

RUTGERS

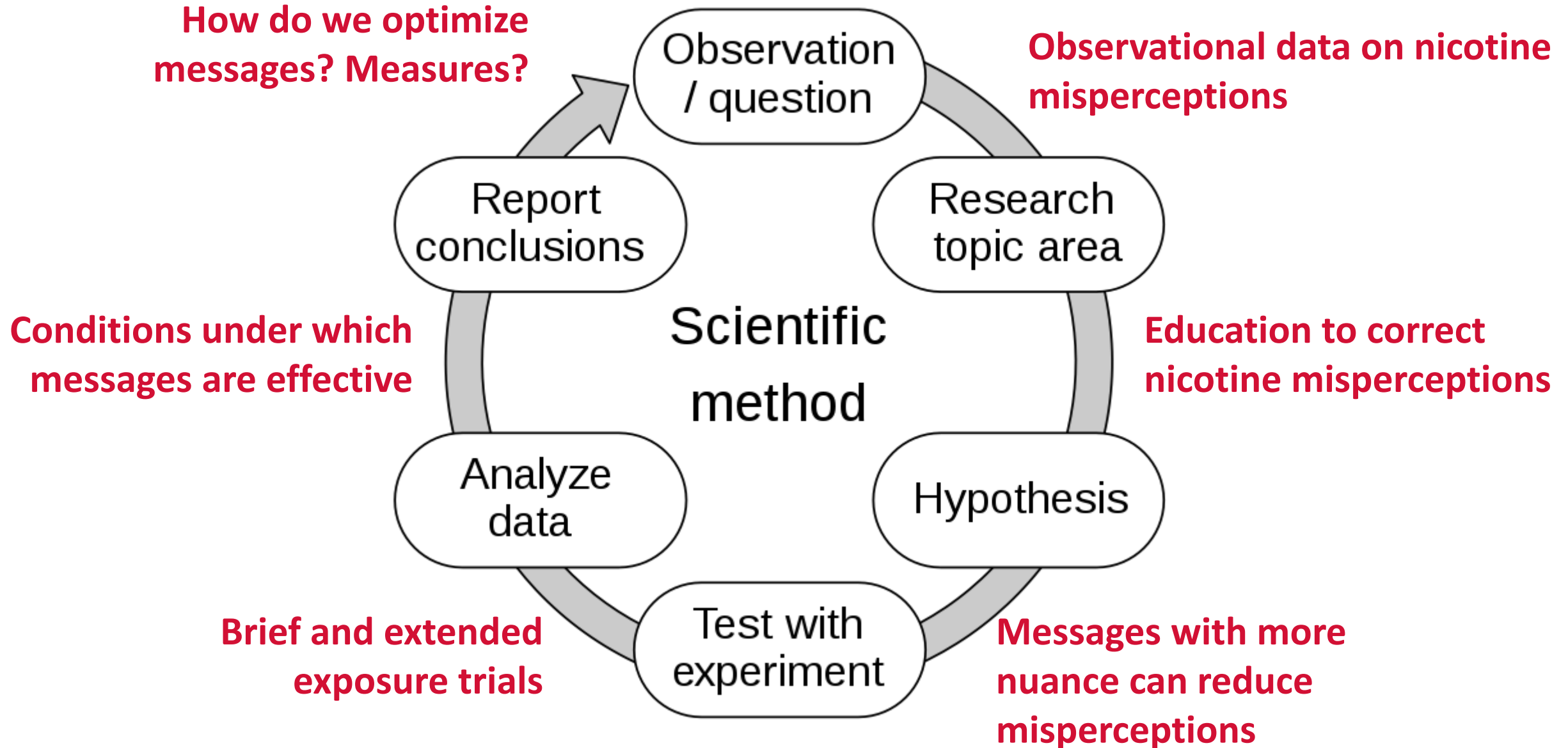
Center for Tobacco Studies

Randomized (Controlled) Trials on Nicotine Messaging

Andrea Villanti, PhD, MPH

Tobacco Online Policy Seminar

- Funding from NIH, FDA, and HRSA
 - Presenting on findings from R03CA212694, R01DA051001
- No other financial relationships to disclose.
- No industry funding; no off-label medications use discussed
- The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health or the Food and Drug Administration.





FINAL DEEMING RULE

Summer 2013 Winter 2014 Fall 2014 Summer 2015 Winter 2016 Fall 2016
4 Wave 5 Wave 6 Wave 7 Wave 8 Wave 9 Wave 10

Nicotine perceptions

FEDERAL REGISTER

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Part III

Department of Health and Human Services

Food and Drug Administration

21 CFR Parts 1100, 1140, and 1143

Deeming Tobacco Products To Be Subject to the Federal Food, Drug, and Cosmetic Act, as Amended by the Family Smoking Prevention and Tobacco Control Act; Restrictions on the Sale and Distribution of Tobacco Products and Required Warning Statements for Tobacco Products; Final Rule

WARNING: This product contains nicotine.
Nicotine is an addictive chemical.

Preventive Medicine 96 (2017) 94–100



Contents lists available at ScienceDirect

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journal homepage: www.elsevier.com/locate/ypmed



U.S. adults' addiction and harm beliefs about nicotine and low nicotine cigarettes☆



Erin Keely O'Brien, Anh B. Nguyen*, Alexander Persoskie, Allison C. Hoffman

Center for Tobacco Products, Food and Drug Administration, United States

Brief report

Public misperception that very low nicotine cigarettes are less carcinogenic

M Justin Byron,^{1,2} Michelle Jeong,^{2,3} David B Abrams,⁴ Noel T Brewer^{2,3}

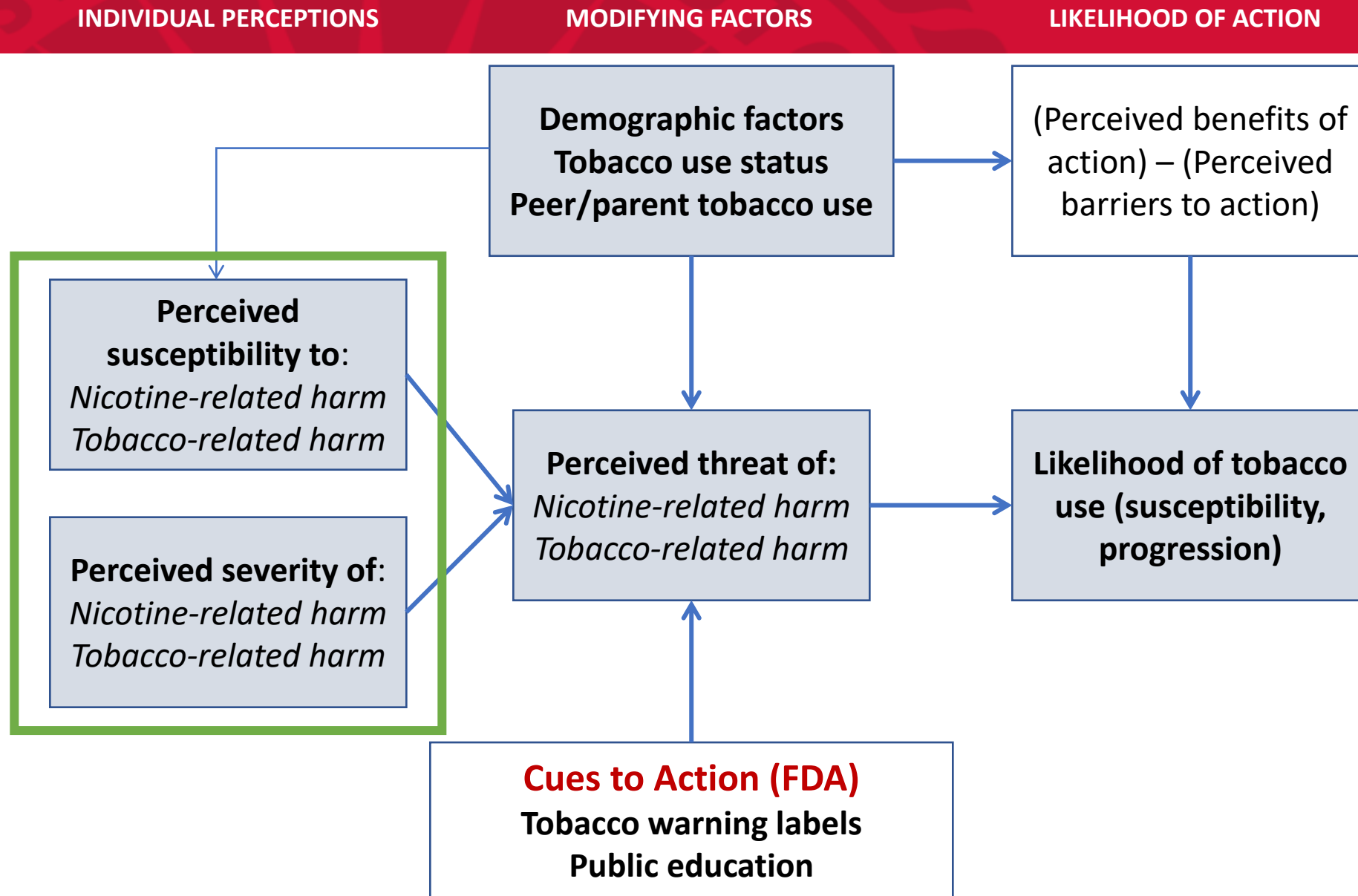
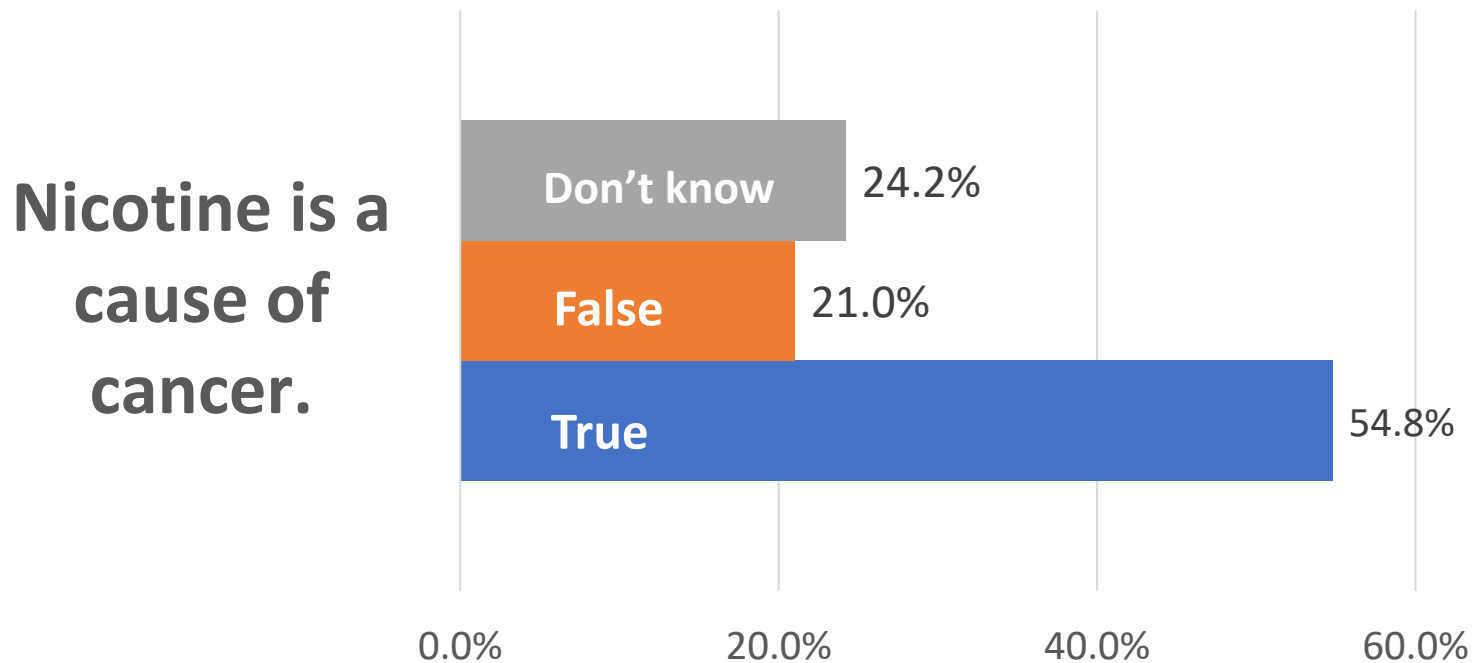
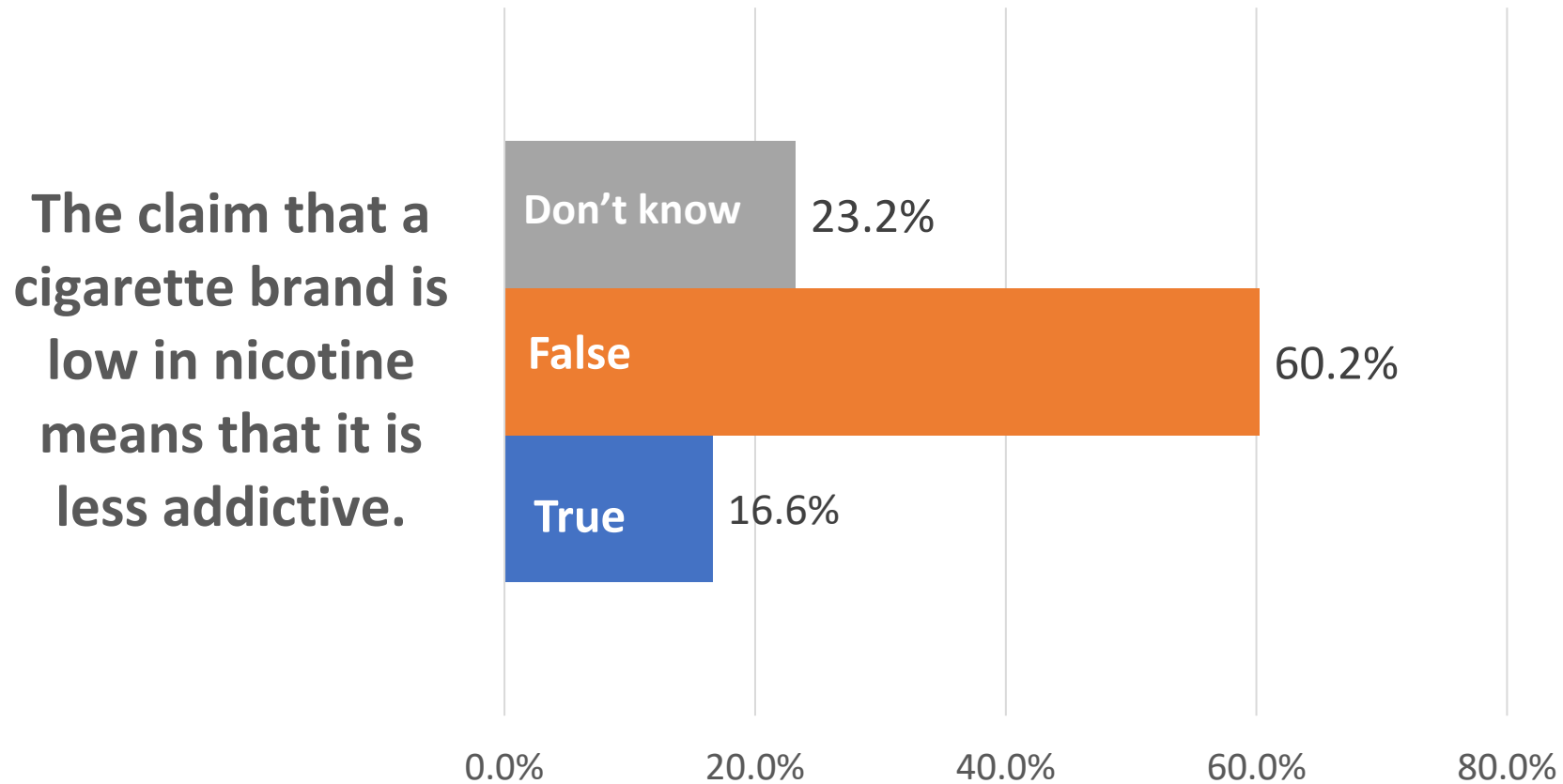


