, dependence
- Behavioral: Smoking Reduction, Quit attempts, Cessation
- Biological*: cotinine, NNAL, CO

Target N: 660
   of which n=120 will be local (biomarker collection)

Actual N: 638 (97%)
   of which n=105 were local, *but still very limited biomarker collection (COVID shutdowns)

Adult Smokers w/ minimal hx of vaping; full spectrum of MTQ

E-Cig: Njoy Tank

2:1
Ecig:control
Stratification: MTQ

No Sampling

4wk sampling period
(daily diaries throughout)

Wk12

Wk24

Minimal Hx of Vaping:
- no purchase in past 6 months,
- no ever regular use (daily or weekly) of tank/mod/advanced personal vaporizer (regular ciga-like usage ok)
- no regular use (daily or weekly) of any e-cig (including cig-a-likes devices) in past 6 months

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Clinical Outcomes of a Naturalistic, Nationwide E-Cigarette Trial

Baseline Characteristics (N=638)- Demographics

	Control (n=211)	E-Cigarette (n=427)	p
Male	43.1%	48.0%	.24
Race			.17
White	69.2%	68.2%	
Black	15.2%	20.1%	
Age, Mean (SD)	42.0 (11.9)	42.4 (11.2)	.63
Education			.12
HS or less	36.0%	28.3%	
Some+ college	64.0%	71.7%	
% Married or Partnered	33.2%	28.1%	.54
Income			.43
< $25,000 USD	31.0%	33.0%	
$25 - $50,000 USD	40.0%	33.7%	
Ever Dx'd with Mental Health Disorder	19.9%	19.9%	.99

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Baseline Characteristics (N=638)- Smoking History

	Control (n=211)	E-Cigarette (n=427)	p
CPD, Mean (SD)	14.8 (7.2)	14.8 (7.2)	.88
Age start smoking, Mean (SD)	17.6 (5.5)	17.7 (5.9)	.76
% w Smoker in home	41.2%	37.9%	.63
% QA in past year	27.5%	22.5%	.61
% Ever used e-cigarette	36.5%	42.4%	.15
% Ever purchased e-cigarette	22.3%	25.5%	.37
% w E-Cigarette user in home	5.2%	4.0%	.47
Motivation to Quit Smoking (0-10)	4.5 (3.1)	4.3 (3.3)	.31
Confidence to Quit Smoking (0-10)	3.3 (2.9)	3.3 (2.9)	.90

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E-Cigarette Uptake

Legend:
- % Using E-Cig (Control)
- % Using E-Cig (E-CIG)
- # days Using E-Cigarettes (CONTROL)*
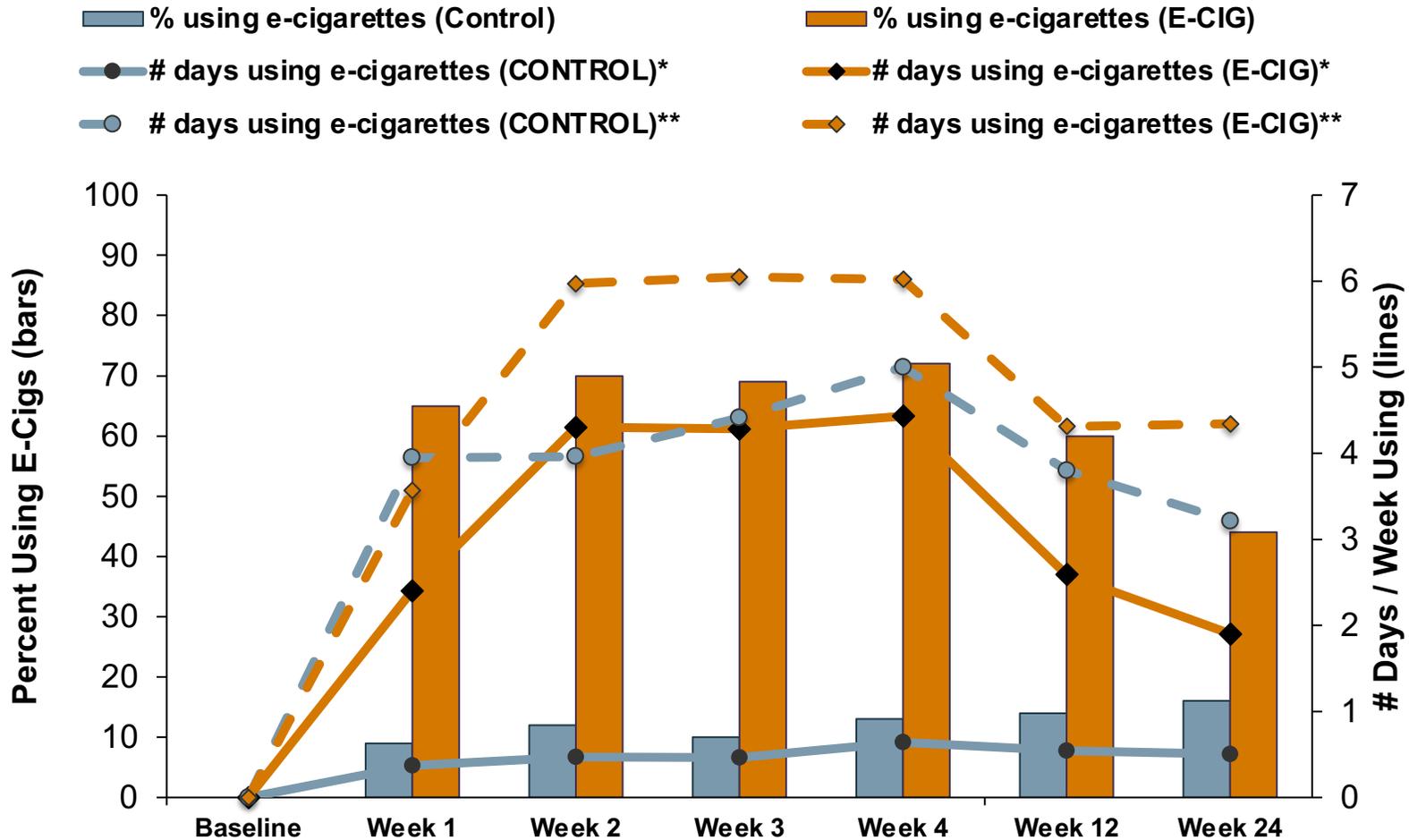- # days Using E-Cigarettes (E-CIG)*

