

#### **DISCLOSURES**

Niaura - Past 3 years: I do work with the FDA CTP via contractual mechanisms. I am a co-Investigator on several NIH grant awards.

Xu -

#### **OUTLINE**

 Who are the (U.S.) smokers? What can national data can tell us (US National Health Interview Survey; Population Assessment of Tobacco and Health Study)?

 Tobacco harm reduction: Can e-cigarettes help cigarette smokers quit?

#### Cigarette smoking is bad for you but quitting helps

# Smoking Cessation and Short-and Longer-Term Mortality

https://evidence.nejm.org/doi/full/10.1056/EVIDoa2300272

Eo Rin Cho, Ilene K. Brill, Inger T. Gram, Patrick E. Brown, Prabhat Jha

Prabhat.jha@utoronto.ca

Twitter/X: @countthedead







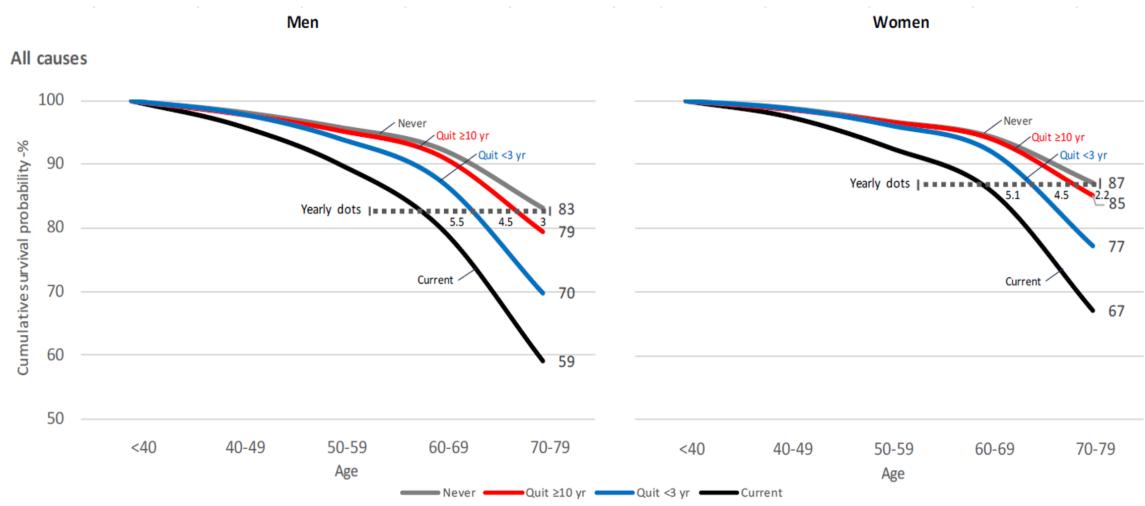


# Worldwide no of smokers, drinkers and obese (B=billions, M=millions)

<u>Exposure</u>	<u>No.</u>	Annual deaths	
Smoking	1.1 B	6-7 M	
Drinking	2.0 B	2 M	
Adiposity (BMI>30)	0.6 B	~ 1.5 M	

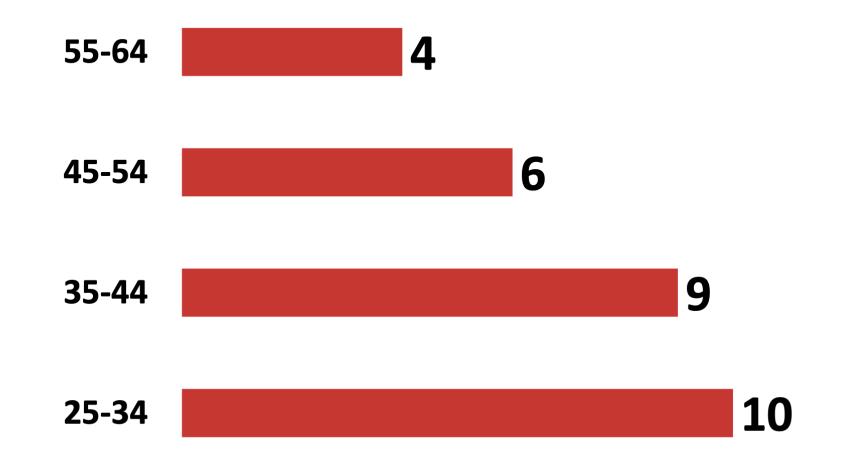


# Survival from ages 40 to 79 years of age by smoking status (never, cessation 10+ years or <3 years, and current) by sex: All causes mortality





# US: Years gained by age at stopping smoking





#### WHO (still) SMOKES CIGARETTES?













#### Who are the smokers?

#### **Priority populations**





## Key Disparities in Current Cigarette Smoking Among Adults and Youth According to Prevalence and/or Harm

- Low socioeconomic status
- Comorbid mental health or substance abuse diagnoses,
- Racial/ethnic minorities
- Individuals with physical disabilities,
- Sexual Orientation and Gender Identity
- Veterans/military
- Criminal justice populations
- Education (low)

- No health insurance
- Medicaid enrollees
- American Indians/Alaska Natives
- Chronic Disease Status
- Geographic Location
- Pregnant Women
- Adolescents
- Dual users
- Light/intermittent smokers

U.S. Department of Health and Human Services. Smoking Cessation. A Report of the Surgeon General. Atlanta, GA: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health, 2020.

#### **US NHIS**

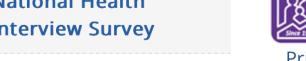


Search NCHS • Search

#### National Center for Health Statistics

CDC > NCHS





**About NHIS** 2019 Redesign What's New



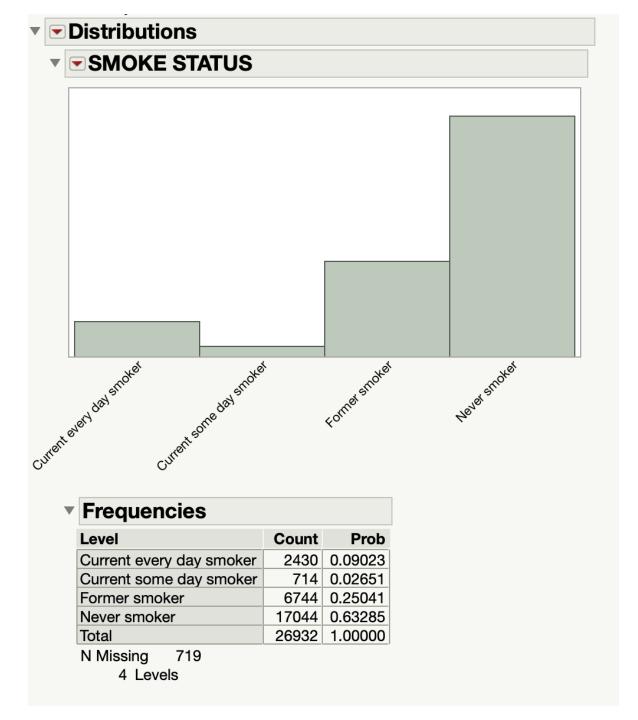
#### National Health Interview Survey

Print

The National Health Interview Survey (NHIS) has monitored the health of the nation since 1957. NHIS data on a broad range of health topics are collected through personal household interviews. Survey results have been instrumental in providing data to track health status, health care access, and progress toward achieving national health objectives.