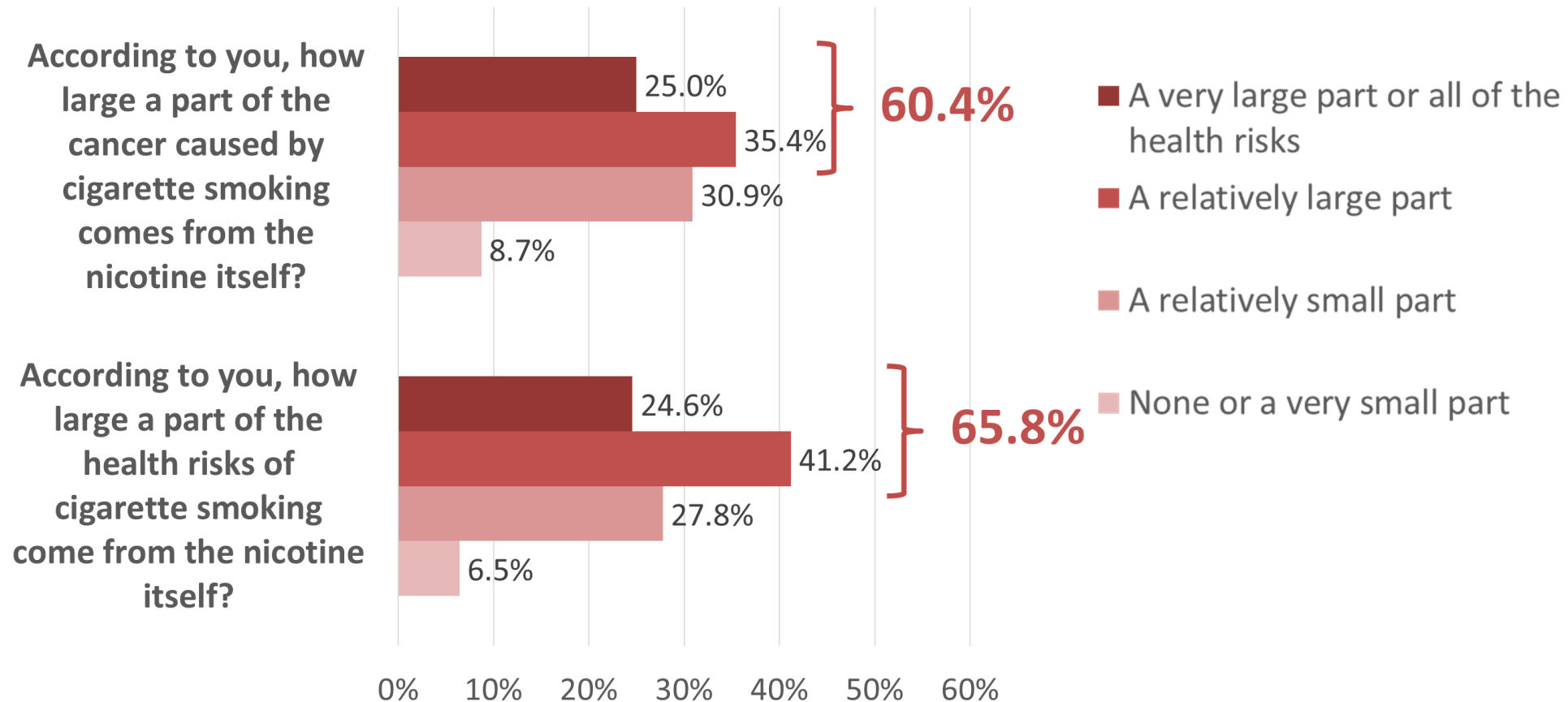
Figure 1. Adapted conceptual framework of Health Belief Model

4,091 participants aged 18-40 completed Wave 10 of the Truth Initiative Young Adult Cohort Study





Nicotine perceptions re: health risks



- In 2019, approximately what proportion of US adults incorrectly believed that nicotine caused cancer – or were unsure (i.e., don't know)?

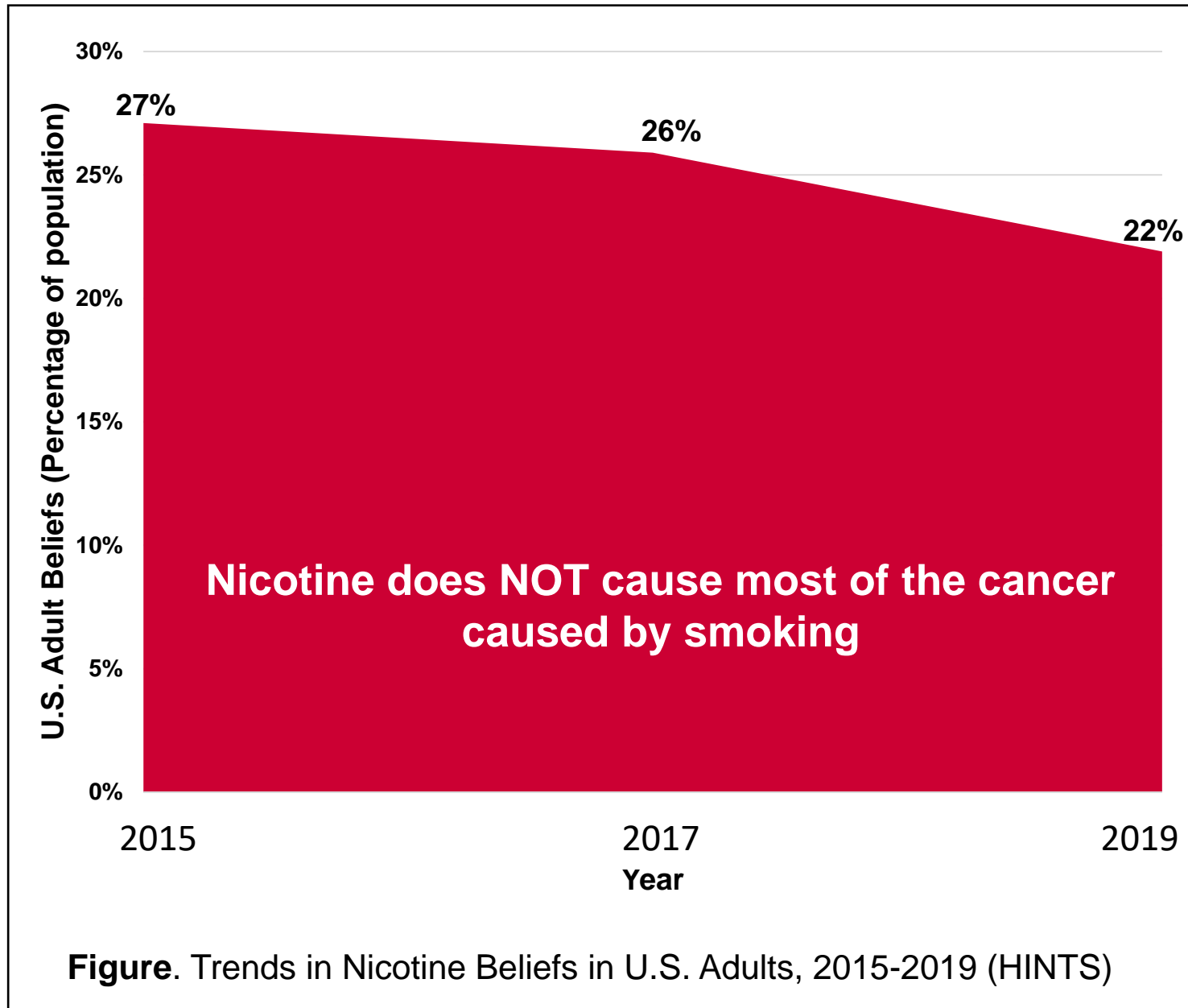
- 50%
- 60%
- 70%
- 80%

HINTS 2019:

The nicotine in cigarettes is the substance that causes most of the cancer.

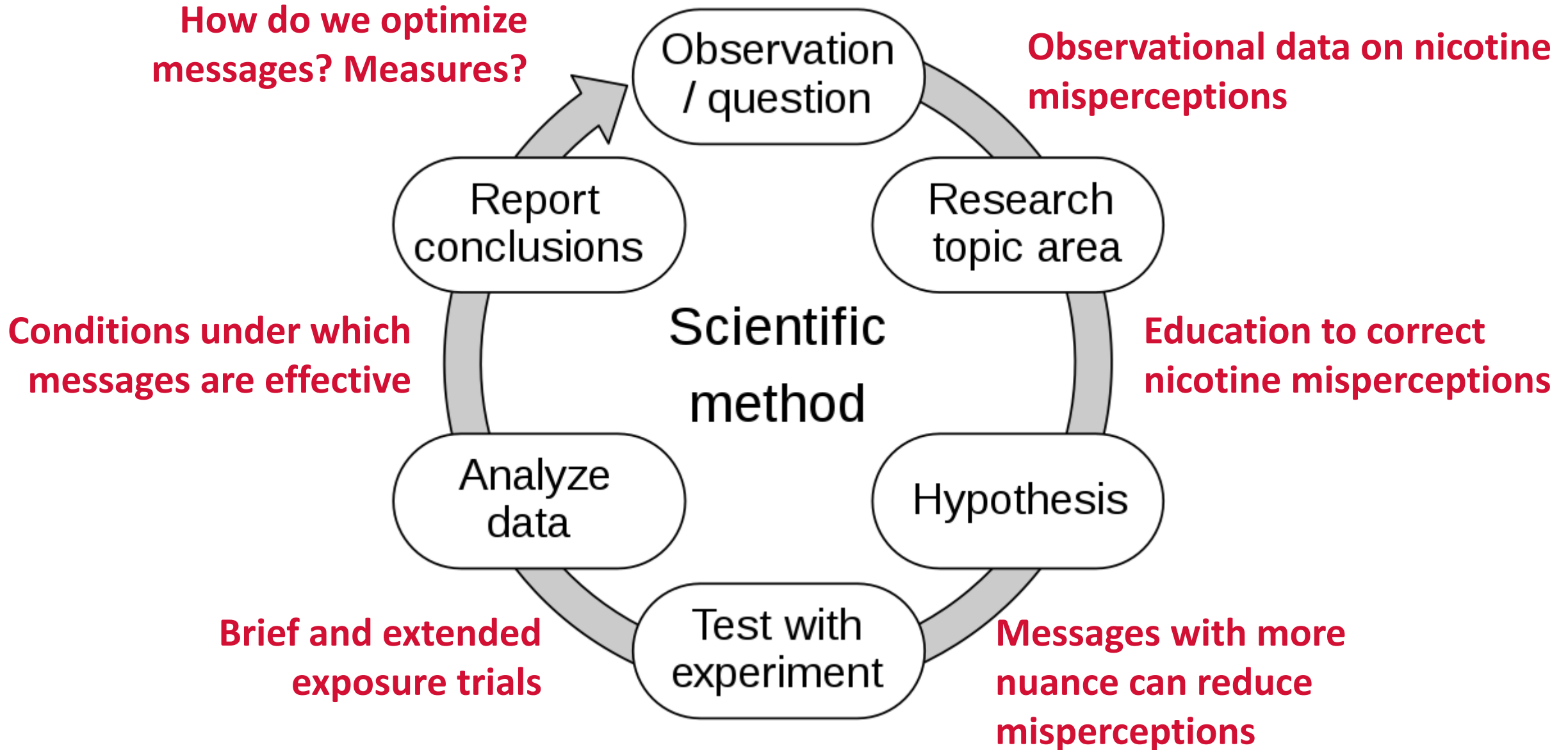
- | | |
|---------------------|-----|
| • Strongly agree | 33% |
| • Agree | 25% |
| • Don't know | 20% |
| • Disagree | 15% |
| • Strongly disagree | 7% |