Y-axis (left): Percent Using E-Cigs (bars)
Y-axis (right): # Days / Week Using (lines)

X-axis: Baseline, Week 1, Week 2, Week 3, Week 4, Week 12, Week 24

* Non-Users included (0 days)

# times/day using e-cig (asked only among users)			
	Control	**E-Cig**	**p**
Week 1	8.15 (6.9)	6.13 (5.3)	
Week 2	6.48 (5.9)	7.31 (7.9)	
Week 3	8.27 (10.3)	8.36 (9.7)	
Week 4	8.70 (9.9)	7.74 (6.5)	All n.s.
Week 12	7.17 (5.7)	6.85 (6.1)	
Week 24	6.58 (9.4)	6.96 (7.6)	

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E-Cigarette Uptake

Legend:
- % using e-cigarettes (Control)
- % using e-cigarettes (E-CIG)
- # days using e-cigarettes (CONTROL)*
- # days using e-cigarettes (E-CIG)*
- # days using e-cigarettes (CONTROL)**
- # days using e-cigarettes (E-CIG)**

Y-axis (left): Percent Using E-Cigs (bars) — 0 to 100
Y-axis (right): # Days / Week Using (lines) — 0 to 7
X-axis: Baseline, Week 1, Week 2, Week 3, Week 4, Week 12, Week 24