US National Health Interview Survey – 2022

Population Outcome: Smoking status- 4 categories



Regression model predicting smoking status via various sociodemographic and other characteristics

#### ■ Nominal Logistic Fit for SMOKE STATUS

#### ▼ Effect Summary

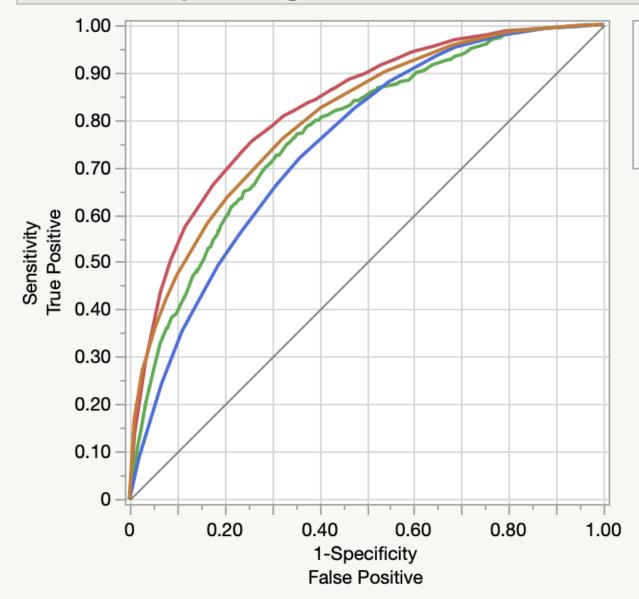
	FDR	
Source	LogWorth	FDR PValue
ECIG	415.960	0.00000
AGE CAT	210.432	0.00000
ALCOHOL	208.418	0.00000
EDUCATION	119.349	0.00000
POVERTY RATIO	31.451	0.00000
SEX	25.302	0.00000
MARITAL	21.534	0.00000
ETHNICITY	13.778	0.00000
VETERAN	9.135	0.00000
DISABILITY	3.769	0.00017
DEPRESSION	3.104	0.00079
ANXIETY	2.542	0.00287
SEX ORIENT	2.065	0.00860
ANXIETY MEDS	1.154	0.07009
EMPLOYMENT	1.143	0.07202
US BORN	0.879	0.13212
<b>DEPRESS MEDS</b>	0.290	0.51323
RACE	0.087	0.81845

Remove Add Edit



FDR

#### **▼** Receiver Operating Characteristic on Training Data



	SMOKE STATUS	Area
_	Current every day smoker	0.8259
	Current some day smoker	0.7723
_	Former smoker	0.7478
	Never smoker	0.8023

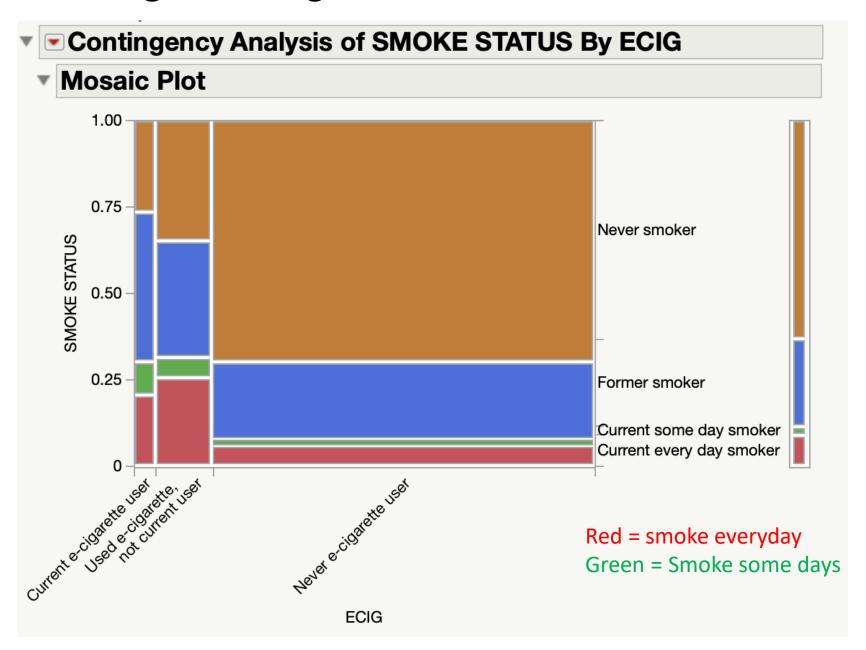
#### **▼** Confusion Matrix

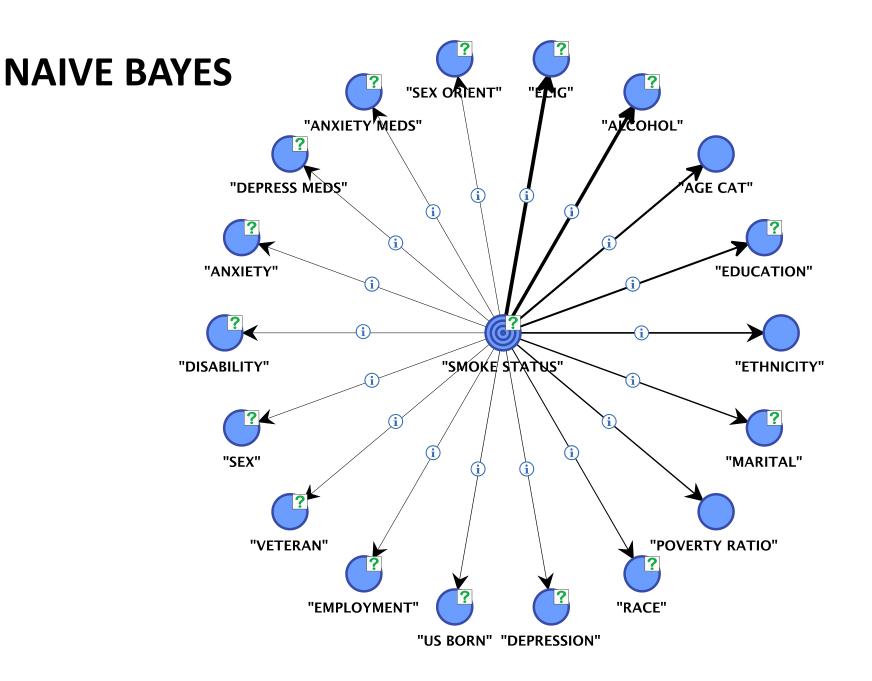
#### Training

	Predicted Count			
Actual SMOKE STATUS	Current every day smoker	Current some day smoker		Never smoker
Current every day smoker	533	0	684	1013
Current some day smoker	75	1	174	376
Former smoker	322	0	2119	3777
Never smoker	174	1	1133	13784