- **How has the proportion of US adults with correct beliefs about nicotine and cancer changed since the first reported estimates from 2015?**
 - **Increased**
 - **Stayed the same**
 - **Decreased**



Widespread misperceptions of nicotine's role in health harms

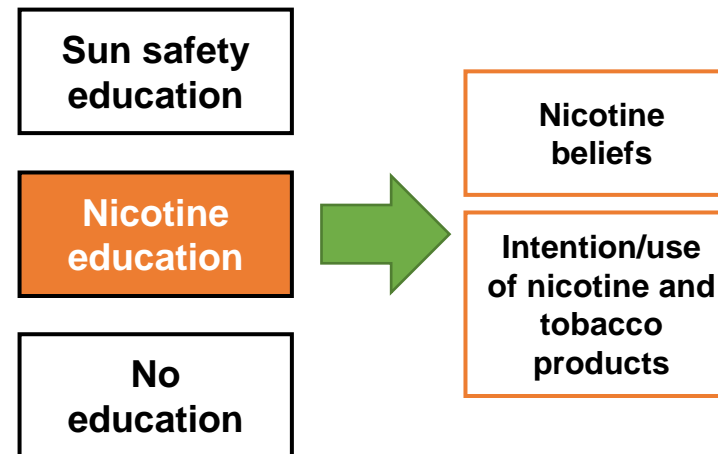
- “Nicotine is responsible for most of the health harms and cancer caused by smoking”
- “Nicotine replacement therapy (NRT) is as harmful to health as smoking”
- “E-cigarettes are as or more harmful to health than cigarettes”
- “Reduced nicotine content (RNC) cigarettes are less harmful than average cigarettes”



- **Study team:**

- Andrea Villanti
- Andrew Strasser
- Joseph Cappella
- Eric Donny
- Darren Mays
- Julia West

GOAL: To test the effect of a single, brief exposure to nicotine education messages on beliefs about nicotine, nicotine replacement therapy (NRT), e-cigarettes, and reduced nicotine content (RNC) cigarettes.



- 521 U.S. adults (aged 18+) on Amazon Mechanical Turk completed a 15-minute survey on “Communicating about cancer risk behaviors.”
 - Paid \$2.50 for survey completion
- After completing items on sociodemographics, literacy, and cancer risk behaviors, participants were randomized in a 2:1:1 ratio to one of three conditions:
 - Nicotine education (n=263)
 - Sun safety education (attention control, n=128)
 - No message control (n=130)

- Messages were adapted from several evidence-based sources for a lay audience:
 - FDA's 2017 comprehensive plan for tobacco and nicotine regulation
 - FDA's 2013 modifications to labeling of NRT products for over-the-counter human use
 - 2014 U.S. Surgeon General's Report on the Health Consequences of Smoking
 - Reports on carcinogens from the International Agency for Research on Cancer.



**All slides presented in order; exposed to each slide for at least 5 seconds.

Sun Safety Education Intervention

Indoor tanning and Ultraviolet (UV) radiation from the sun cause skin cancer and premature aging.

UV radiation from the sun is just as strong on cloudy and partly cloudy days.

Indoor tanning beds, booths, and lamps emit UV radiation at much higher levels than typical sunlight.

Conditions such as snow, water, or even reflections off of buildings intensify the sun's ultraviolet radiation.

Wearing sunscreen alone does NOT prevent skin cancer.

Limit sun exposure, wear protective clothing, and avoid indoor tanning to reduce your risk of skin cancer.

**All slides presented in order; exposed to each slide for at least 5 seconds.

Results – Nicotine beliefs

	Study condition		p-value
	Nicotine messaging (n = 263)	Combined controls (n = 258)	
Nicotine is a cause of cancer. ^b			<0.001
False	78.3	36.8	
Don't know	5.3	26.0	
True	16.4	37.2	
In your opinion, how large a part of the health risks of cigarette smoking comes from the nicotine itself? ^b			<0.001
None/small part	76.4	55.8	
Large/very large part	23.6	44.2	
In your opinion, how large a part of the cancer caused by cigarette smoking comes from the nicotine itself? ^b			<0.001
None/small part	84.0	62.8	
Large/very large part	16.0	37.2	
Nicotine false beliefs scale (alpha = 0.86) ^{a,c}	4.90 (2.06)	6.71 (2.48)	<0.001

Nicotine, NRT, E-cigarette, RNC beliefs

	Study condition		p-value
	Nicotine messaging (n = 263)	Control (n = 258)	
Nicotine false beliefs scale (alpha = 0.86) ^{a,c}	4.90 (2.06)	6.71 (2.48)	<0.001
NRT false beliefs scale (alpha = 0.74) ^{a,d}	9.89 (2.63)	11.07 (2.84)	<0.001
E-cigarette false beliefs scale (alpha = 0.79) ^{a,e}	6.58 (2.21)	6.97 (2.24)	<0.05
RNC cigarette false beliefs scale (alpha = 0.91) ^{a,f}	20.99 (6.80)	22.16 (6.53)	<0.05

^a Mean (SD); ^b Column percent

^c Nicotine false beliefs scale comprised of 3 items (listed above in this table; range 3 - 11)

^d NRT false beliefs scale comprised of 6 items (range 6 - 18)

^e E-cigarette false beliefs scale comprised of 4 items (range 3 -12)

^f RNC cigarette false beliefs scale comprised of 9 items (range 9 - 39)

American Journal of
Preventive Medicine

RESEARCH BRIEF

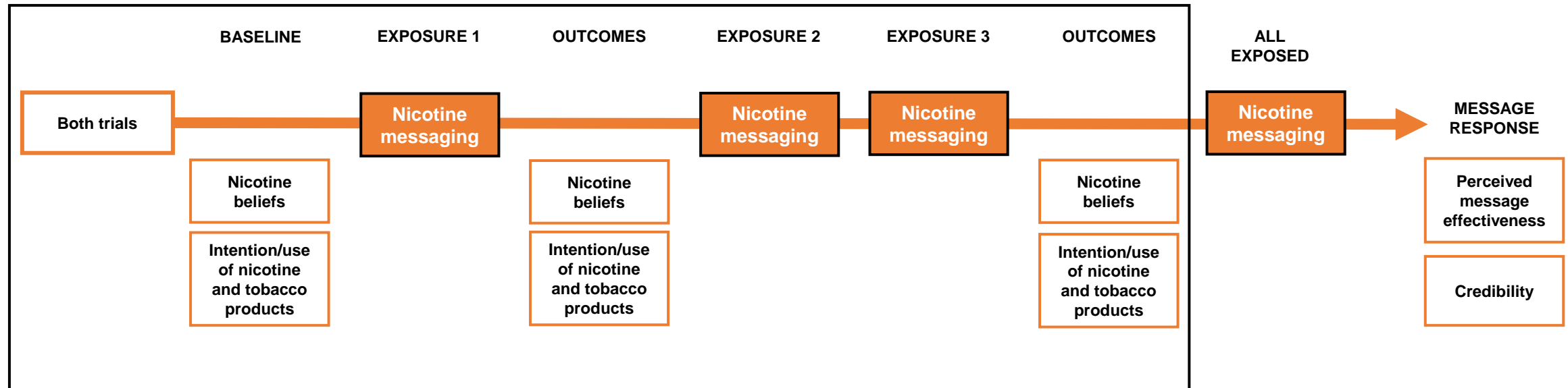
Impact of Brief Nicotine Messaging on Nicotine-
Related Beliefs in a U.S. Sample



Andrea C. Villanti, PhD, MPH,¹ Julia C. West, BA,¹ Darren Mays, PhD, MPH,² Eric C. Donny, PhD,³
Joseph N. Cappella, PhD,⁴ Andrew A. Strasser, PhD⁵

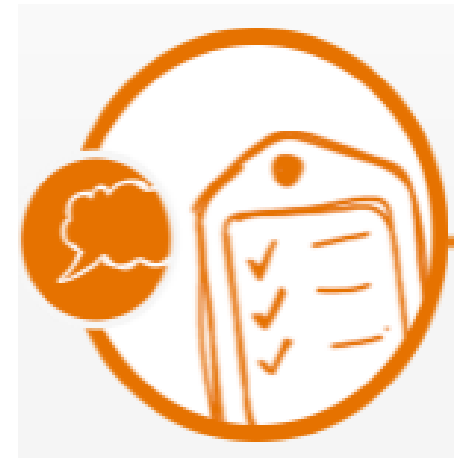
R01: Multiple exposures

- **Aim 1:** Population-based trial in U.S. adults (Villanti)
- **Aim 2:** Lab-based trial in adults who smoke cigarettes AND receive normal vs. low nicotine content cigarettes (Strasser)



- Test the impact of nicotine corrective messaging (NCM) on nicotine beliefs and the subsequent impact on intention and use of tobacco and nicotine products in adult smokers and non-smokers followed for 12 weeks.

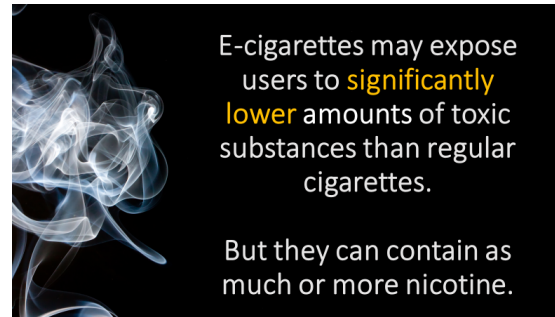
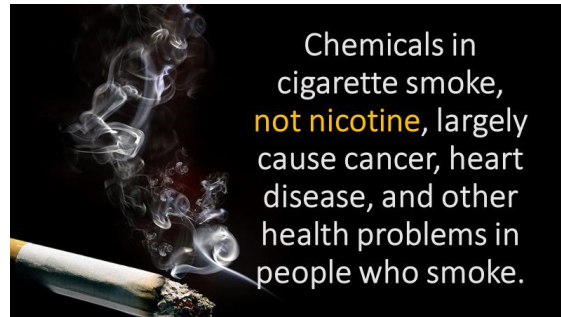
- 794 U.S. English-speaking adults aged 18+ recruited in spring 2021 from NORC's *AmeriSpeak*® national consumer market research panel.
- Amerispeak® panelists 18+ sent email invitation describing the study; interested panel members directed to the initial baseline survey.



- At end of baseline survey, participants randomized in 1:1 ratio:
 - Nicotine Corrective Messaging (NCM) intervention (n=393)
 - Delayed Message (DM) control condition (n=401).
- Four waves of data collection over 13 weeks between 2/12/21 and 5/14/21.