* Non-Users included (0 days)
** Users only
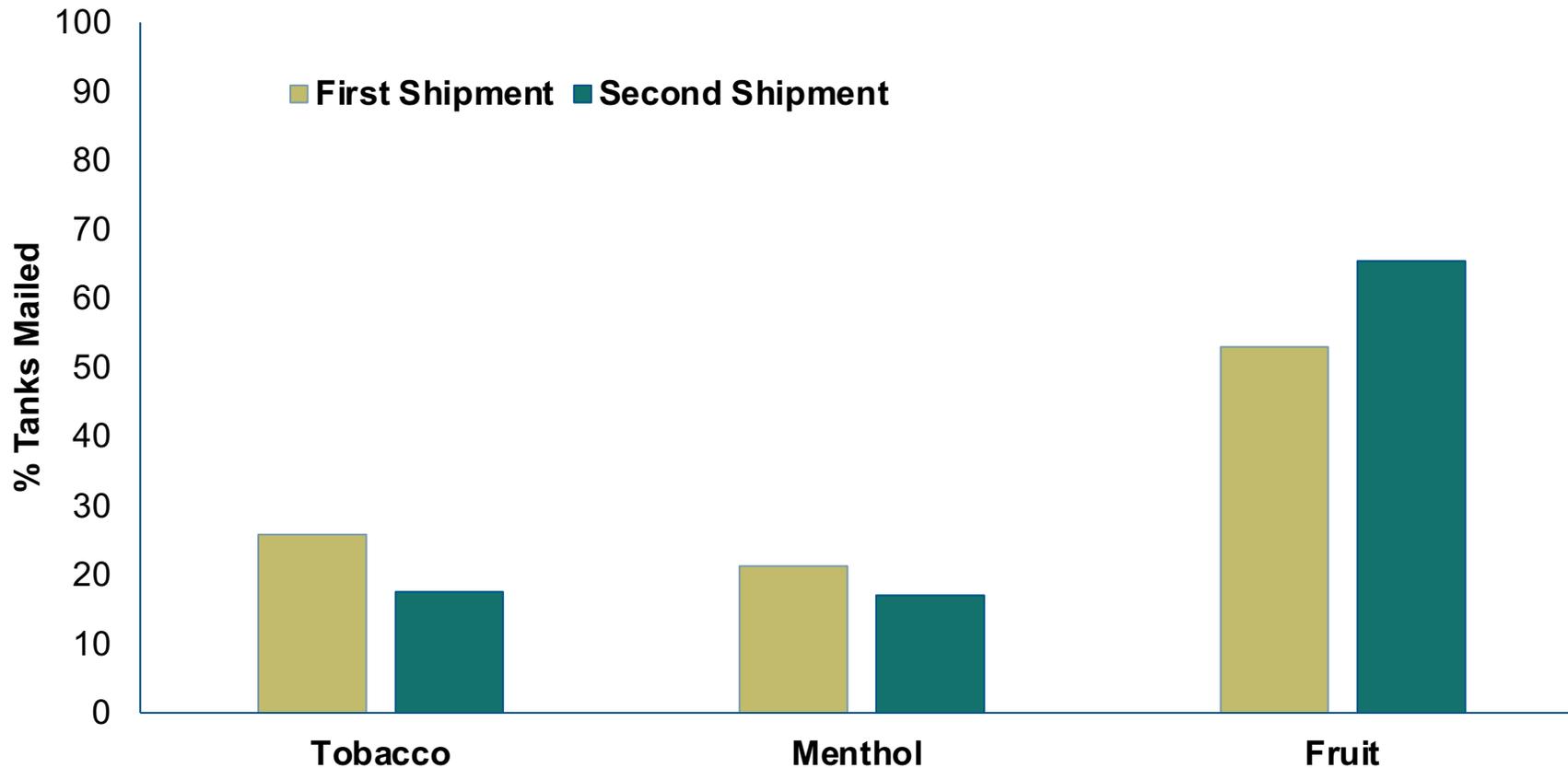
# times/day using e-cig (asked only among users)			
	Control	**E-Cig**	**p**
Week 1	8.15 (6.9)	6.13 (5.3)	
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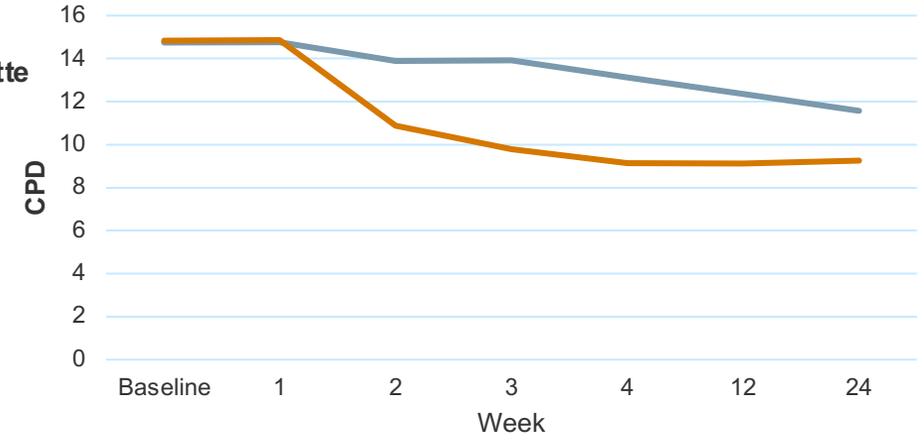Clinical Outcomes of a Naturalistic, Nationwide E-Cigarette Trial

Other Outcomes

Significant Time x Group Interactions	Motivation to Quit Cigarettes
	Confidence to Quit Cigarettes
	CPD
	HSI
	Penn State Dependence (cigarettes)
Interaction: n.s.; Time: p=0.012; Group: n.s.	Penn State Dependence (ecigs)

What About Dependence?