	Predicted Rate			
Actual	<b>Current every</b>	<b>Current some</b>	Former	Never
SMOKE STATUS	day smoker	day smoker	smoker	smoker
Current every day smoker	0.239	0.000	0.307	0.454
Current some day smoker	0.120	0.002	0.278	0.601
Former smoker	0.052	0.000	0.341	0.607
Never smoker	0.012	0.000	0.075	0.913

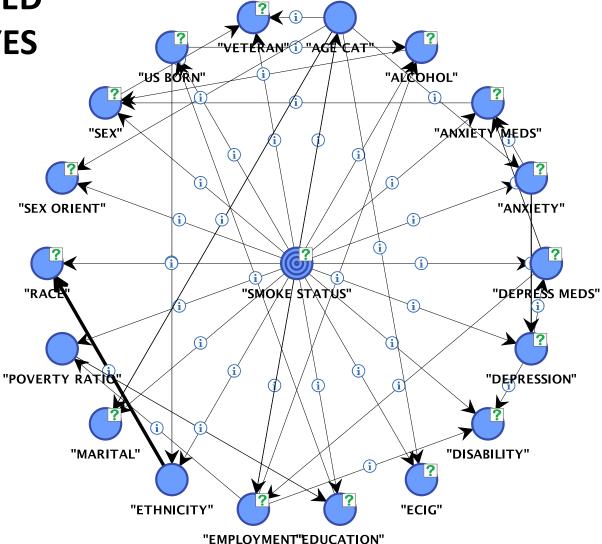
#### Cigs and E-cigs co-occurrence: NHIS 2022





Naive learning on "SMOKE STATUS": Delete All Arcs Variable Selection: false

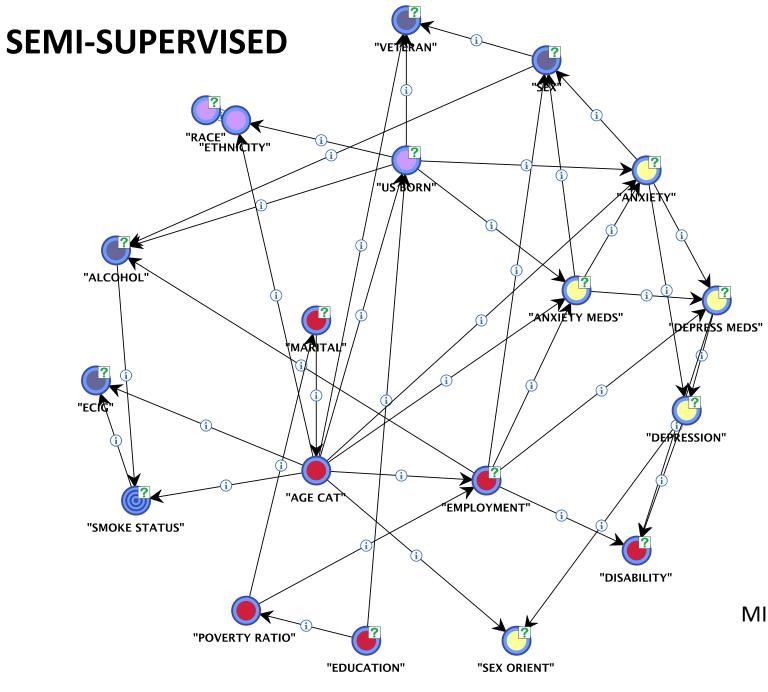
Missing values treated with Structural EM Total Weight: 27,651 Initial MDL score: 745,005.421 Final MDL score: 735,828.106 Total learning time: 0s AUGMENTED NAIVE BAYES



Augmented Naive learning on "SMOKE STATUS": Delete All Arcs Variable Selection: false

Missing values treated with Structural EM Total Weight: 27,651 Initial MDL score: 745,005.421 Final MDL score: 658,672.252

Total learning time: 18s



Semi-Supervised learning on "SMOKE STATUS":

Variable Selection:

false

Radius: 8 Algorithm:

Taboo

Missing values treated with Structural EM Total Weight: 27,651

Initial MDL score:

745,005.421

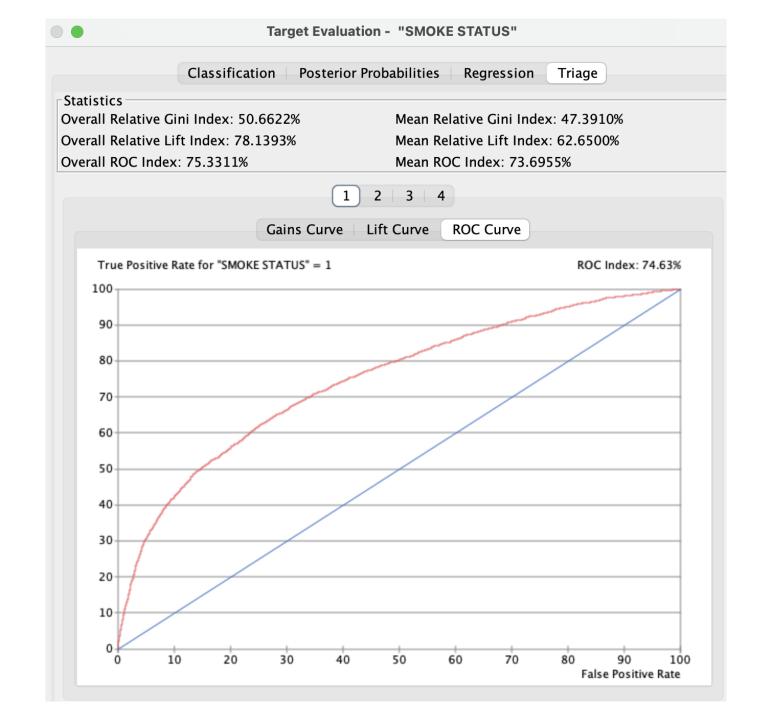
Final MDL score:

651,939.97

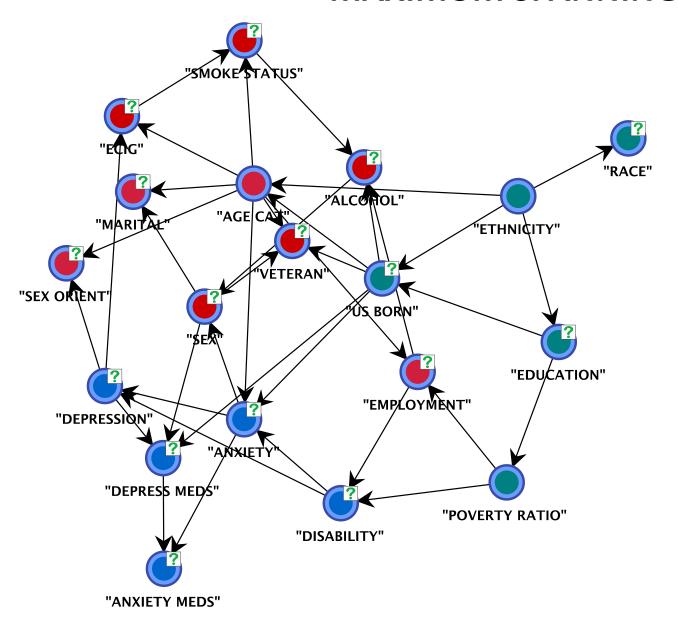
Total learning time:

**12s** 

MI distance mapping; Variable clustering



#### **MAXIMUM SPANNING TREE**



Maximum Spanning
Tree learning:
Delete All Arcs
Post-Processed with
Taboo (78)
Score Type: MDL

Missing values treated with Structural EM Total Weight: 27,651 Initial MDL score: 745,005.421 Final MDL score: 652,020.374 Total learning time: 9s

#### **Tobacco Harm Reduction**

Tobacco Harm Reduction depends on changing behaviors, or switching states of behavior, from more to less harmful.