	Baseline	Randomized + Exposure 1	Key measures + Exposure 2	Exposure 3	Key measures	Exposure 4
Aim 1: Population trial	Wave 1 (Weeks 1-3: 2/12/21-3/5/21)		Wave 2 (Weeks 5-6: 3/12/21- 3/26/21)	Wave 3* (Weeks 8-9: 4/2/21-4/16/21)	Wave 4 (Weeks 11-13: 4/23/21-5/14/21)	
Intervention (NCM)	n = 393		N = 313 (80%)	N = 295 (75%)	N = 290 (74%)	
Control (DM)	N = 401		N = 318 (79%)	-	N = 319 (80%)	

*Wave 3 provided only to Intervention condition, by design



- **Primary outcomes:**

- Nicotine false beliefs (3 items)
- NRT false beliefs (6 items)
- E-cigarette false beliefs (4 items)
- Reduced nicotine content (RNC) cigarette false beliefs (9 items)

- **Secondary outcomes:**

- Intention to use nicotine/tobacco products
- Nicotine/tobacco use and behavior

	Aim 1: Population study	Aim 2: Lab study
Intervention/Exposure		
Nicotine messaging vs. control	Wave 1	Week 1
Normal nicotine vs. RNC cigarette		Week 1
Heatmapping	Waves 1-4	
Perceived message effectiveness	Wave 4	Week 5
Message credibility	Wave 4	Week 5
Eye-tracking		Weeks 1-4
Biomarkers		Weeks 0, 5
Outcomes		
Nicotine beliefs	Waves 1, 2, 4	Weeks 0, 2, 5
Intention to use nicotine/tobacco products	Waves 1, 2, 4	Weeks 0, 2, 5
Nicotine/tobacco use and behavior	Waves 1, 2, 4	Weeks 0, 2, 5
Subjective rating of study cigarette		Weeks 1-5
Manipulation check	Waves 1, 2, 4	Weeks 0, 2, 5
Moderators		
Sociodemographics	Wave 1	Week 0
Literacy	Wave 1	Week 0
Cancer risk beliefs	Wave 1	Week 0
Cancer risk behaviors	Wave 1	Week 0
Fagerstrom test for nicotine dependence	Wave 1	Week 0
Other key constructs		
Attitudes about nicotine	Waves 1, 2, 4	Weeks 0, 2, 5
Nicotine-related norms	Waves 1, 2, 4	Weeks 0, 2, 5
Behavioral control	Waves 1, 2, 4	Weeks 0, 2, 5
Stages of change	Wave 1, 4	Week 0, 5
Policy support	Wave 4	Week 5

- **Bivariate analyses** examined differences in:
 - Distribution of demographic characteristics by study condition
 - Primary outcomes by study condition at Wave 4
- **Linear regression models** examined differences in false belief scale scores (nicotine, NRT, e-cigarette, RNC cigarette) by study condition at Waves 2 and 4
 - Exploratory analyses examined effect of message dose on Wave 4 false belief scales

- No differences in distribution of demographic characteristics by study condition

Table 1a. Demographics (Unweighted)

	All (<i>n</i> = 794)	Intervention (<i>n</i> = 393)	Control (<i>n</i> = 401)	<i>P</i>
Sex				0.089
Female	400 (50%)	186 (47%)	214 (53%)	
Male	394 (50%)	207 (53%)	187 (47%)	
Age				0.747
18-24	55 (7%)	25 (6%)	30 (7%)	
25-34	162 (20%)	78 (20%)	84 (21%)	
35-44	124 (16%)	57 (14%)	67 (17%)	
45-54	123 (15%)	61 (15%)	62 (15%)	
55-64	145 (18%)	74 (19%)	71 (18%)	
65-74	135 (17%)	68 (17%)	67 (17%)	
75+	50 (6%)	30 (8%)	20 (5%)	
Smoker^a	119 (15%)	61 (15%)	58 (14%)	0.676
Daily smoker^b	76 (10%)	37 (9%)	39 (10%)	0.882

Results: Primary outcomes at Wave 4 follow-up (n = 609)

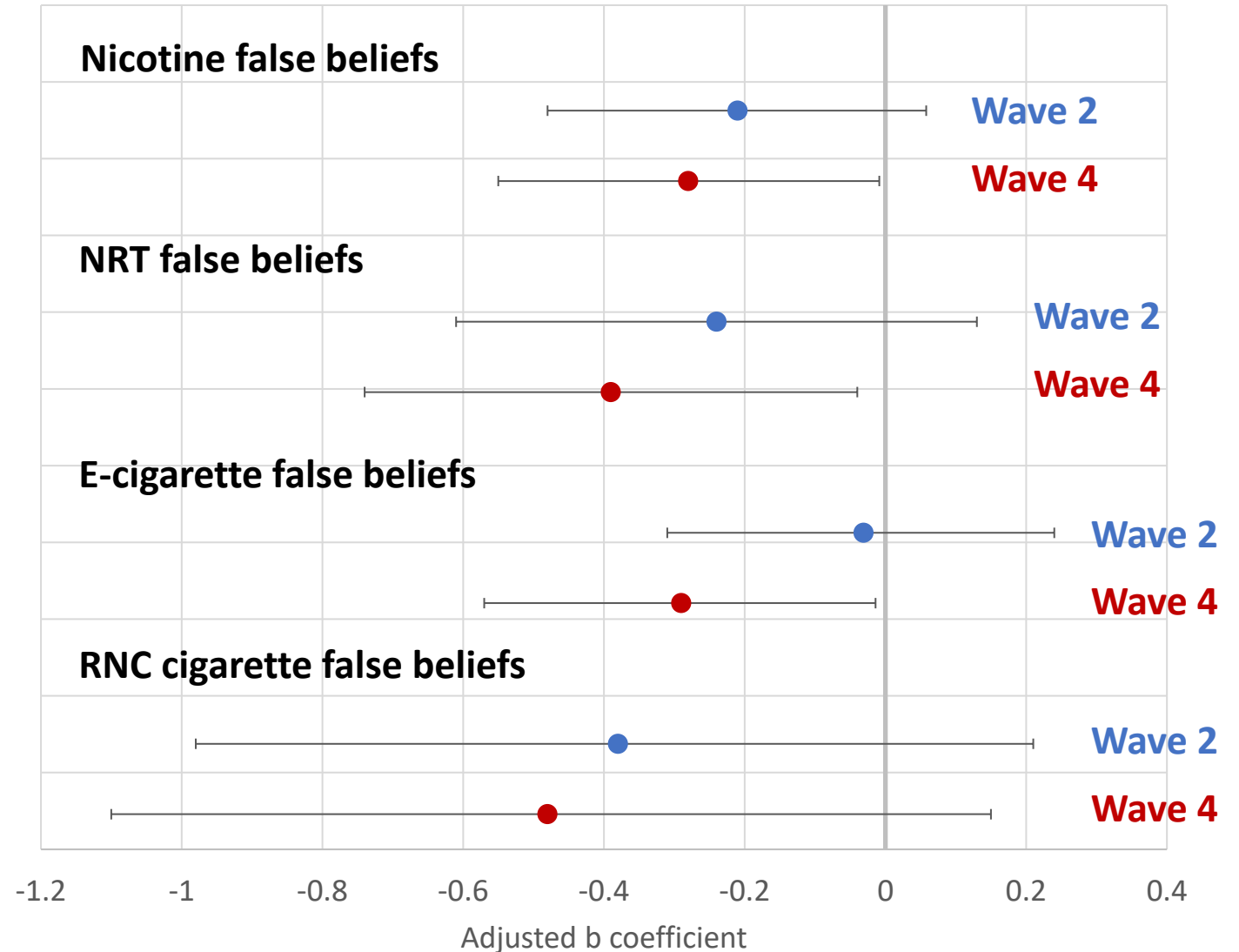
	Intervention (NCM) (n = 290) Mean (SD)	Control (DM) (n = 319) Mean (SD)	p-value
Nicotine false beliefs	7.5 (2.3)	7.8 (2.1)	0.084
NRT false beliefs	10.9 (2.8)	11.3 (2.8)	0.048
E-cigarette false beliefs	8.9 (2.2)	9.2 (2.1)	0.032
RNC cigarette false beliefs	29.8 (4.7)	30.3 (4.1)	0.174

Preliminary findings. Please do not distribute.

Results at both follow-ups

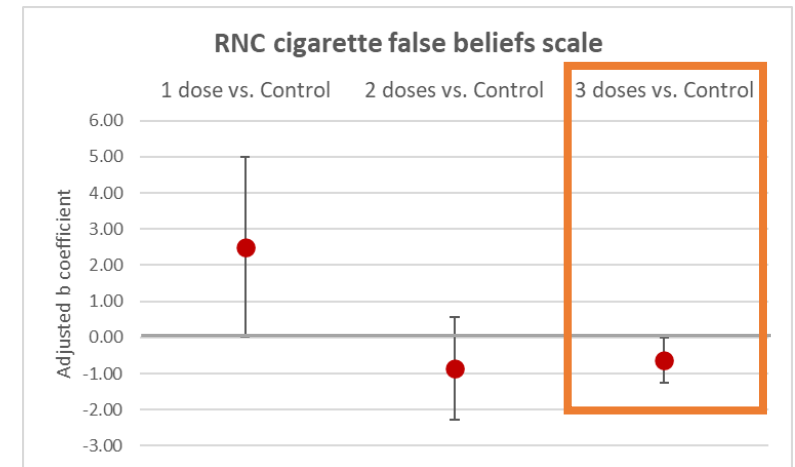
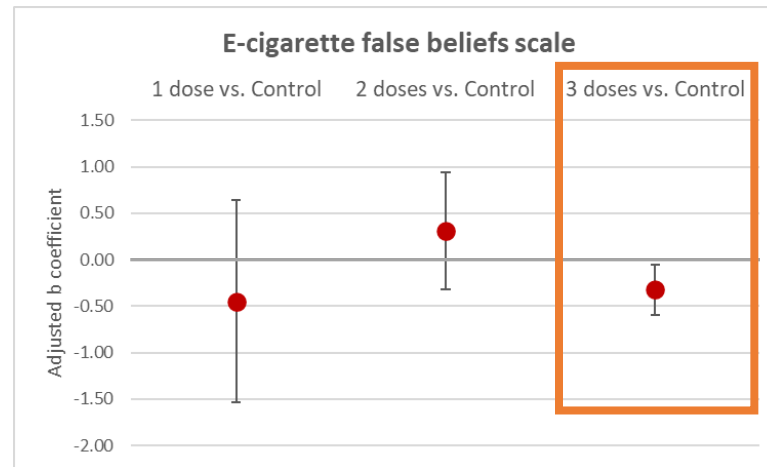
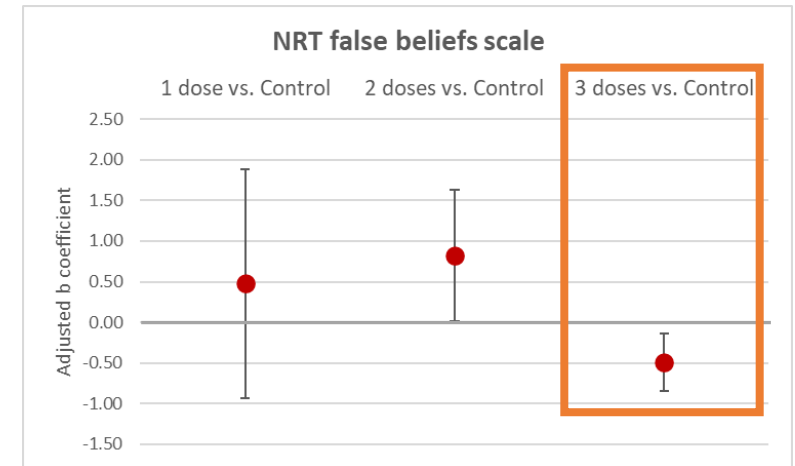
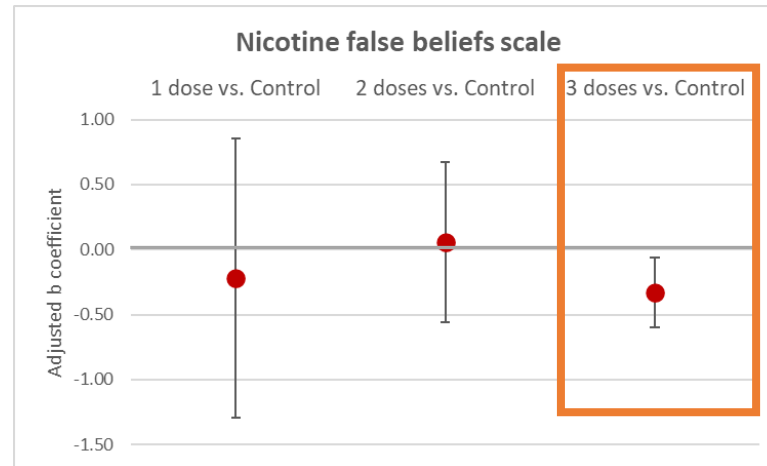
- Greater change in beliefs at Wave 4 follow-up than Wave 2 follow-up, controlling for baseline false beliefs in participants completing both follow-ups

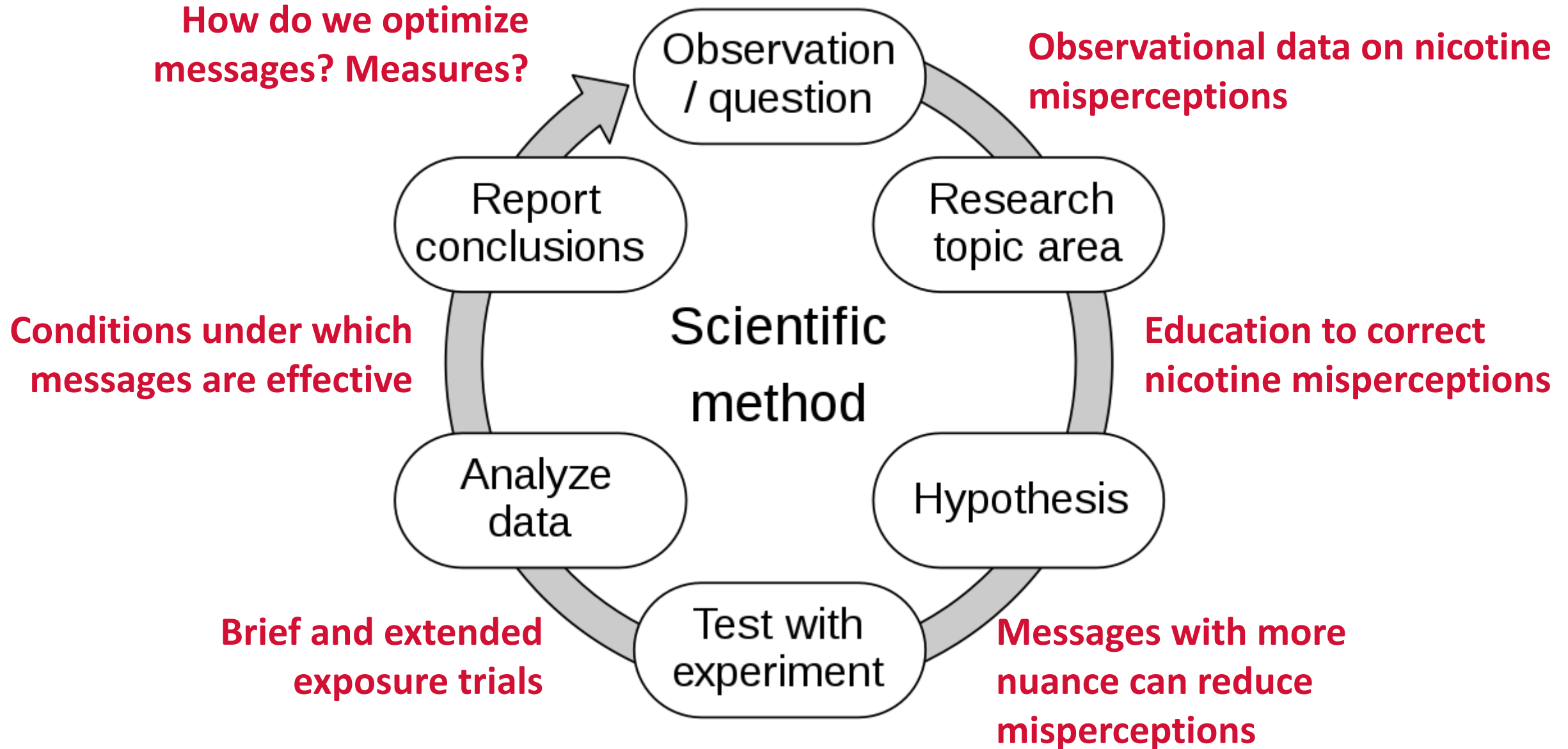
Complete case analysis (n = 551)