Significant Time x Group interaction

Chart legend:
- Cig Dependence: CONTROL group
- Cig Dependence: ECIG group
- E-Cig Dependence: ECIG group

Y-axis: Penn St Dependence Scale (0-20)

X-axis: Baseline, Week 1, Week 2, Week 3, Week 4, Week 12, Week 24

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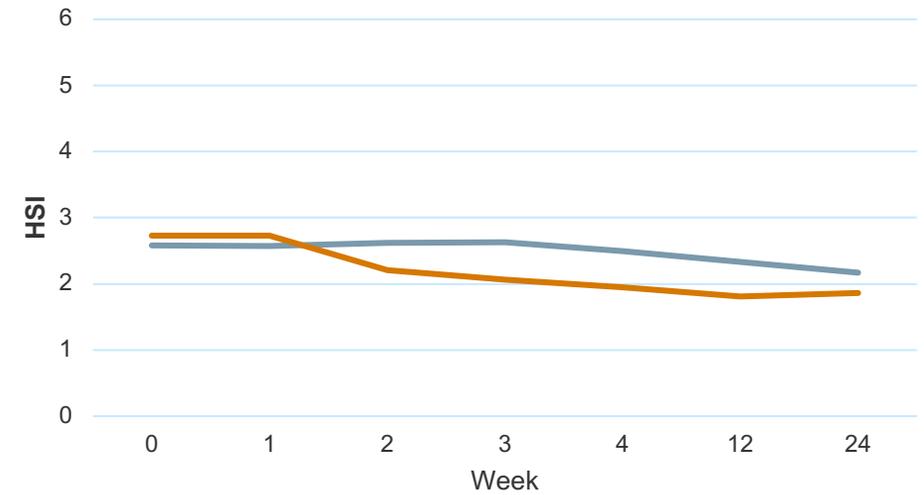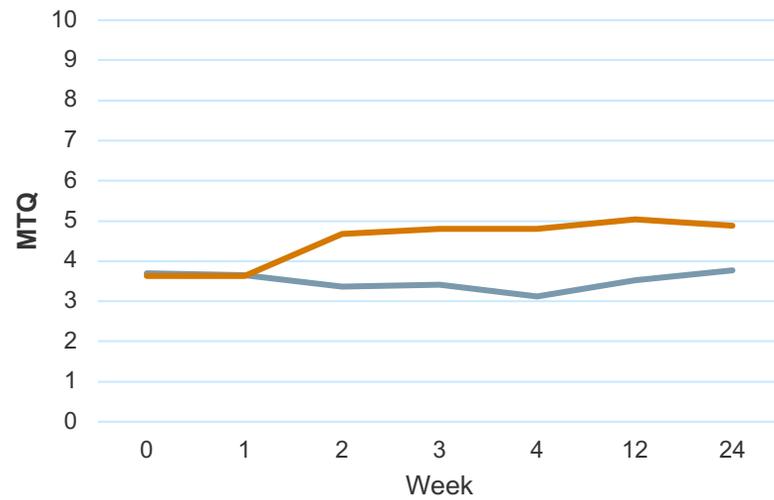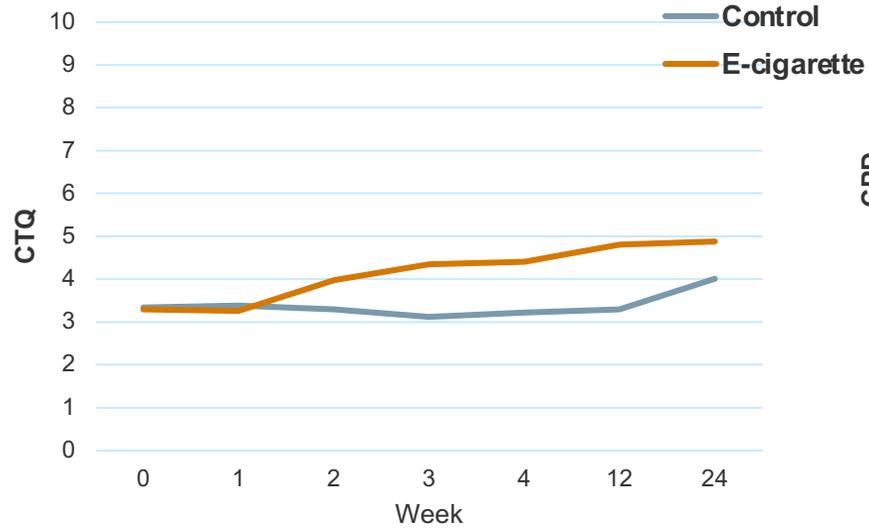