Cigarette -> E-cigarette (or some other reduced risk tobacco/nicotine product)

#### DO E-CIGS HELP SMOKERS QUIT SMOKING?

2023



**RCTs** 

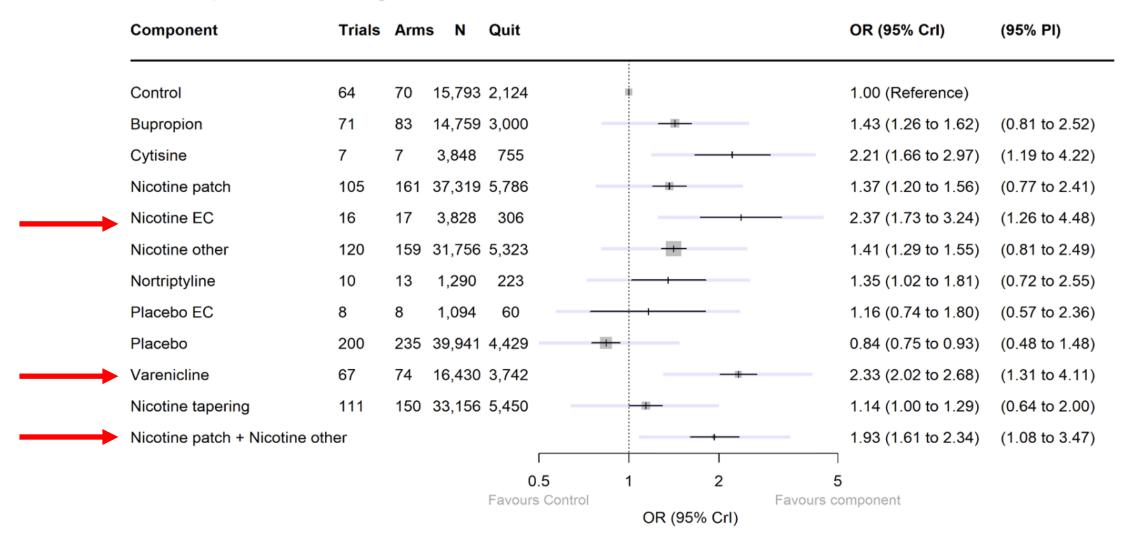
**Cochrane** Database of Systematic Reviews

Pharmacological and electronic cigarette interventions for smoking cessation in adults: component network meta-analyses (Review)

Lindson N, Theodoulou A, Ordóñez-Mena JM, Fanshawe TR, Sutton AJ, Livingstone-Banks J, Hajizadeh A, Zhu S, Aveyard P, Freeman SC, Agrawal S, Hartmann-Boyce J

#### DO E-CIGS HELP SMOKERS QUIT SMOKING? - YES

Figure 3. Forest plot illustrating final model for abstinence (efficacy) outcome. Note, darker intervals represent CrI and lighter intervals represent PI. Control: no pharmacological or EC intervention. *Abbreviations*CrI: credibility interval; EC: e-cigarette; N: number of participants; OR: odds ratio; PI: prediction interval



#### BUT WAIT, NOT SO FAST! WHAT ABOUT THE "REAL WORLD?"

#### **OBSERVATIONAL STUDIES TO THE RESCUE?**



#### Stop-smoking methods used by adults who stopped smoking completely from 2020-2022, **US National Health Interview Survey**

100

(12.0–18.1; 1.1 million)

(50.6–58.7; 4.1 million)

(3.1–6.7; 0.4 million)

4.7

54.6

**Weighted Percent** (95% CI\*; Weighted N)

	(Unweighted n=756)	(7.5 million)
	Nicotine-containing methods	
	E-cigarettes	42.5 (38.3–46.8; 3.2 million)
,	Exclusively	27.2 (23.4–31.2; 2.0 million)
	Nicotine gum/lozenge	17.1 (14.0–20.6; 1.3 million)
	Exclusively	2.5 (1.5–3.8; 0.2 million)
	Nicotine patch	14.8

Exclusively

Nicotine nasal spray/inhaler

Exclusively

One or more of above

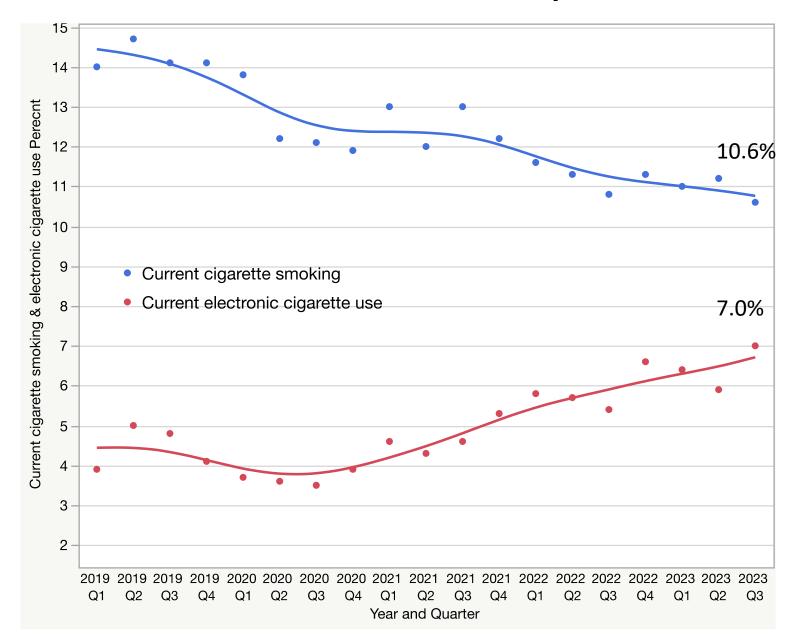
Any method

**E-cigarette and** nicotine replacement are the most popular methods

#### Stop-smoking methods used by adults who stopped smoking completely from 2020–2022

Prescription drug methods		
Chantix/Varenicline	6.4 (4.6–8.5; 0.5 million)	
Exclusively	2.4 (1.4–3.7; 0.2 million)	
Zyban/Bupropion/Wellbutrin	4.5 (3.1–6.3; 0.3 million)	
Exclusively	†	
One or more of above	9.6 (7.4–12.2; 0.7 million)	
Non-nicotine, non-prescription drug methods		
Quit line	2.5 (1.5–3.9; 0.2 million)	
Exclusively	†	

### Current cigarette smoking & electronic cigarette use % vs. Year and Quarter- US National Health Interview Survey



Are they connected?