Results by dose at Wave 4 (n = 609)

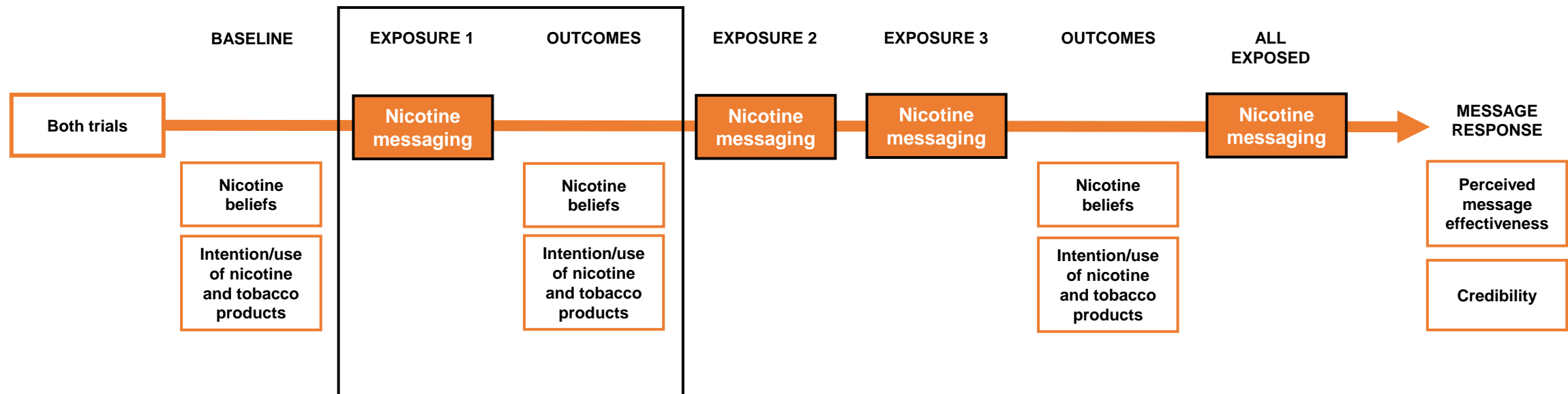
Intervention participants receiving all three message exposures had the greatest reductions in false beliefs vs. control.





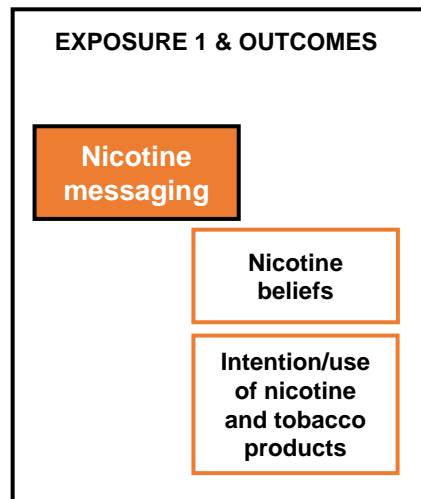
Key findings and questions

- Brief nicotine corrective messaging can reduce nicotine misperceptions after a single exposure
- Multiple exposures to nicotine corrective messaging reduces nicotine misperceptions at sufficient dose (3 exposures)
- **Why the difference???**



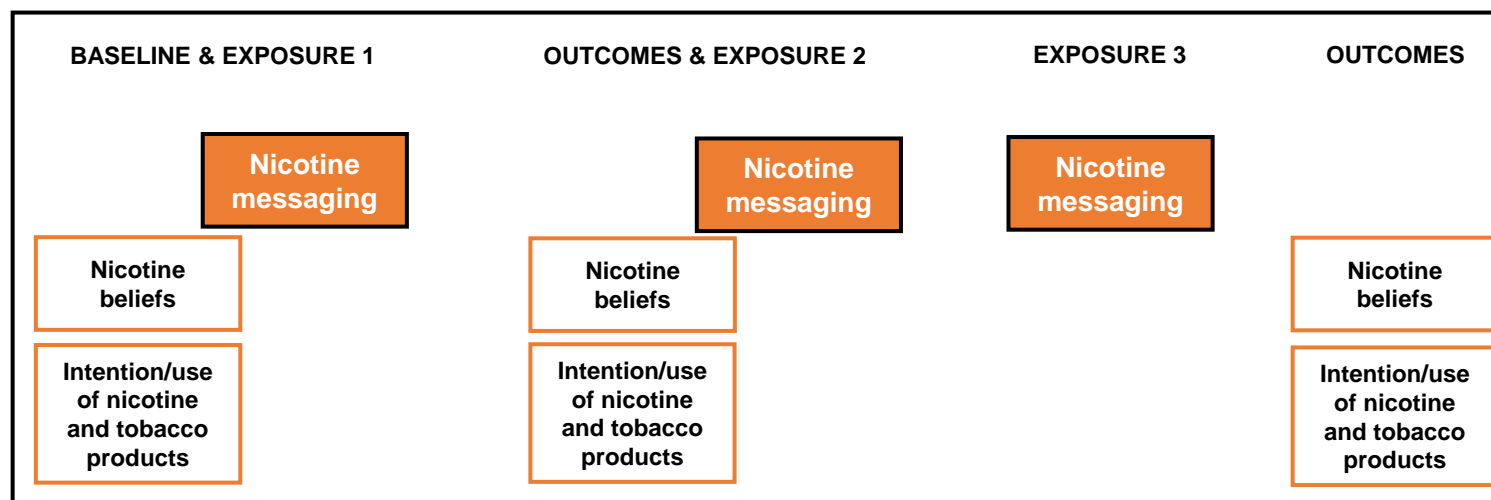
Comparison of two trials

**Brief
exposure
trial***



*Exposure and outcome assessment separated by seconds

**Multiple
exposures
trial****



Beliefs assessed at baseline prior to exposure.

Did this prime respondents in any way?

**Exposure and outcome assessment separated by ~1-4 weeks at each wave

- The public health impact of FDA's proposed nicotine reduction policy hinges on the extent to which tobacco users and non-users understand the harms of nicotine in relation to specific products, including nicotine replacement therapy (NRT).
- Results from two messaging trials support that corrective messaging about nicotine can reduce nicotine misperceptions, including those related to e-cigarettes, NRT and reduced nicotine content cigarettes.
 - Population-level efforts will require multiple campaign exposures to achieve reductions in false beliefs
- **Limitation:**
 - Even if we change beliefs, we know little about how nicotine corrective messaging will impact uptake/use of reduced nicotine content cigarettes, e-cigarettes, OR NRT.

VLN
America's Only MRTP Cigarette

NOW AVAILABLE IN COLORADO!
AND EXPANDING ACROSS ILLINOIS

HELPS YOU SMOKE LESS

BEST NEW PRODUCTS AWARDS 2022

MENTHOL

95% LESS NICOTINE

95% LESS NICOTINE

Nicotine is addictive. Less nicotine does NOT mean safer. All cigarettes can cause disease and death.

Nicotine is addictive. Less nicotine does NOT mean safer. All cigarettes can cause disease and death.

**True tobacco satisfaction
95% Less Nicotine**

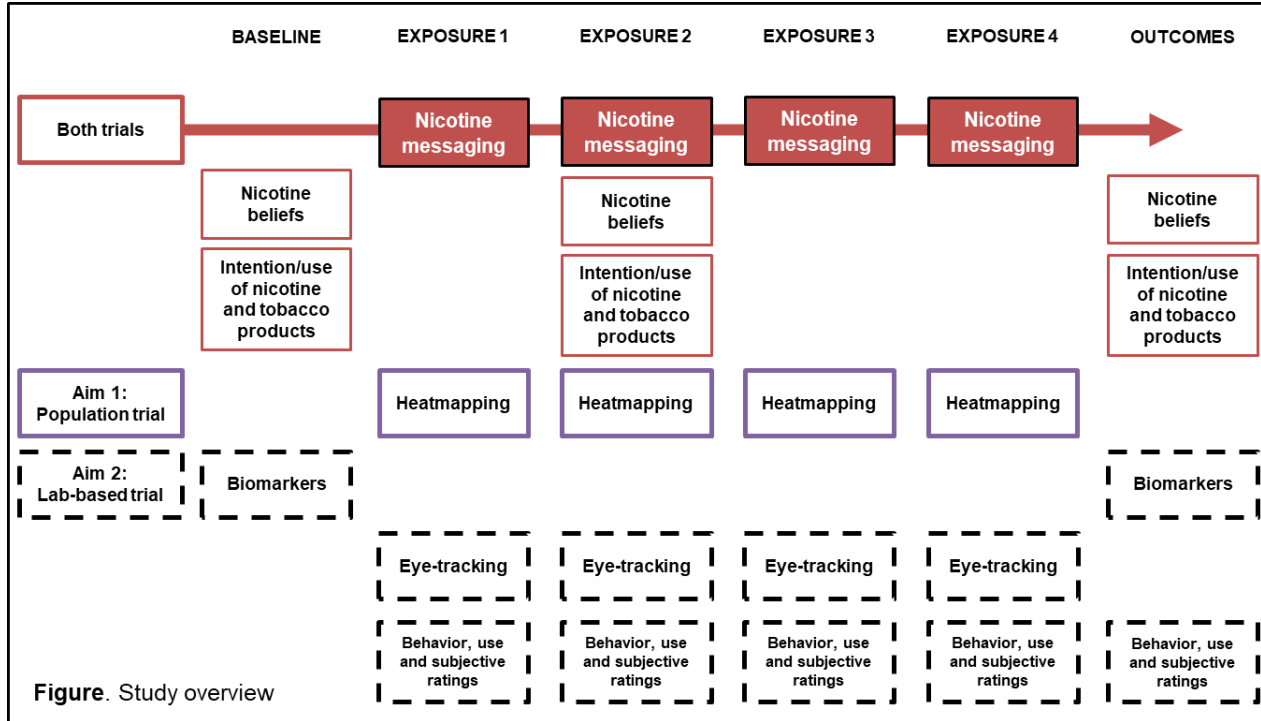
VLN® HELPS YOU SMOKE LESS

SURGEON GENERAL'S WARNING: Smoking By Pregnant Women May Result in Fetal Injury, Premature Birth, And Low Birth Weight.

Nicotine is addictive. Less nicotine does NOT mean safer. All cigarettes can cause disease and death.