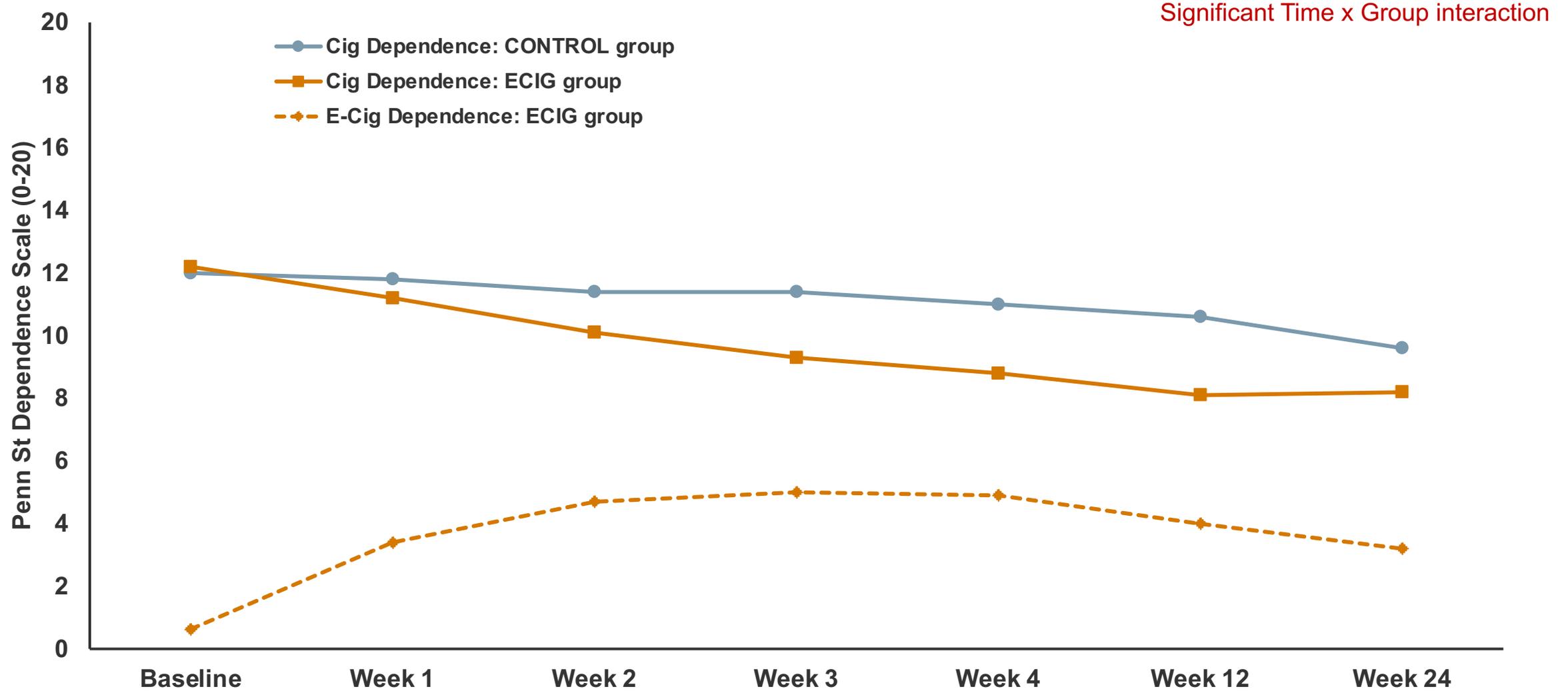
Example: Trajectories of Use Buckets over Time
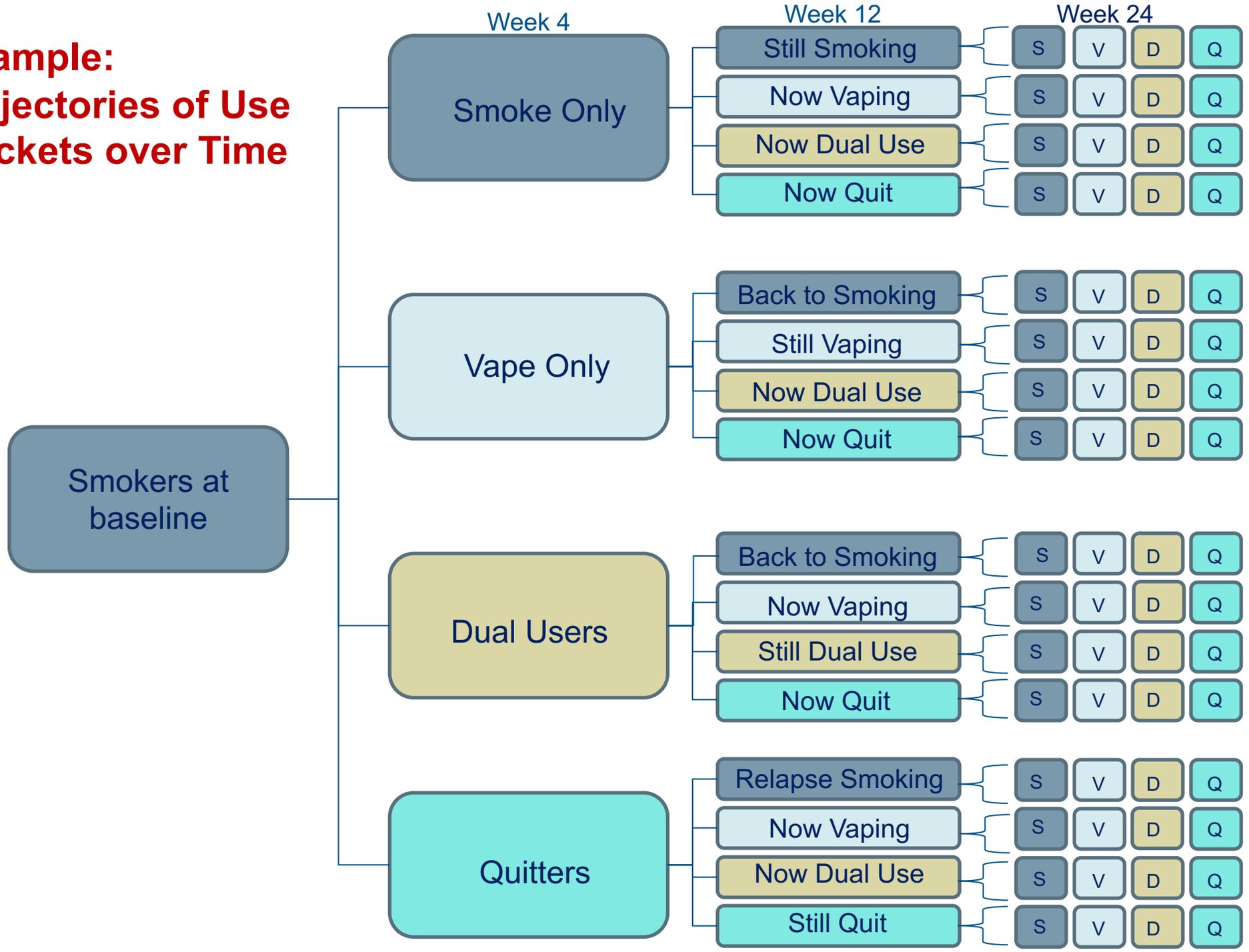
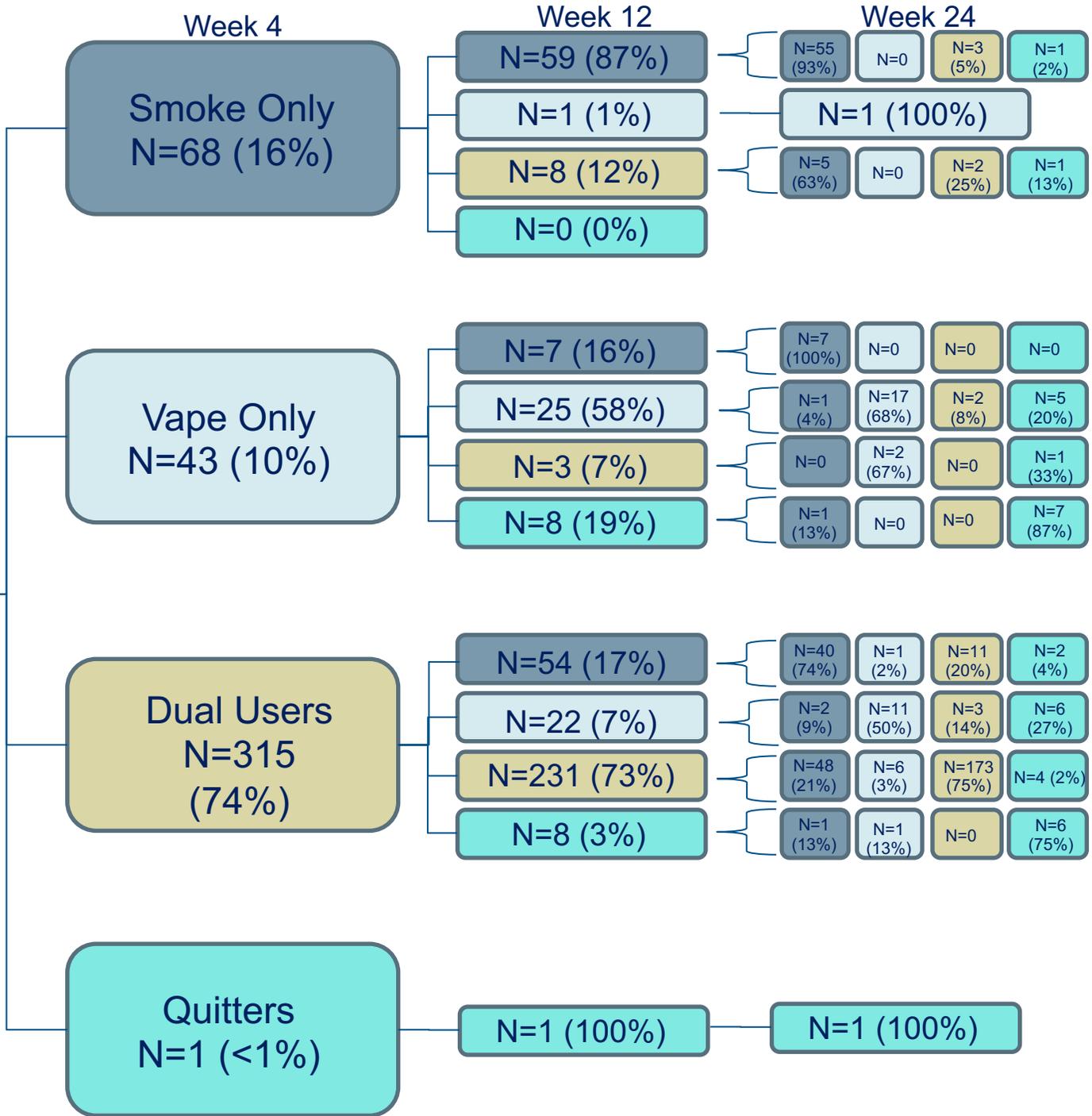- All "buckets" defined by product use in past 7 days