#### Population Assessment of Tobacco and Health (PATH) Study

- The PATH Study is a collaboration between the National Institute on Drug Abuse (NIDA), National Institutes of Health (NIH), and the Center for Tobacco Products (CTP), Food and Drug Administration (FDA).<sup>14</sup>
- It was launched in 2011 to inform FDA's regulatory activities under the Family Smoking Prevention and Tobacco Control Act.<sup>14</sup>
- The PATH Study is an ongoing longitudinal cohort study on tobacco use behavior, attitudes, beliefs, and tobacco-related health outcomes.<sup>14</sup>

	_	
ч.	/	
	7770	
	/ave	

Sep. 2013-Dec. 2014

Adult: **32,320** 

Youth: **13,651** 

#### Wave 2

Oct. 2014-Oct. 2015

Adult: 28,362

Youth: 12,172

#### Wave 3

Oct. 2015-Oct. 2016

Adult: 28,148

Youth: 11,814

#### Wave 4

Dec. 2016-Jan. 2018

Adult: 33,822

Youth: 14,798

### Wave 4.5 Special Collection: Youth Only

Dec. 2017-Nov. 2018

Youth: 13,131

#### Wave 5

Dec. 2018-Nov. 2019

Adult: **34,309** 

Youth: 12,098

#### Wave 5.5 & PATH-ATS

Special Collection: Adult & Youth

Wave 5.5: Jul. – Dec. 2020 PATH-ATS: Sep. – Dec. 2020

Adult (PATH-ATS): 8,874

Young Adult (W5.5): **3,628** 

Youth (W5.5): 7,129

#### Wave 6

Mar. – Nov. 2021

Adult: **30,516** 

Youth: **5,652** 

#### Wave 7

Jan. 2022 – Apr. 2023 Data not yet available

Adult: xx,xxx

Youth: xx,xxx

The overall weighted response rate for adults was 74% in Wave 1 and 65.1% in Wave 5.15

Source: NIDA.NIH.gov

#### Analyses: Wave 1 – 6 adults with complete longitudinal data

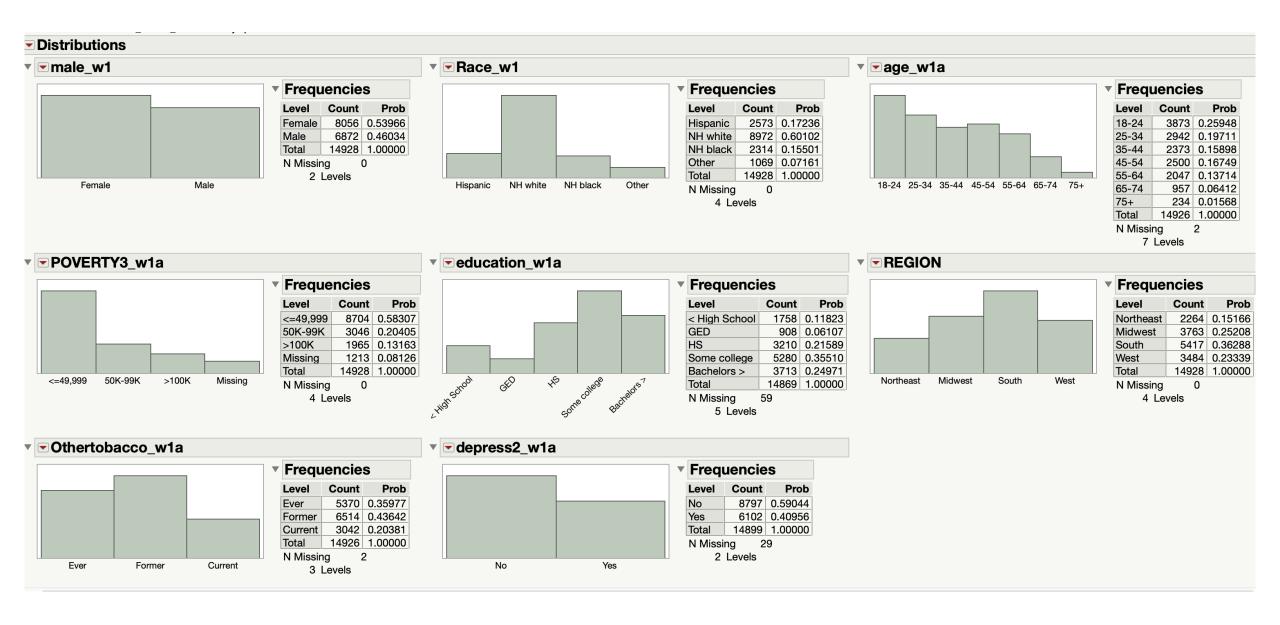
**Basic sociodemographic info:** Age, sex, education, race, region, poverty, depression

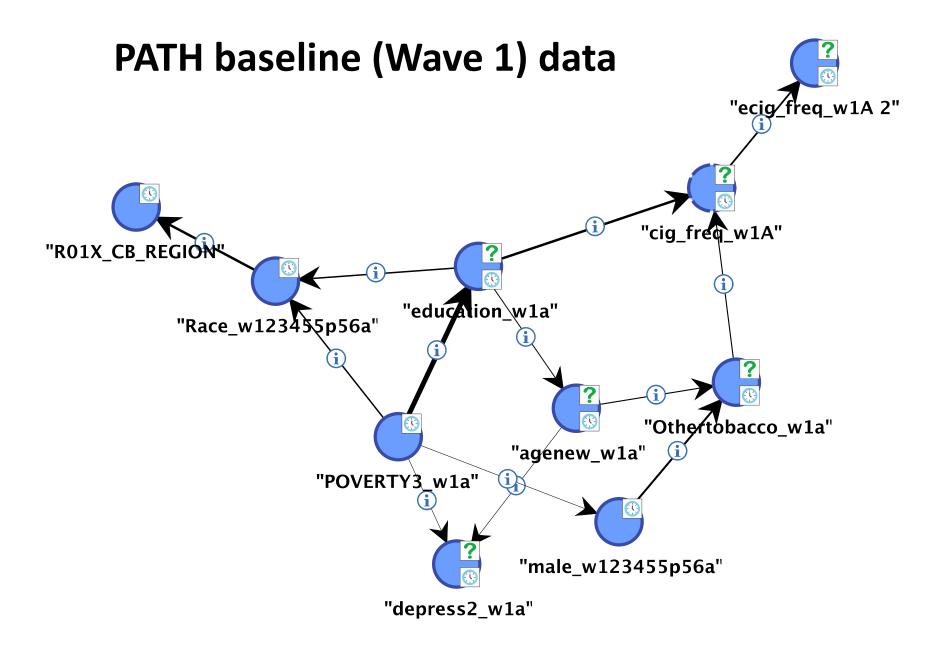
**Exposure:** E-cigarette use frequency (days used in past month); Past month use – yes/no

Outcomes: Cigarette use frequency (days used in past month); Past month use – yes/no