Interested retailers, contact us at: MARKETING@axilcentury.com

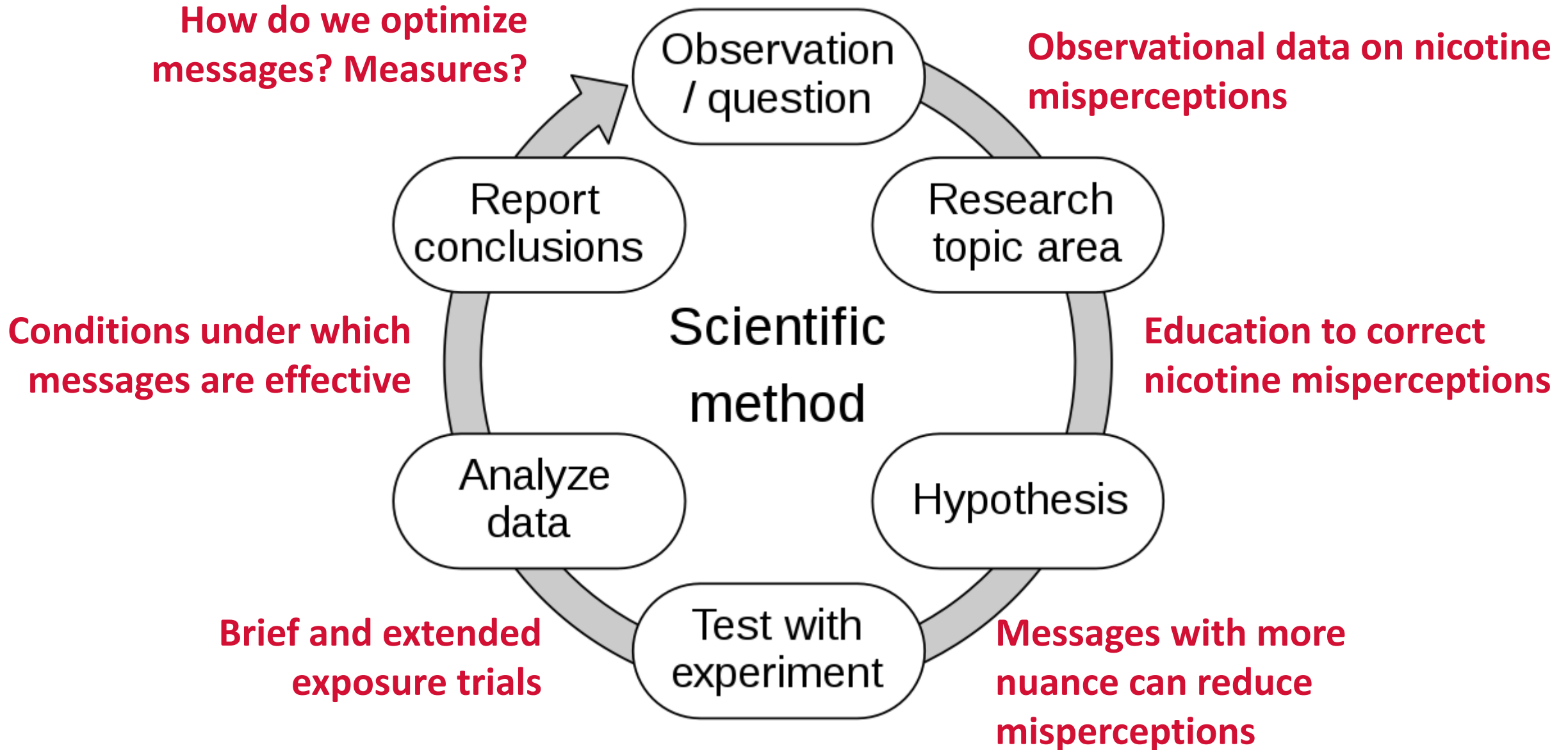
R01: Aim 2 Lab-based trial

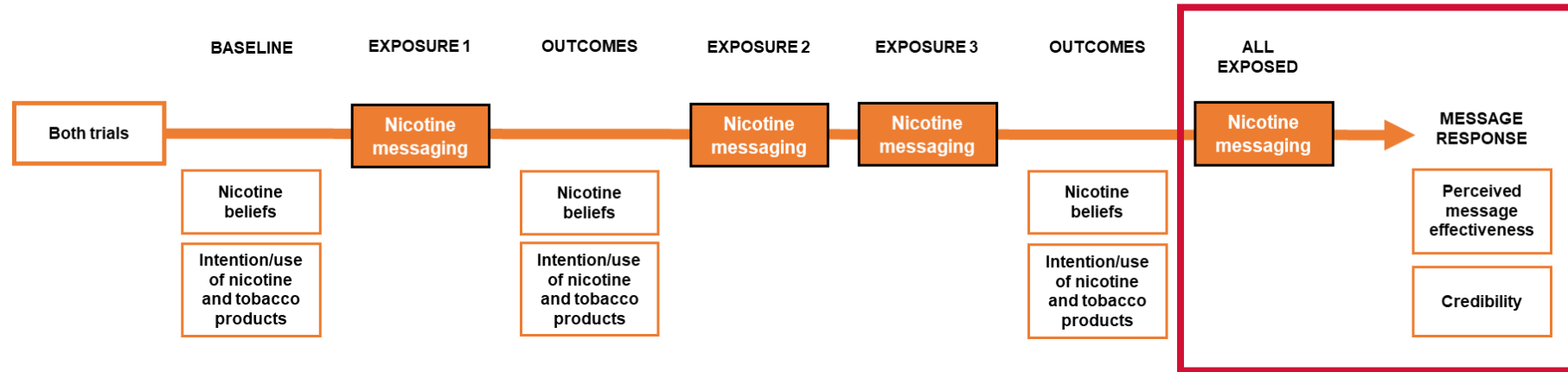


Ongoing: Aim 2 lab-based study testing interaction of NCM intervention and reduced nicotine content cigarettes

Table 1. Factorial design of Aim 2 lab-based study

	Nicotine Corrective Messaging (NCM) Intervention	Delayed Message Control
Normal nicotine content cigarettes	n = 40	n = 40
Reduced nicotine content cigarettes	n = 40	n = 40





- Repeated exposures vs. single exposure did not impact message response

	Intervention (Mean, SD)	Control (Mean, SD)
Perceived message effectiveness (range 1-5)	3.78 (0.90)	3.80 (0.98)
Accurate (range 1-7)	5.07 (1.57)	4.97 (1.50)
Authentic (range 1-7)	4.93 (1.52)	4.89 (1.50)
Believable (range 1-7)	5.07 (1.62)	5.13 (1.56)

Message experiment

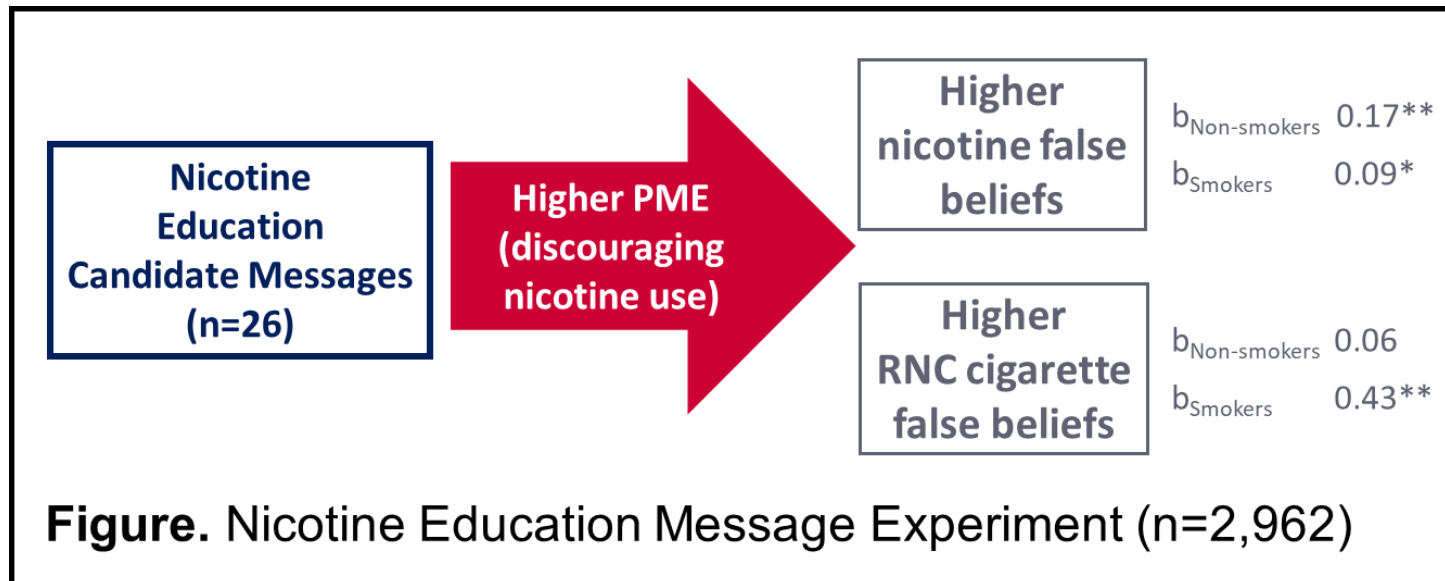
- May 2022
- N = 2,962
 - 18-45 year olds in the U.S. (mTurk)
- **Goal:** To test message response and impact on nicotine/RNC beliefs

- Participants were randomized to one of 26 text-based messages compiled from:
 - Our ongoing research (n=8; R01DA051001)
 - VLN messages authorized by FDA (n=6), and
 - Messages from FDA's "From Plant to Product to Puff" education campaign (n=12).
- Participants then completed:
 - three-item scale of perceived message effectiveness (PME)
 - single item on nicotine beliefs (cause of cancer) and
 - six items assessing RNC cigarette beliefs

- Range, n=100-124 participants per message
- Analyses examined:
 1. Relationships between mean PME, nicotine and RNC cigarette beliefs; and
 2. Effect of exposure to specific messages on nicotine and RNC cigarette beliefs in the full sample.

Results - PME and nicotine/RNC beliefs

- Across all messages, a one-unit increase in mean PME was correlated with higher odds of endorsing a false belief about nicotine (nicotine causes cancer; odds ratio (OR) 1.33, 95% CI 1.24, 1.42).
- Mean PME was not correlated with false beliefs about RNC cigarettes in crude analyses, but it was correlated with greater false beliefs about RNC cigarettes in current cigarette smokers (b 0.43, 95% CI 0.22, 0.65).



Results – Individual message effects

- Examination of individual messages suggested that:
 - Exposure to 5 of the candidate messages increased the odds of a correct belief about nicotine;
 - 1 message substantively increased correct beliefs about RNC cigarettes.

Source	Message	Correct belief about nicotine/cancer	Correct beliefs about RNC cigarettes
R01_5	Chemicals in cigarette smoke, not nicotine, largely cause cancer, heart disease, and other health problems in people who smoke.	X	
VLN_1	Very low nicotine cigarettes have 95% less nicotine than regular brands.	X	
VLN_3	Very low nicotine cigarettes greatly reduce your nicotine consumption.	X	
VLN_4	Very low nicotine cigarettes help you smoke less.	X	
FDAN_3	Nicotine can change the way your brain works, causing you to crave more nicotine.	X	
R01_8	Low nicotine cigarettes are as harmful as regular cigarettes. But they may help people quit and prevent new users from becoming addicted to cigarettes.		X

Message experiment

- May 2022
- N = 2,962
 - 18-45 year olds in the U.S. (mTurk)
- **Goal:** To test message response and impact on nicotine/RNC beliefs

Measures experiment

- August 2022
- N = 2,526
 - 18-45 year olds in the U.S. (mTurk)
- **Goal:** To determine how the survey item itself affects prevalence of nicotine misperceptions






International Journal of
*Environmental Research
and Public Health*



Article

Persistent Misperceptions about Nicotine among US Physicians: Results from a Randomized Survey Experiment

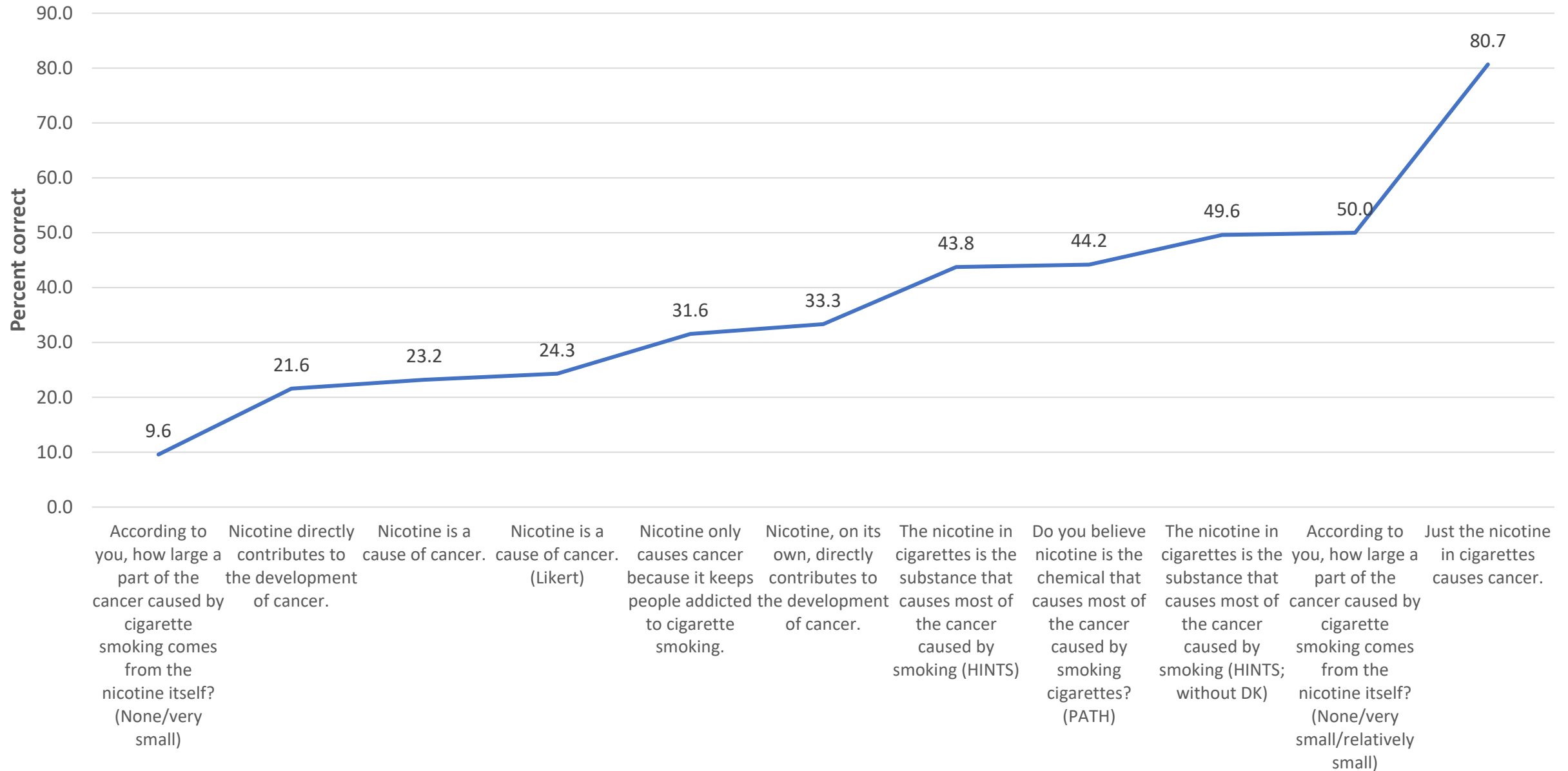
Michelle T. Bover Manderski ^{1,2,*} , Michael B. Steinberg ^{3,4} , Olivia A. Wackowski ^{2,5}, Binu Singh ²,
William J. Young ² and Cristine D. Delnevo ^{2,5} 