E-cigarette Group Completed Week 4 Now at Week 24

	Week 4	Week 12	Week 24			
Smokers at baseline N=427	**Smoke Only N=68 (16%)**	N=59 (87%)	N=55 (93%)	N=0	N=3 (5%)	N=1 (2%)
		N=1 (1%)	N=1 (100%)			
		N=8 (12%)	N=5 (63%)	N=0	N=2 (25%)	N=1 (13%)
		N=0 (0%)				
	Vape Only N=43 (10%)	N=7 (16%)	N=7 (100%)	N=0	N=0	N=0
		N=25 (58%)	N=1 (4%)	N=17 (68%)	N=2 (8%)	N=5 (20%)
		N=3 (7%)	N=0	N=2 (67%)	N=0	N=1 (33%)
		N=8 (19%)	N=1 (13%)	N=0	N=0	N=7 (87%)
	Dual Users N=315 (74%)	N=54 (17%)	N=40 (74%)	N=1 (2%)	N=11 (20%)	N=2 (4%)
		N=22 (7%)	N=2 (9%)	N=11 (50%)	N=3 (14%)	N=6 (27%)
		N=231 (73%)	N=48 (21%)	N=6 (3%)	N=173 (75%)	N=4 (2%)
		N=8 (3%)	N=1 (13%)	N=1 (13%)	N=0	N=6 (75%)
	Quitters N=1 (<1%)	N=1 (100%)	N=1 (100%)			

By Week 24:

Of W4 mono smokers:
- 60 (88.2%) maintained mono smoking
- 1 (1.5%) became a mono-vaper
- 5 (7.3%) became dual users
- 2 (2.9%) achieved underline complete abstinence
- **i.e, 4.4% not smoking**

Of W4 mono vapers:
- 9 (20.9%) relapsed to mono-smoking
- 19 (44.2%) still mono vapers
- 2 (4.7%) dual users (went back to smoking)
- 13 (30.2%) achieved complete abstinence
- **i.e., 74.4% not smoking**

Of W4 dual users:
- 91 (28.9%) relapsed to mono smoking
- 19 (6%) became mono-vapers
- 187 (59.4%) still dual users
- 18 (5.7%) achieved complete abstinence
- **i.e., 11.7% not smoking**

All percents based on denominator from previous step

For individuals with missing data, the last observation reported was carried forward

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Did We Create Dual Users? Yes but. . .