Covariates: Other tobacco product use, depression

#### **PATH Study Wave 1 Sociodemographic characteristics**



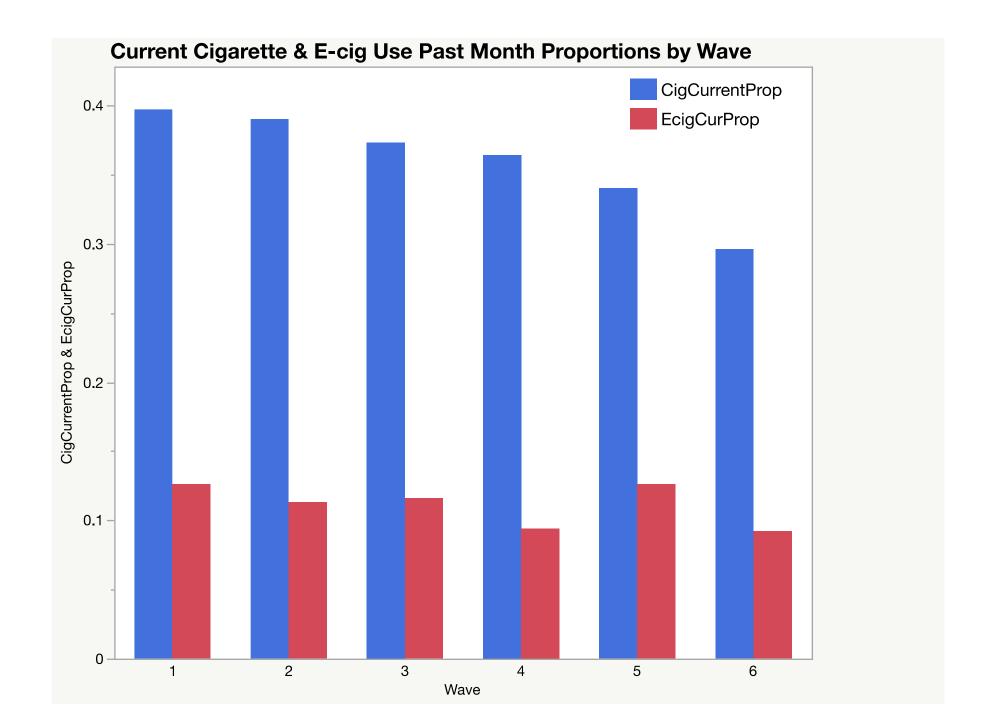


Taboo learning:
Delete All Arcs
Taboo List Size: 36

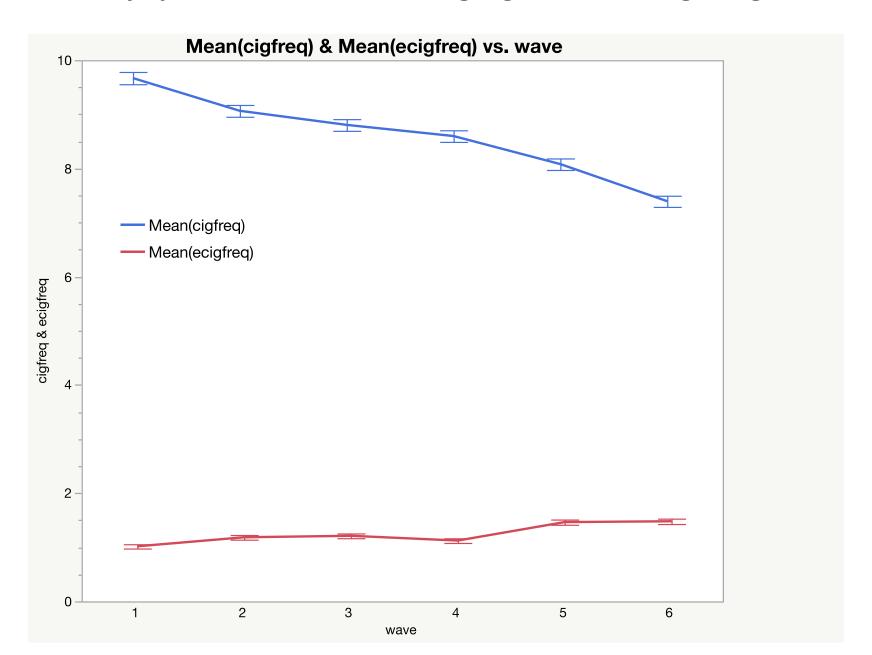
Missing values treated with Structural EM Total Weight: 14,928 Initial MDL score: 227,476.42

Final MDL score: 219,343.079

Total learning time: 0s



#### Mean days per last month smoking cigarettes, using e-cigarettes



## wave 30 10 10 cigfreq cigfreq 30 wave

#### **Fixed Effects Tests**

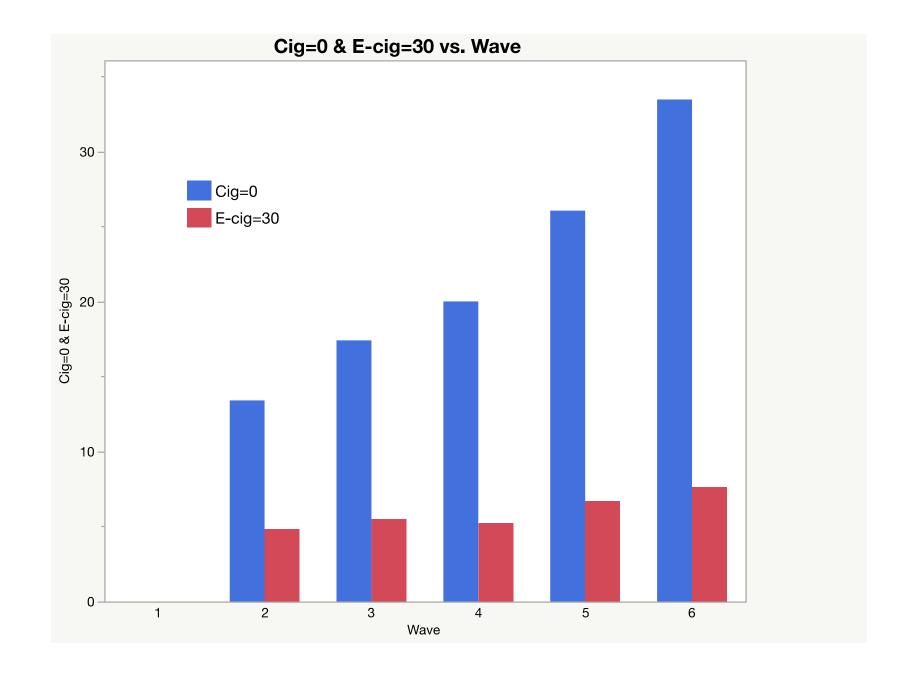
Source	Nparm	<b>DFNum</b>	<b>DFDen</b>	F Ratio	Prob > F
wave	5	5	14460	144.69765	<.0001*
ecigfreq	1	1	15124	2.7563292	0.0969
wave*ecigfreq	5	5	27034	54.125811	<.0001*

Random effects model: Time (wave), ecigarette frequency (days per month) and interaction effect (time x frequency)

Outcome: Cigarette frequency (days per month)