- Participants were randomized to **one of 10 survey items** about the role of nicotine in causing cancer from:
 - HINTS
 - PATH
 - Prior research
 - Newly-developed items
- Participants then completed:
 - An open-ended cognitive interview question about their response

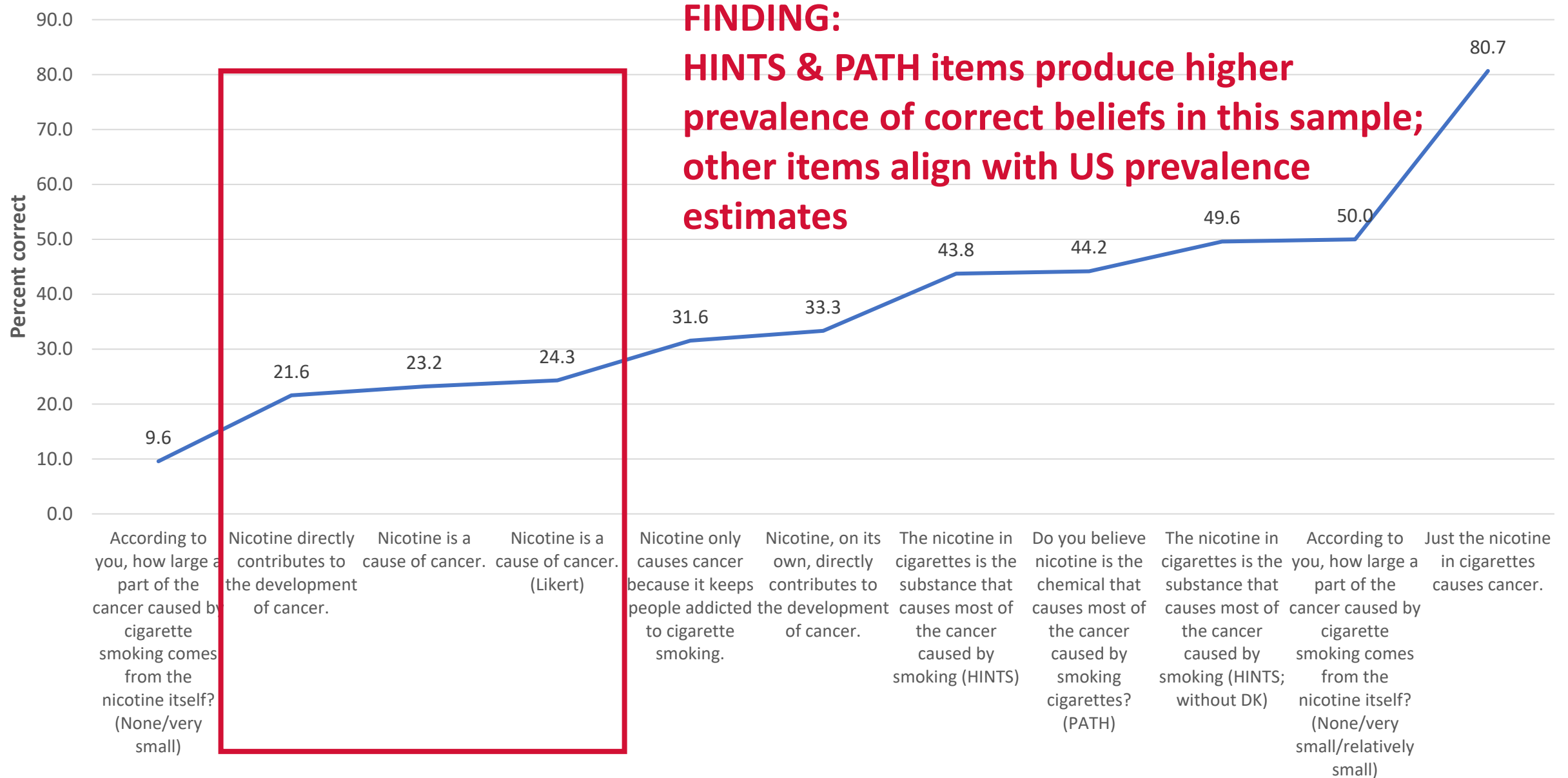
- Range, n=240-267 participants per survey item
- Three embedded experiments:
 - **Difference in response options**
 - HINTS item (with and without “don’t know)
 - Nicotine is a cause of cancer (T/F/DK vs. Likert agreement)
 - **Difference in stem:**
 - Nicotine directly contributes to the development of cancer.
 - Nicotine, on its own, directly contributes to the development of cancer.
- Analyses examined prevalence of correct beliefs by study condition

Wording	Response options	Source	Alternate	
The nicotine in cigarettes is the substance that causes most of the cancer caused by smoking.	1. Strongly agree 2. Agree 3. Disagree 4. Strongly disagree 5. Don't know	HINTS	1. Strongly agree 2. Agree 3. Disagree 4. Strongly disagree	Adapted from HINTS
Do you believe nicotine is the chemical that causes most of the cancer caused by smoking cigarettes?	1. Definitely yes 2. Probably yes 3. Probably not 4. Definitely not	PATH		
Nicotine <u>directly</u> contributes to the development of cancer.	1. Strongly agree 2. Agree 3. Disagree 4. Strongly disagree	Adapted from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8306881/	Nicotine, <u>on its own</u>, directly contributes to the development of cancer.	Adapted from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8306881/
Nicotine is a cause of cancer	1. True 2. False 3. Don't know	Villanti et al, 2019	1. Strongly agree 2. Agree 3. Disagree 4. Strongly disagree 5. Don't know	*New*
According to you, how large a part of the cancer caused by cigarette smoking comes from the nicotine itself?"	1. None or a very small part 2. A relatively small part 3. A relatively large part 4. A very large part or all	Perceived severity - nicotine; Wikmans & Ramstrom 2010		
Just the nicotine in cigarettes causes cancer.	1. Strongly agree 2. Agree 3. Disagree 4. Strongly disagree	*New*		
Nicotine only causes cancer because it keeps people addicted to cigarette smoking.	1. Strongly agree 2. Agree 3. Disagree 4. Strongly disagree	*New*		

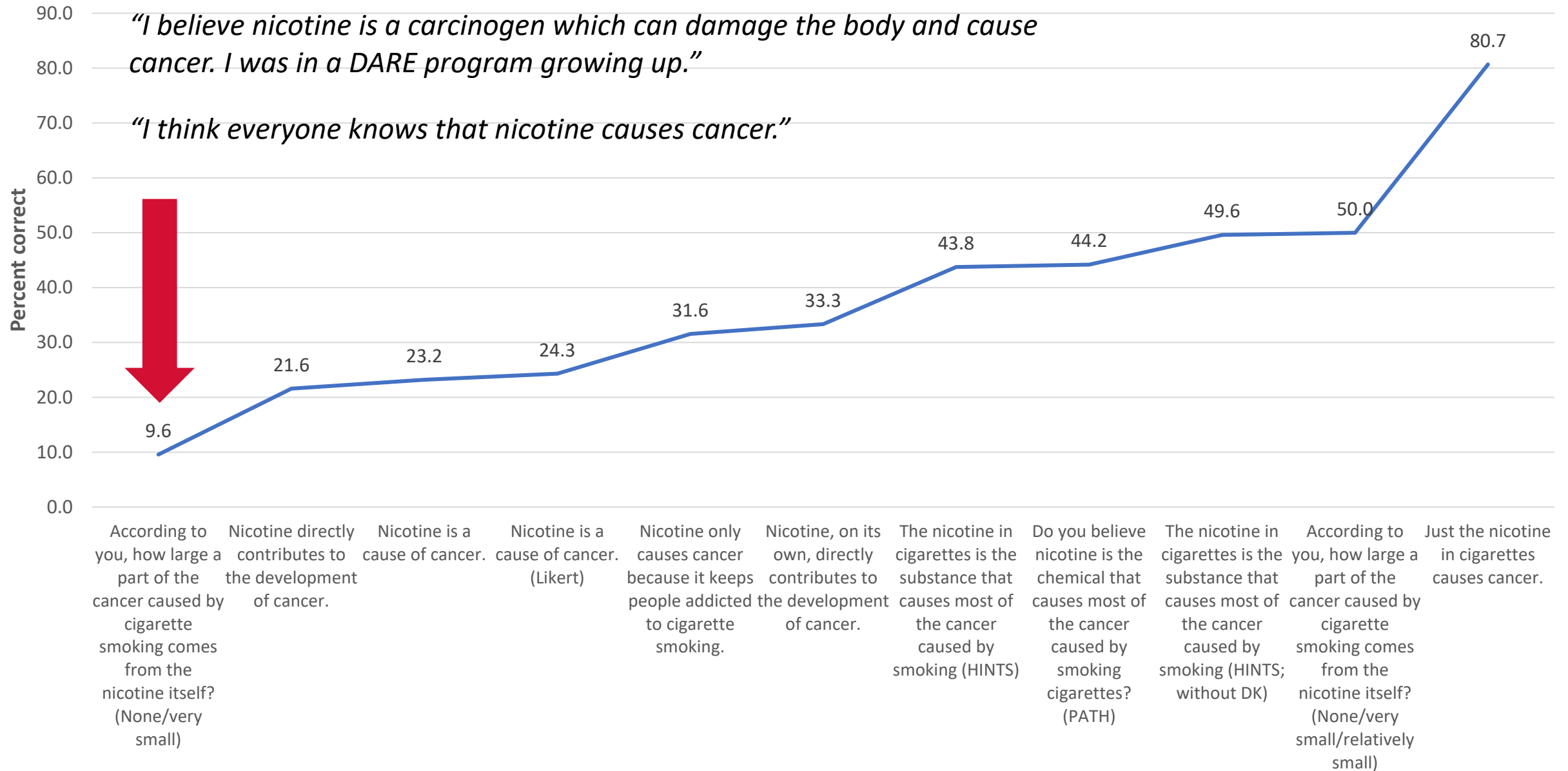
Survey item influences prevalence!



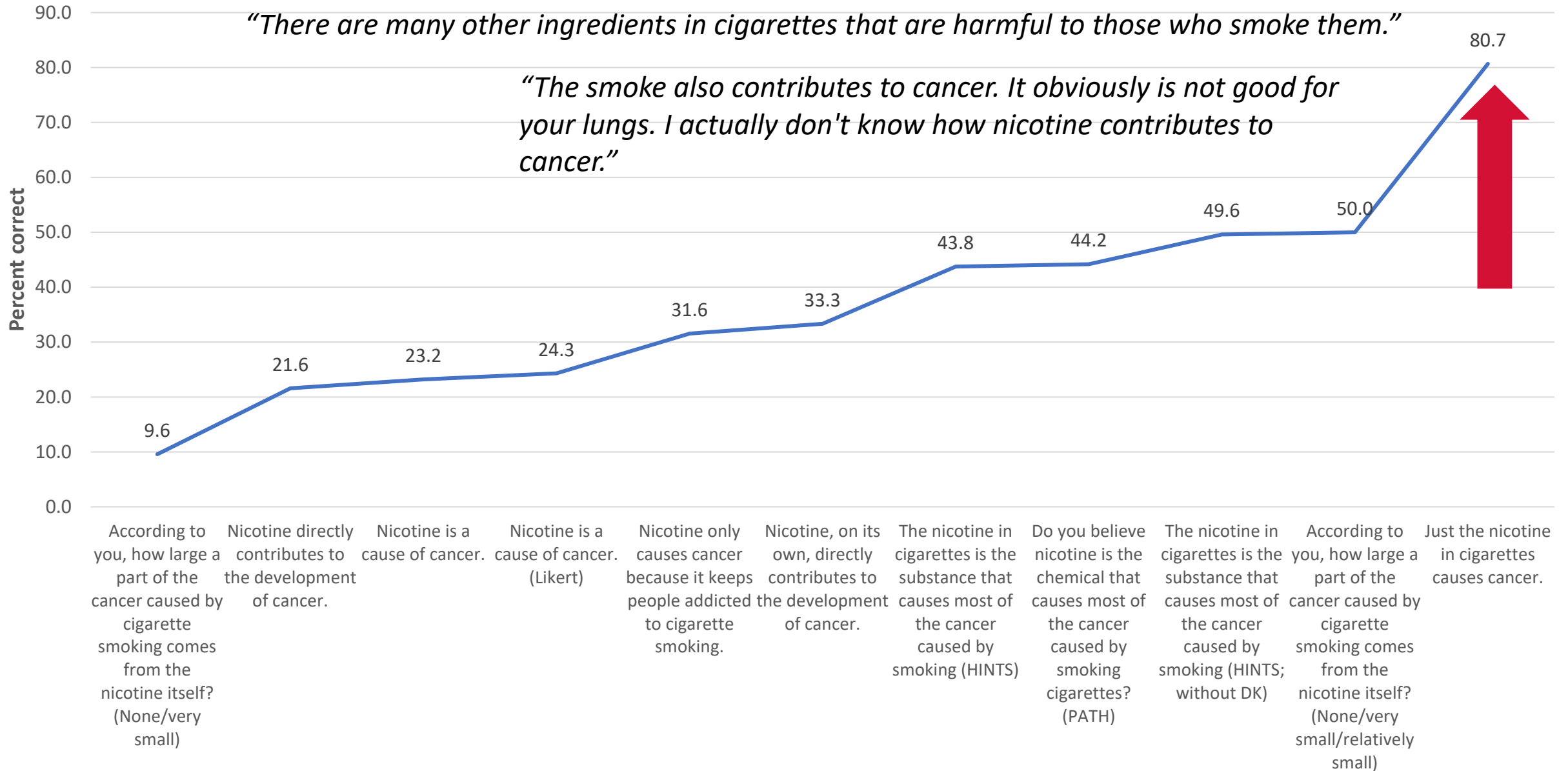
Survey item influences prevalence!