	>50% Reduction in CPD (since baseline)	
Among Dual Users at Week:	**At Week 4**	32%
	At Week 12	33%
	At Week 24	32%
Among Ever Dual Users throughout Follow-Up	40%	
	36% mean reduction in CPD (31% -- 41%)	
Among Ever Dual Users NOT Achieving >50% CPD reduction (n=199)	14% mean reduction in CPD (9% -- 19%)	

. . . Dual Users had substantial reductions in CPD

If missing: LOCF

Did We Create Dual Users? Yes but. . .

		Outcomes at Week 24:		
		Mono Smokers	**Mono E-Cig Users**	**Dual Users**	**Achieved Completed Abstinence (of both)**
Within E-CIG Group, At Week 4, Among:				
Mono Smokers (n=68)	60 (88.2%)	1 (1.5%)	5 (7.3%)	3 (4.4%)
Mono E-Cig Users (n=43)	9 (20.9%)	19 (44.2%)	2 (4.7%)	13 (30.2%)
Dual Users (n=315)	91 (28.9%)	19 (6.0%)	187 (59.4%)	18 (5.7%)
Total: 426 **(1ppt quit at week 4; Total N in E-CIG Group = 427)**				

. . . Dual Users had substantial reductions in CPD
. . . Greater Proportion of Dual Users achieved abstinence than the entirety of the control group

If missing: LOCF

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Conclusions; Moving Forward

- Study findings complement existing RCTs of e-cigarettes, which were primarily cessation focused & supported
- Our results show that unstructured/unguided e-cigarette use leads to increase quitting, <u>across a range of outcomes</u>
- Effect sizes were comparable among those who were and were not ready to quit
- Dual use was the predominant outcome, but moderate reduction in CPD exist even among dual users

- **Limitations**: Lack of bioverification (the curse of covid)
- **Manuscript(s) in development**:
  - Main outcomes
  - Impact of flavors relative to outcomes
  - Reasons for Use → Actual Use
  - Remote recruitment process
  - Invitation to others!
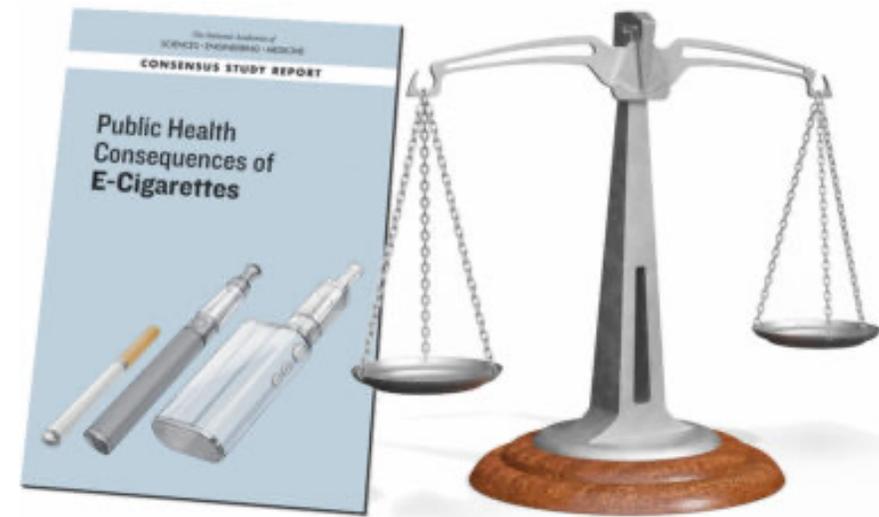
- **SRNT Symposium** (Thurs, 3/2): Podium Session #2

And remember. . .

ALL e-cig cessation trials should be balanced with public health needs and science focused on prevention of youth initiation

Us vs. Them: Only 1 side wins

Balance: How do we get e-cigarettes in the right hands of smokers, AND out of the hands of kids?

Slide credit: Tracy Smith

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Thank you!

Questions?

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