#### **Selection:**

Smokers only selected at Wave 1



#### 

#### **▼** Frequencies

Level	Count	Prob
0	795	0.13434
1	137	0.02315
2	98	0.01656
3	81	0.01369
4	54	0.00912
5	116	0.01960
6	54	0.00912
7	28	0.00473
8	40	0.00676
9	24	0.00406
10	106	0.01791
11	4	0.00068
12	25	0.00422
13	5	0.00084
14	8	0.00135
15	111	0.01876
16	5	0.00084
17	2	0.00034
18	12	0.00203
19	8	0.00135
20	133	0.02247
21	5	0.00084
22	11	0.00186
23	6	0.00101
24	7	0.00118
25	71	0.01200
26	10	0.00169
27	8	0.00135
28	19	0.00321
29	4	0.00068
30	3931	0.66424
Total	5918	1.00000

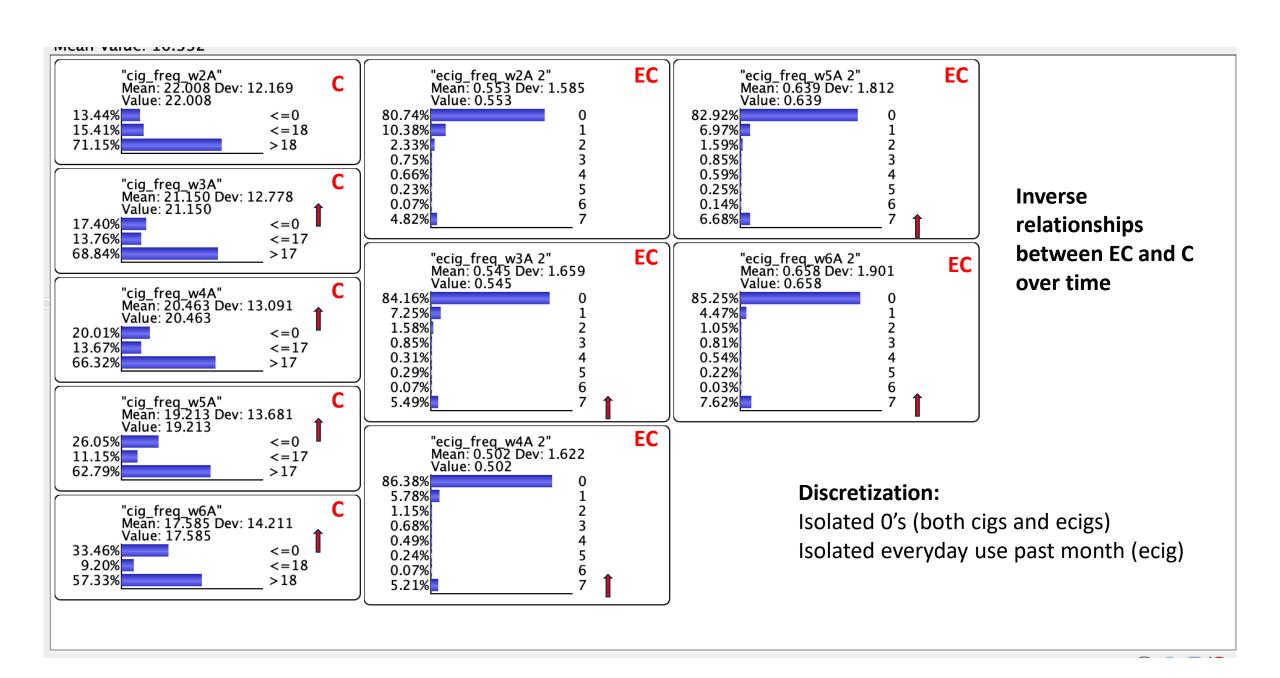
N Missing 31 Levels

#### **▼** Frequencies

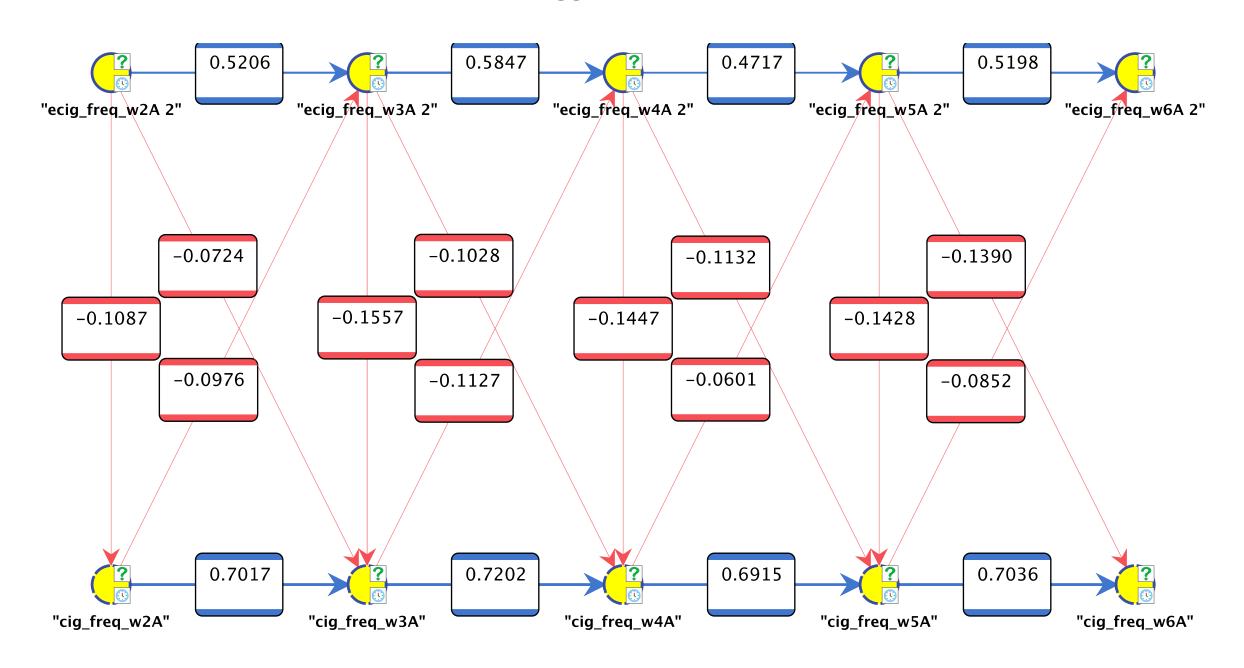
Level	Count	Prob
0	4509	0.80676
1	182	0.03256
2	157	0.02809
3	69	0.01235
4	33	0.00590
5	137	0.02451
6	25	0.00447
7	14	0.00250
8	14	0.00250
9	14	0.00250
10	63	0.01127
11	1	0.00018
12	5	0.00089
13	4	0.00072
14	3	0.00054
15	29	0.00519
16	1	0.00018
17	1	0.00018
18	5	0.00089
19	1	0.00018
20	29	0.00519
21	1	0.00018
25	12	0.00215
26	1	0.00018
27	2	0.00036
29	1	0.00018
30	276	0.04938
Total	5589	1.00000