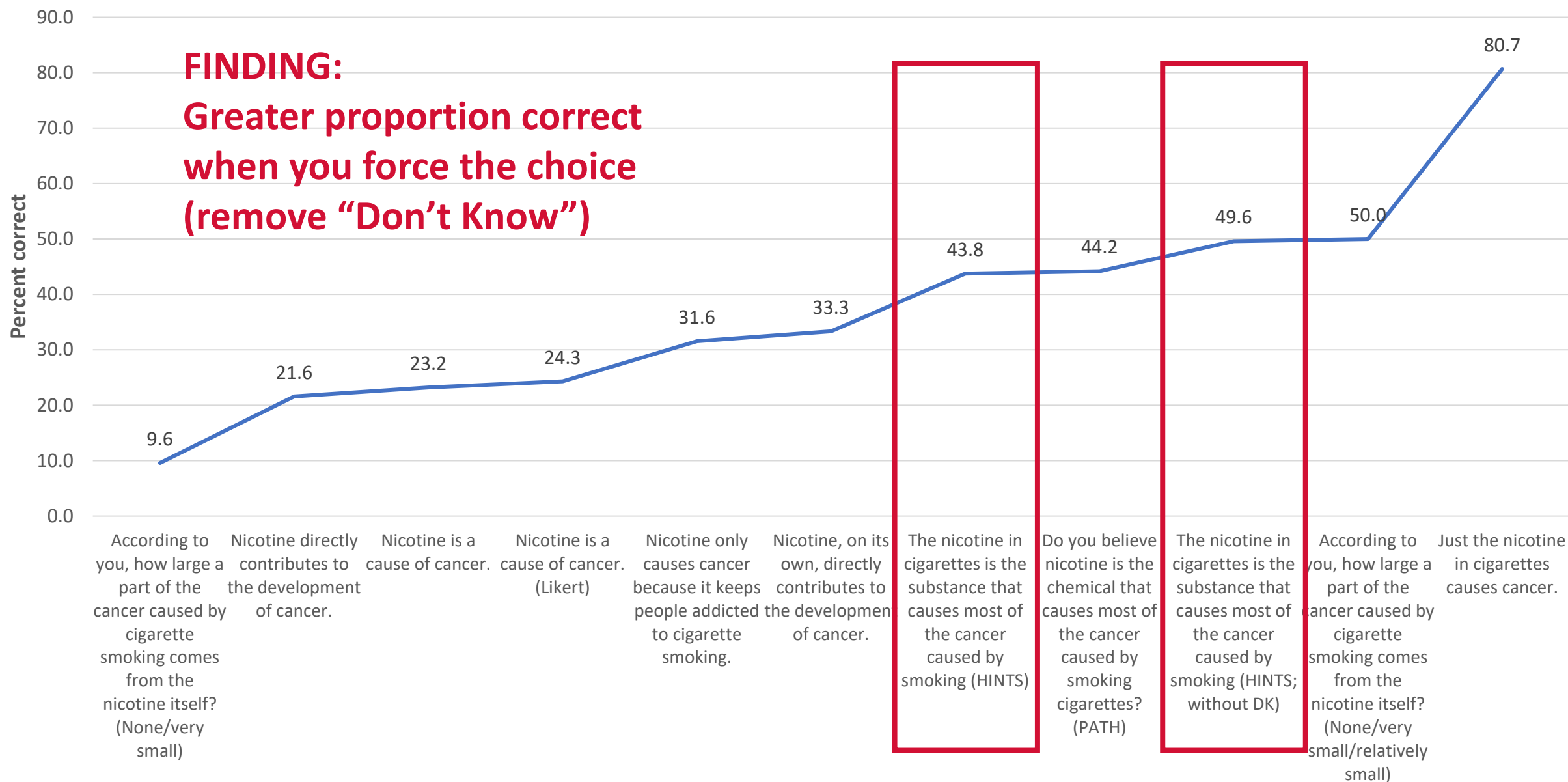
Survey item influences prevalence!



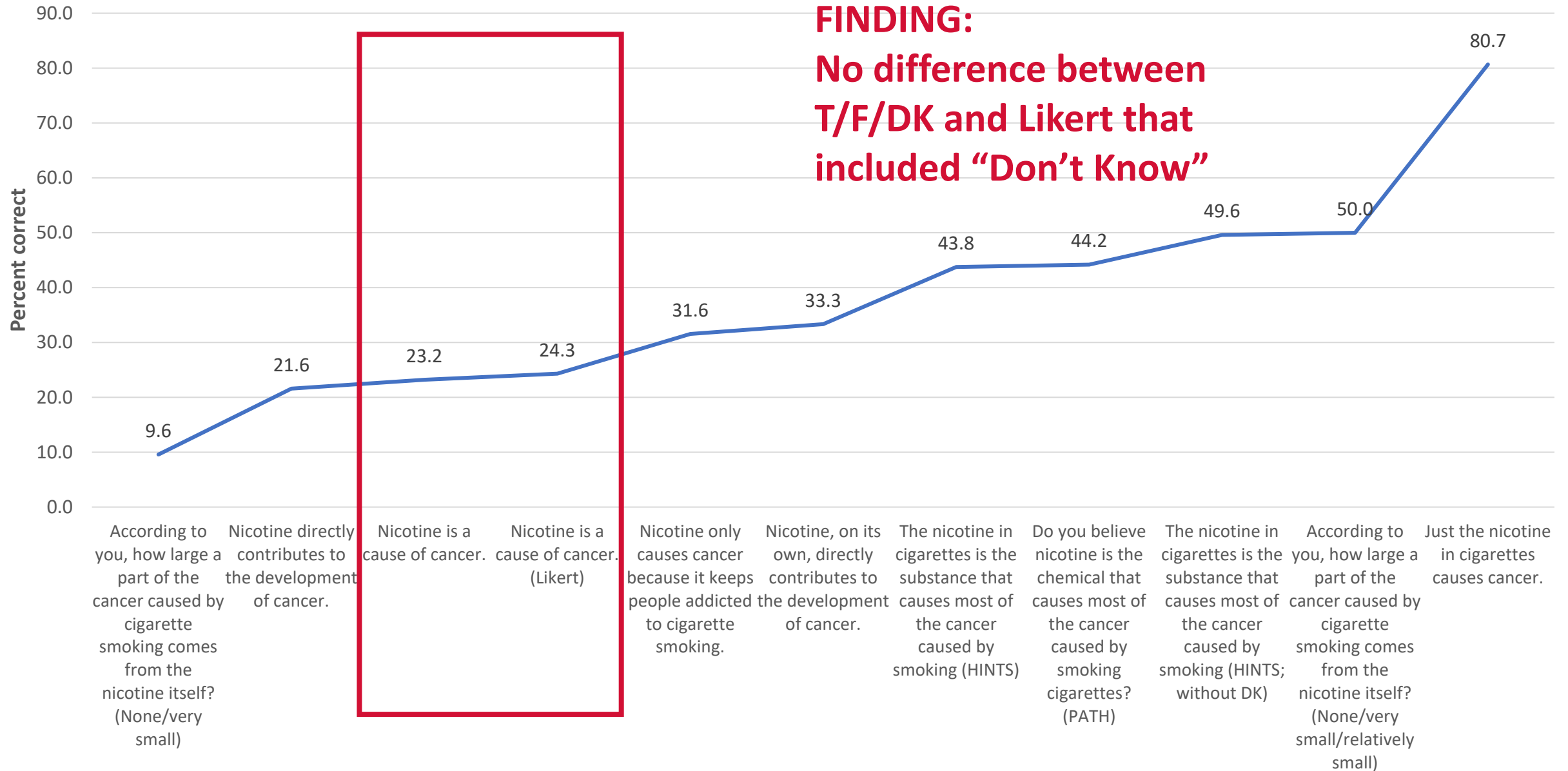
Survey item influences prevalence!



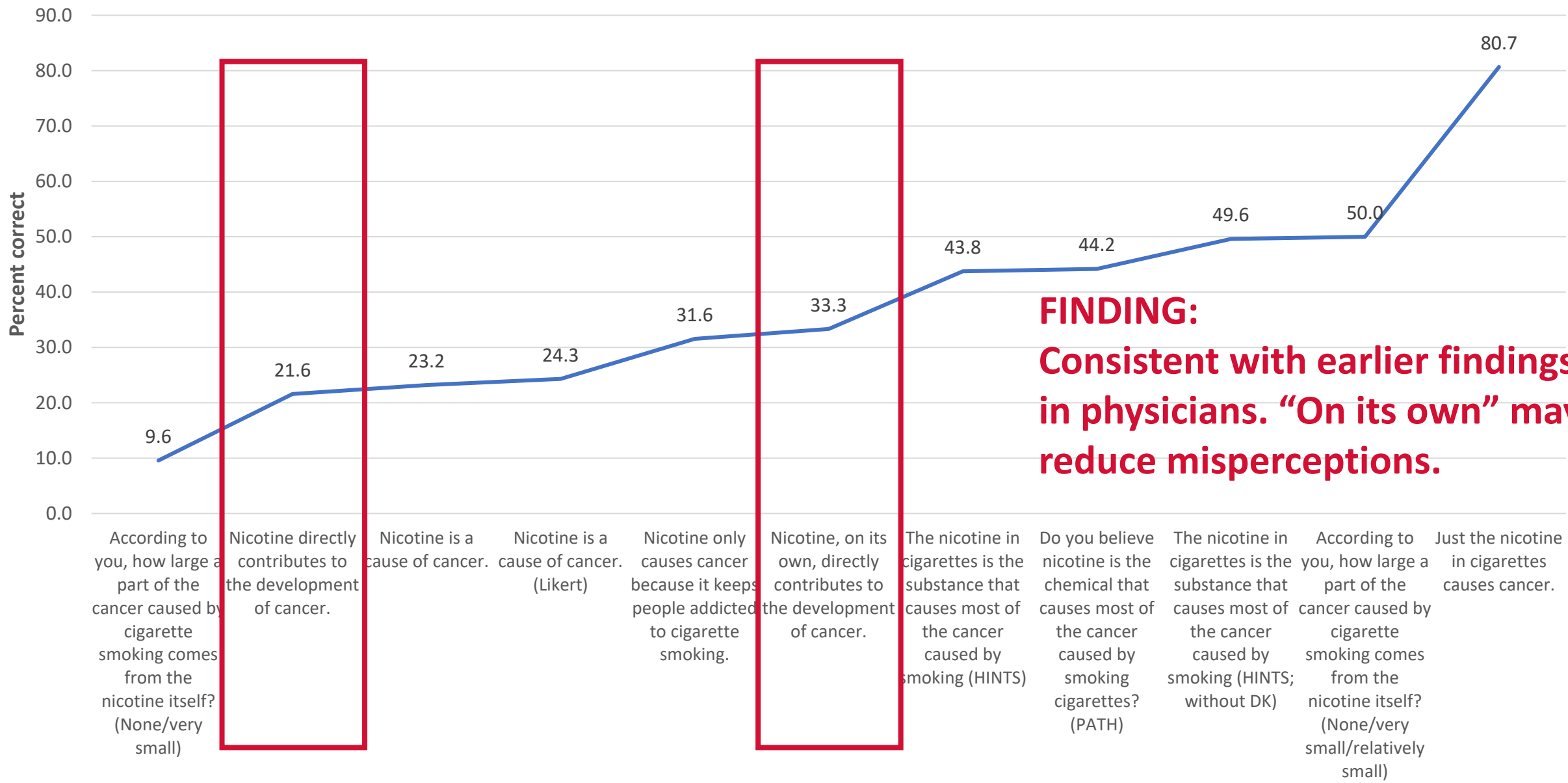
Embedded experiment 1: HINTS



Embedded experiment 2: T/F/DK vs. Likert



Embedded experiment 3: “Directly” vs. “on its own”



FINDING:
Consistent with earlier findings in physicians. “On its own” may reduce misperceptions.

More questions than answers!