N Missing 338 27 Levels

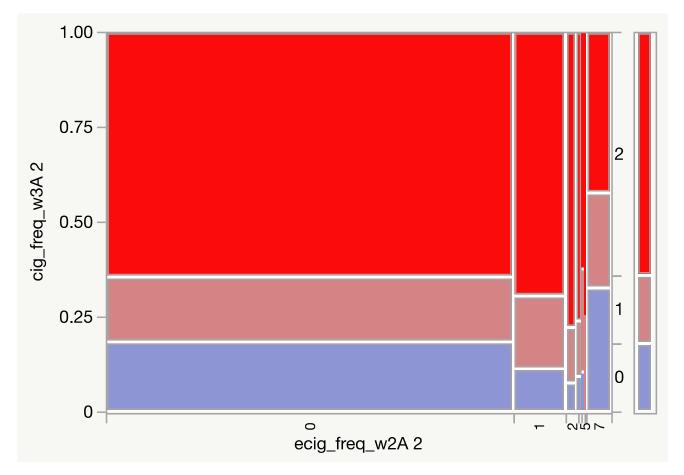
#### **Skewed distributions**



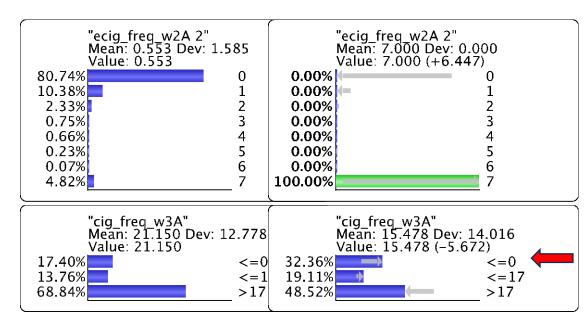
#### **Cross-lagged Panel Model**



**Wave 2-3 lagged relationship** 



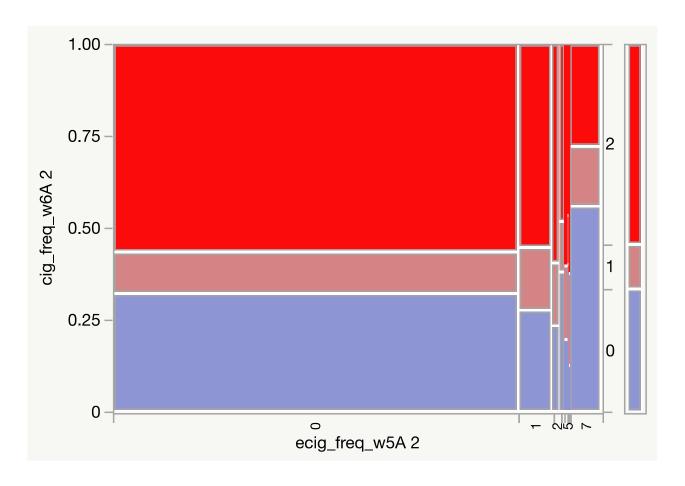
### Setting evidence: 100% of smokers switch to daily e-cig use



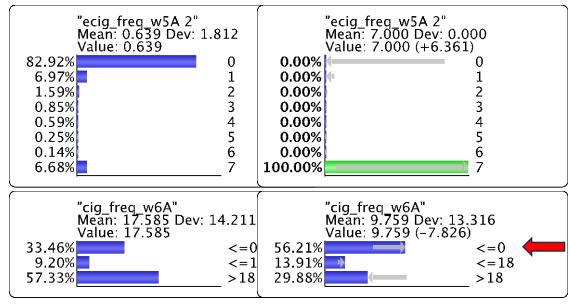
N	D	F	-LogLi	ke	RSquare (U)
5581	1	4	49.9751	58	0.0099
Test		C	hiSquare	Pı	ob>ChiSq
Likelihoo	d Ratio		99.950		<.0001*
Pearson			99.672		<.0001*

Daily use of e-cigs show the strongest association

Wave 5-6 lagged relationship



## Setting evidence: 100% of smokers switch to daily e-cig use



N D		F -LogLike		RSquare (U)	
5904	14	77.6585	03	0.013	
Test	C	hiSquare	are Prob>ChiSq		
Likelihood Ratio		155.317		<.0001*	
Pearson		155.205	<.0001*		

Daily use of e-cigs show the strongest association

#### **Accidental Quitting**

by Jemma Wolfe Sep 20, 2022



#### ANOTHER LOOK AT PATH STUDY DATA: SMOKERS NOT PLANNING TO QUIT





**Original Investigation | Public Health** 

# Association of e-Cigarette Use With Discontinuation of Cigarette Smoking Among Adult Smokers Who Were Initially Never Planning to Quit

Karin A. Kasza, PhD; Kathryn C. Edwards, PhD; Heather L. Kimmel, PhD; Andrew Anesetti-Rothermel, PhD, MPH; K. Michael Cummings, PhD; Raymond S. Niaura, PhD; Akshika Sharma, MDS; Erin M. Ellis, PhD; Rebecca Jackson, MPH; Carlos Blanco, MD, PhD; Marushka L. Silveira, PhD; Dorothy K. Hatsukami, PhD; Andrew Hyland, PhD

JAMA Network Open. 2021;4(12):e2140880. doi:10.1001/jamanetworkopen.2021.40880

Table 2. Cigarette Discontinuation and Discontinuing Daily Cigarette Smoking at Follow-up Wave, Among Daily Cigarette Smokers Who Had No Plans to Ever Quit for Good and Who Were Not Using e-Cigarettes at Baseline Wave, as a Function of e-Cigarette Use at Follow-up Wave<sup>a</sup>

	Cigarette discontinuation at follow-up wave (ie, no cigarette smoking)		Discontinuing daily cigarette smoking at follow-up wave (ie, no daily cigarette smoking)		
e-Cigarette use at follow-up	No. of observations (%) [95% CI]	aOR (95% CI) <sup>b</sup>	No.of observations (%) [95% CI]	aOR (95% CI) <sup>b</sup>	
Overall (n = 2489)	158 (6.2) [5.0-7.5]	NA	271 (10.7) [9.1-12.5]	NA	
No e-cigarette use (n = 2273)	138 (5.8) [4.7-7.2]	1 [Reference]	228 (9.9) [8.2-11.8]	1 [Reference]	
Nondaily e-cigarette use (n = 156)	3 (3.1) [0.8-11.1] <sup>c</sup>	0.53 (0.08-3.35)	16 (10.2) [5.8-17.3]	0.96 (0.44-2.09)	
Daily e-cigarette use (n = 60)	17 (28.0) [15.2-45.9]	8.11 (3.14-20.97)	27 (45.5) [27.4-64.9]	9.67 (4.02-23.25)	

# Yes, BUT...



#### **CONCLUSIONS**

- Who are the (U.S.) smokers? National data can point us to important inequalities, but we need more to reach the majority of smokers with effective cessation tools.
- What works to help smokers quit?
  - E-cigarettes are a popular method. They are consumer not therapeutic products. They may have greater reach and availability and they may benefit smokers who are not even trying to quit, but they must be used daily for complete switching.

